*Supplementary Material*

# Clinical Significance and Patterns of Potential Drug-Drug Interactions in Cardiovascular Patients: Observational Cross-Sectional Analytical Study

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**Table S1.** Medical conditions other than diseases of the cardiovascular system coded with ICD categories in study sample ($n$ = 1030).

| ICD category | Condition | Percentage, % |
|---|---|---|
| J06.9 | Acute upper respiratory infection | 3.6 |
| E11.7 | Type 2 diabetes mellitus with multiple complications | 2.7 |
| E11.9 | Type 2 diabetes mellitus without complications | 1.7 |
| N40 | Benign prostatic hyperplasia without lower urinary tract symptoms | 1.6 |
| U07.1 | COVID-19 | 1.5 |
| J06.8 | Other acute upper respiratory infections of multiple sites | 1.3 |
| J12.8 | Other viral pneumonia | 1.3 |
| J18.9 | Pneumonia, unspecified organism | 1.3 |
| K29.9 | Gastroduodenitis | 1.1 |
| M42.1 | Adult osteochondrosis of spine | 1.1 |
| K81.1 | Chronic cholecystitis | 1 |
| J44.8 | Other specified chronic obstructive pulmonary disease | 0.9 |
| E04.2 | Nontoxic multinodular goiter | 0.8 |
| E11.8 | Type 2 diabetes mellitus with unspecified complications | 0.8 |
| K80.1 | Calculus of gallbladder with other cholecystitis | 0.8 |
| M54.4 | Lumbago with sciatica | 0.8 |
| N18.3 | Chronic kidney disease, stage 3 | 0.8 |
| J44.9 | Chronic obstructive pulmonary disease, unspecified | 0.7 |
| D64.9 | Anemia, Unspecified | 0.6 |
| E66.0 | Obesity due to excess calories | 0.6 |
| J20.9 | Acute Bronchitis, Unspecified | 0.6 |

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| M19.9 | Osteoarthritis, unspecified site | 0.6 |
| M51.1 | Lumbar and other intervertebral disc disorders with radiculopathy | 0.6 |
| Z76.0 | Encounter for issue of repeat prescription | 0.6 |
| C83.0 | Small cell B-cell lymphoma | 0.5 |
| D50.9 | Iron deficiency anemia, unspecified | 0.5 |
| E78.8 | Other disorders of lipoprotein metabolism | 0.5 |
| N11.8 | Other chronic tubulo-interstitial nephritis | 0.5 |
| E11.6 | Type 2 diabetes mellitus With other specified complications | 0.4 |
| G62.8 | Other specified polyneuropathies | 0.4 |
| G93.8 | Other specified disorders of brain | 0.4 |
| H25.1 | Age-related nuclear cataract | 0.4 |
| J02.9 | Acute pharyngitis, unspecified | 0.4 |
| J42 | Unspecified chronic bronchitis | 0.4 |
| J45.9 | Other and unspecified asthma | 0.4 |
| K25.9 | Gastric ulcer Unspecified as acute or chronic, without haemorrhage or perforation | 0.4 |
| K26.7 | Chronic duodenal ulcer without hemorrhage or perforation | 0.4 |
| K29.6 | Other gastritis | 0.4 |
| K76.0 | Fatty (change of) liver, not elsewhere classified | 0.4 |
| K86.1 | Other chronic pancreatitis | 0.4 |
| N28.1 | Cyst of kidney, acquired | 0.4 |
| R73.9 | Hyperglycemia, unspecified | 0.4 |
| T75.2 | Effects of vibration | 0.4 |
| Z00.8 | Encounter for other general examination | 0.4 |
| B18.2 | Chronic viral hepatitis C | 0.3 |
| E06.3 | Autoimmune thyroiditis | 0.3 |
| H35.3 | Degeneration of macula and posterior pole | 0.3 |
| H90.3 | Sensorineural hearing loss, bilateral | 0.3 |
| J41.0 | Simple chronic bronchitis | 0.3 |
| J45.8 | Mixed asthma | 0.3 |
| K21.0 | Gastro-esophageal reflux disease with esophagitis, without bleeding | 0.3 |
| K29.5 | Chronic gastritis | 0.3 |
| K52.9 | Noninfective gastroenteritis and colitis | 0.3 |
| K91.5 | Postcholecystectomy syndrome | 0.3 |
| L90.8 | Other atrophic disorders of skin | 0.3 |
| M05.8 | Other rheumatoid arthritis with rheumatoid factor | 0.3 |
| M15.9 | Polyosteoarthritis, unspecified | 0.3 |
| M17.0 | Bilateral primary osteoarthritis of knee | 0.3 |
| M50.3 | Other cervical disc degeneration | 0.3 |
| M53.1 | Cervicobrachial syndrome | 0.3 |
| M54.6 | Pain in thoracic spine | 0.3 |

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| M54.8 | Other dorsalgia | 0.3 |
| M65.8 | Other synovitis and tenosynovitis | 0.3 |
| N20.0 | Calculus of kidney | 0.3 |
| C44.3 | Other malignant neoplasms: Skin of other and unspecified parts of face | 0.2 |
| C54.1 | Malignant neoplasm: Endometrium | 0.2 |
| C67.8 | Malignant neoplasm of overlapping sites of bladder | 0.2 |
| D44.1 | Neoplasm of uncertain or unknown behaviour: Adrenal gland | 0.2 |
| D64.8 | Other specified anemias | 0.2 |
| E01.8 | Other iodine-deficiency-related thyroid disorders and allied conditions | 0.2 |
| E06.5 | Other chronic thyroiditis | 0.2 |
| E10.7 | Type 1 diabetes mellitus With multiple complications | 0.2 |
| E11.2 | Type 2 diabetes mellitus with kidney complications | 0.2 |
| E11.5 | ype 2 diabetes mellitus with circulatory complications | 0.2 |
| H25.8 | Other age-related cataract | 0.2 |
| J12.9 | Viral pneumonia, unspecified | 0.2 |
| J16.8 | Pneumonia due to other specified infectious organisms | 0.2 |
| J90 | Pleural effusion, not elsewhere classified | 0.2 |
| K21.9 | Gastro-oesophageal reflux disease | 0.2 |
| K29.4 | Chronic atrophic gastritis | 0.2 |
| K29.7 | Gastritis | 0.2 |
| K58.9 | Irritable bowel syndrome without diarrhea | 0.2 |
| K59.0 | Constipation | 0.2 |
| K59.9 | Functional intestinal disorder, unspecified | 0.2 |
| K64.1 | Second degree hemorrhoids | 0.2 |
| K64.8 | Other hemorrhoids | 0.2 |
| K71.2 | Toxic liver disease with acute hepatitis | 0.2 |
| K81.0 | Acute cholecystitis | 0.2 |
| K85.9 | Acute pancreatitis | 0.2 |
| M10.0 | Idiopathic gout | 0.2 |
| M15.8 | Other polyosteoarthritis | 0.2 |
| M16.5 | Unilateral post-traumatic osteoarthritis of hip | 0.2 |
| M17.1 | Unilateral primary osteoarthritis of knee | 0.2 |
| M17.2 | Bilateral post-traumatic osteoarthritis of knee | 0.2 |
| M17.9 | Osteoarthritis of knee, unspecified | 0.2 |
| M53.8 | Other specified dorsopathies. | 0.2 |
| M54.2 | Cervicalgia | 0.2 |
| M54.5 | Low back pain | 0.2 |
| M54.9 | Dorsalgia, unspecified | 0.2 |
| N18.2 | Chronic kidney disease, stage 2 (mild) | 0.2 |
| N18.4 | Chronic kidney disease, stage 4 (severe) | 0.2 |

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|---|---|---|
| N41.1 | Chronic prostatitis | 0.2 |
| R73.0 | Abnormal glucose | 0.2 |
| S00.0 | Unspecified superficial injury of scalp | 0.2 |
| S52.50 | Fracture of lower end of radius: Unspecified | 0.2 |
| T91.1 | Sequelae of fracture of spine | 0.2 |
| Z00.0 | Encounter for general adult medical examination without abnormal findings | 0.2 |
| Z25.1 | Need for immunization against influenza | 0.2 |
| A02.0 | Salmonella enteritis | 0.1 |
| A41.1 | Sepsis due to other specified staphylococcus | 0.1 |
| A46 | Erysipelas | 0.1 |
| B25.9 | Cytomegaloviral disease, unspecified | 0.1 |
| B66.0 | Opisthorchiasis | 0.1 |
| B99 | Other and unspecified infectious diseases | 0.1 |
| C18.0 | Malignant neoplasm of cecum | 0.1 |
| C18.7 | Malignant neoplasm: Sigmoid colon | 0.1 |
| C18.8 | Malignant neoplasm: Overlapping lesion of colon | 0.1 |
| C20 | Malignant neoplasm of rectum | 0.1 |
| C34.1 | Malignant neoplasm: Upper lobe, bronchus or lung | 0.1 |
| C50.3 | Malignant neoplasm: Lower-inner quadrant of breast | 0.1 |
| C50.4 | Malignant neoplasm: Upper-outer quadrant of breast | 0.1 |
| C50.9 | Malignant neoplasm: Breast, unspecified | 0.1 |
| C61 | Malignant neoplasm of prostate | 0.1 |
| C67.4 | Malignant neoplasm: Posterior wall of bladder | 0.1 |
| C78.0 | Secondary malignant neoplasm of lung | 0.1 |
| C81.1 | Nodular sclerosis (classical) Hodgkin lymphoma | 0.1 |
| D12.0 | Benign neoplasm of cecum | 0.1 |
| D14.3 | Benign neoplasm: Bronchus and lung | 0.1 |
| D23.5 | Other benign neoplasm of skin of trunk | 0.1 |
| D30.0 | Benign neoplasm of kidney | 0.1 |
| D33.4 | Benign neoplasm of spinal cord | 0.1 |
| D37.7 | Neoplasm of uncertain or unknown behaviour: Other digestive organs | 0.1 |
| D38.1 | Neoplasm of uncertain behavior of trachea, bronchus and lung | 0.1 |
| D45 | Polycythemia vera | 0.1 |
| D47.9 | Neoplasm of uncertain or unknown behaviour of lymphoid, haematopoietic and related tissue, unspecified | 0.1 |
| D68.8 | Other specified coagulation defects | 0.1 |
| D69.6 | Thrombocytopenia, unspecified | 0.1 |
| D75.9 | Disease of blood and blood-forming organs, unspecified | 0.1 |
| E03.8 | Other specified hypothyroidism | 0.1 |
| E04.1 | Nontoxic single thyroid nodule | 0.1 |

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|---|---|---|
| E05.9 | Thyrotoxicosis | 0.1 |
| E10.6 | Type 1 diabetes mellitus With other specified complications | 0.1 |
| E11.3 | Type 2 diabetes mellitus with ophthalmic complications | 0.1 |
| E11.4 | Type 2 diabetes mellitus With neurological complications | 0.1 |
| E11.7 | Type 2 diabetes mellitus With multiple complications | 0.1 |
| E16.8 | Other specified disorders of pancreatic internal secretion | 0.1 |
| E21.1 | Secondary hyperparathyroidism, not elsewhere classified | 0.1 |
| E66.8 | Other obesity | 0.1 |
| E68 | Sequelae of hyperalimentation | 0.1 |
| E78.0 | Pure hypercholesterolemia | 0.1 |
| E78.5 | Hyperlipidemia, Unspecified | 0.1 |
| E79.0 | Hyperuricemia without signs of inflammatory arthritis and tophaceous disease | 0.1 |
| E87.5 | Hyperkalemia | 0.1 |
| F10.3 | Mental and behavioural disorders due to use of alcohol Withdrawal state | 0.1 |
| G00.9 | Bacterial meningitis, unspecified | 0.1 |
| G20 | Parkinson's disease | 0.1 |
| G40.2 | Localization-related (focal)(partial) symptomatic epilepsy and epileptic syndromes with complex partial seizures | 0.1 |
| G40.3 | Generalized idiopathic epilepsy and epileptic syndromes | 0.1 |
| G45.0 | Vertebro-basilar artery syndrome | 0.1 |
| G50.0 | Trigeminal neuralgia | 0.1 |
| G52.8 | Disorders of other specified cranial nerves | 0.1 |
| G57.1 | Meralgia paresthetica | 0.1 |
| G63.2 | Diabetic polyneuropathy | 0.1 |
| G70.0 | Myasthenia gravis | 0.1 |
| G91.8 | Other hydrocephalus | 0.1 |
| G93.4 | Other and unspecified encephalopathy | 0.1 |
| H00.0 | Hordeolum and other deep inflammation of eyelid | 0.1 |
| H04.1 | Other disorders of lacrimal gland | 0.1 |
| H10.4 | Chronic conjunctivitis | 0.1 |
| H10.8 | Other conjunctivitis | 0.1 |
| H26.2 | Complicated cataract | 0.1 |
| H26.9 | Unspecified cataract | 0.1 |
| H40.0 | Glaucoma suspect | 0.1 |
| H40.8 | Other glaucoma | 0.1 |
| H52.0 | Hypermetropia | 0.1 |
| H52.4 | Presbyopia | 0.1 |
| H60.5 | Acute noninfective otitis externa | 0.1 |
| H68.0 | Eustachian salpingitis | 0.1 |
| H81.1 | Benign paroxysmal vertigo | 0.1 |

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| H90.0 | Conductive hearing loss | 0.1 |
| H90.8 | Mixed conductive and sensorineural hearing loss, unspecified. | 0.1 |
| J00 | Acute nasopharyngitis | 0.1 |
| J01.0 | Acute maxillary sinusitis | 0.1 |
| J02.8 | Acute pharyngitis due to other specified organisms | 0.1 |
| J32.9 | Chronic sinusitis | 0.1 |
| J37.0 | Chronic laryngitis | 0.1 |
| J94.8 | Other specified pleural conditions | 0.1 |
| K10.2 | Inflammatory conditions of jaws | 0.1 |
| K31.7 | Polyp of stomach and duodenum | 0.1 |
| K31.9 | Disease of stomach and duodenum | 0.1 |
| K35.8 | Other and unspecified acute appendicitis | 0.1 |
| K40.9 | Unilateral or unspecified inguinal hernia, without obstruction or gangrene | 0.1 |
| K51.9 | Ulcerative colitis | 0.1 |
| K56.5 | Intestinal adhesions [bands] with obstruction (postinfection) | 0.1 |
| K64.3 | Fourth degree hemorrhoids | 0.1 |
| K65.9 | Peritonitis, unspecified | 0.1 |
| K66.0 | Peritoneal adhesions (postprocedural) (postinfection) | 0.1 |
| K75.9 | Inflammatory liver disease, unspecified | 0.1 |
| K80.2 | Calculus of gallbladder without cholecystitis | 0.1 |
| K80.8 | Other cholelithiasis | 0.1 |
| K82.8 | Other specified diseases of gallbladder | 0.1 |
| K86.0 | Alcohol-induced chronic pancreatitis | 0.1 |
| L02.4 | Cutaneous abscess, furuncle and carbuncle of limb | 0.1 |
| L20.9 | Atopic dermatitis, unspecified | 0.1 |
| L30.1 | Dyshidrosis | 0.1 |
| L30.9 | Dermatitis, unspecified | 0.1 |
| L40.0 | Psoriasis vulgaris | 0.1 |
| L40.8 | Other psoriasis | 0.1 |
| L98.4 | Chronic ulcer of skin, not elsewhere classified | 0.1 |
| L98.9 | Disorder of the skin and subcutaneous tissue, unspecified | 0.1 |
| M10.9 | Gout, Unspecified | 0.1 |
| M15.0 | Primary generalized (osteo)arthritis | 0.1 |
| M16.0 | Bilateral primary osteoarthritis of hip | 0.1 |
| M16.2 | Bilateral osteoarthritis resulting from hip dysplasia | 0.1 |
| M16.3 | Unilateral osteoarthritis resulting from hip dysplasia | 0.1 |
| M17.5 | Other unilateral secondary osteoarthritis of knee | 0.1 |
| M19.0 | Primary osteoarthritis of other joints | 0.1 |
| M19.8 | Other specified arthrosis | 0.1 |
| M23.2 | Derangement of meniscus due to old tear or injury | 0.1 |

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| M24.5 | Contracture of joint | 0.1 |
| M35.3 | Polymyalgia rheumatica | 0.1 |
| M42.9 | Spinal osteochondrosis | 0.1 |
| M45.0 | Ankylosing spondylitis of multiple sites in spine | 0.1 |
| M50.1 | Cervical disc disorder with radiculopathy | 0.1 |
| M51.0 | Thoracic, thoracolumbar and lumbosacral intervertebral disc disorders with myelopathy | 0.1 |
| M53.0 | Cervicocranial syndrome | 0.1 |
| M65.3 | Trigger finger | 0.1 |
| M65.9 | Synovitis and tenosynovitis, unspecified | 0.1 |
| M67.1 | Other contracture of tendon (sheath) | 0.1 |
| M70.2 | Olecranon bursitis | 0.1 |
| M75.1 | Rotator cuff tear or rupture, not specified as traumatic | 0.1 |
| M75.8 | Other shoulder lesions | 0.1 |
| M79.2 | Neuralgia and neuritis | 0.1 |
| M81.8 | Other osteoporosis without current pathological fracture | 0.1 |
| M87.0 | Idiopathic aseptic necrosis of bone | 0.1 |
| N11.0 | Nonobstructive reflux-associated chronic pyelonephriti | 0.1 |
| N11.9 | Chronic tubulo-interstitial nephritis | 0.1 |
| N18.5 | Chronic kidney disease, stage 5 | 0.1 |
| N18.9 | Chronic kidney disease | 0.1 |
| N20.1 | Calculus of ureter | 0.1 |
| N20.2 | Calculus of kidney with calculus of ureter | 0.1 |
| N20.9 | Urinary calculus, unspecified | 0.1 |
| N23 | Unspecified renal colic | 0.1 |
| N30.1 | Interstitial cystitis | 0.1 |
| N30.2 | Other chronic cystitis | 0.1 |
| N30.9 | Cystitis, unspecified | 0.1 |
| N43.0 | Encysted hydrocele | 0.1 |
| N45.9 | Orchitis, epididymitis and epididymo-orchitis without abscess | 0.1 |
| N60.1 | Diffuse cystic mastopathy | 0.1 |
| N60.8 | Other benign mammary dysplasias | 0.1 |
| N63 | Unspecified lump in breast | 0.1 |
| N85.0 | Endometrial hyperplasia | 0.1 |
| N95.0 | Postmenopausal bleeding | 0.1 |
| N95.2 | Postmenopausal atrophic vaginitis | 0.1 |
| Q24.9 | Congenital malformation of heart, unspecified | 0.1 |
| R09.1 | Pleurisy | 0.1 |
| R51 | Headache | 0.1 |
| R59.9 | Enlarged lymph nodes, unspecified | 0.1 |

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| R71 | Abnormality of red blood cells | 0.1 |
| R73.9 | Hyperglycemia, unspecified | 0.1 |
| S05.0 | Injury of conjunctiva and corneal abrasion without mention of foreign body | 0.1 |
| S20.2 | Contusion of thorax | 0.1 |
| S40.0 | Contusion of shoulder and upper arm | 0.1 |
| S50.1 | Contusion of forearm | 0.1 |
| S51.0 | Open wound of elbow | 0.1 |
| S70.1 | Contusion of thigh | 0.1 |
| S80.0 | Contusion of knee | 0.1 |
| S93.4 | Sprain of ankle | 0.1 |
| T15.1 | Foreign body in conjunctival sac | 0.1 |
| T26.6 | Chemical burn of cornea and conjunctival sac | 0.1 |
| T29.3 | Burns of multiple regions, at least one burn of third degree mentioned | 0.1 |
| T31.1 | Burns involving 10-19% of body surface | 0.1 |
| T78.3 | Angioneurotic edema | 0.1 |
| T90.5 | Sequelae of intracranial injury | 0.1 |
| T91.3 | Sequelae of injury of spinal cord | 0.1 |
| U08.9 | Personal history of COVID-19, unspecified | 0.1 |
| U09.9 | Post–COVID-19 condition, unspecified | 0.1 |
| W00.4 | Fall on same level involving ice and snow | 0.1 |
| W22.4 | Striking against wall of swimming pool | 0.1 |
| Z01.4 | Encounter for gynecological examination | 0.1 |
| Z03.1 | Observation for suspected malignant neoplasm | 0.1 |
| Z03.8 | Encounter for observation for other suspected diseases and conditions ruled out | 0.1 |
| Z54.8 | Convalescence following other treatment | 0.1 |
| Z71.2 | Person consulting for explanation of examination or test findings | 0.1 |
| Z96.1 | Presence of intraocular lens | 0.1 |

**Table S2. Median numbers of drugs, pDDIs, and pDDI index values per record in the T-List and the P-List in cardiovascular patients depending on primary diagnosis category established during the medical encounter.**

| Clinical entity | Number of EHRs, *n* | | Drug number, median (IQR) | | *P*-value | pDDI number, median (IQR) | | *P*-value | pDDI index, median (IQR) | | *P*-value |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | T-List | P-List | T-List | P-List | | T-List | P-List | | T-List | P-List | |
| A | 2 | 3 | 15 (1-19) | 6 (3.5-11) | .4000 | 27 (13.5-40.5) | 0 (0-18) | .7469 | 51 (25-76) | 0 (0-35) | .7469 |
| C | 6 | 11 | 2 (1.25-4.25) | 4 (2-4) | .5723 | 0 (0-0) | 0 (0-0.5) | .7354 | 0 (0-0) | 0 (0-1) | .7354 |
| D | 5 | 9 | 4 (3-4) | 4 (1-4) | 1.000 | 2 (1-3) | 1 (0-1) | .4475 | 4 (2-6) | 2 (0-3) | .4939 |
| E | 35 | 38 | 3 (1-7) | 3 (1-7) | .9469 | 1 (0-6) | 0 (0-2.75) | .2485 | 2 (0-12) | 0 (0-8.25) | .4630 |
| G | 6 | 16 | 6.5 (4.5-7) | 5 (2-5) | .1640 | 2 (0.5-7.25) | 0 (0-1) | .0898 | 4.5 (1-14) | 0 (0-1) | .0553 |
| H | 1 | 14 | 7 (-7-7) | 3 (2.25-4) | - | 7 (7-7) | 0 (0-0.75) | - | 14 (14-14)s | 0 (0-1.75) | - |
| I | 292 | 536 | 6 (3-8) | 7 (5-9) | **1.928e-7** | 5 (1-10.25) | 6 (2-11) | .0747 | 11 (1-20) | 13 (4-21) | **.0291** |
| J | 45 | 97 | 5 (2-9) | 6 (4-9) | .0853 | 2 (0-9) | 0 (0-3) | .0688 | 3 (0-18) | 0 (0-6) | .0807 |
| K | 15 | 41 | 5 (1.5-6) | 4 (2-6) | .7727 | 0 (0-4) | 0 (0-1) | .1909 | 0 (0-7.5) | 0 (0-2) | .1911 |
| L | 2 | 5 | 4.5 (2.75-6.25) | 2 (2-3) | .8407 | 3 (1.5-4.5) | 0 (0-0) | .2059 | 6.5 (3.25-9.75) | 0 (0-0) | .2059 |
| M | 33 | 60 | 3 (1-5) | 5 (2-7) | **.0291** | 0 (0-3) | 0 (0-1.25) | .8808 | 0 (0-6) | 0 (0-2.25) | .9299 |
| N | 18 | 36 | 4 (2.25-7) | 3.5 (1.75-5) | .2395 | 1.5 (0-7.5) | 0 (0-0) | **.0048** | 2.5 (0-15.25) | 0 (0-0) | **.0041** |
| Q | 1 | 1 | 8 (8-8) | 9 (9-9) | - | 3 (3-3) | 0 (0-0) | - | 6 (6-6) | 12 (12-12) | - |
| R | 1 | 4 | 9 (9-9) | 7.5 (3.25-11) | - | 12 (12-12) | 6 (6-6) | - | 24 (24-24) | 7.5 (0.75-15) | - |
| S and T | 1 | 4 | 14 (14-14) | 1.5 (1-2) | - | 23 (23-23) | 7.5 (0.75-15) | - | 43 (43-43) | 0 (0-0.5) | - |
| U07.1 | 12 | 11 | 12.5 (8.75-16) | 7 (5-13) | .1643 | 12 (4.5-15.25) | 1 (0-2) | **.0010** | 21.5 (8.75-27.5) | 1 (0-4) | **.0153** |
| U (other than U07.1) | 1 | 1 | 0 (0-0) | 9 (9-9) | - | 0 (0-0) | 5 (5-5) | - | 0 (0-0) | 11 (1-11) | - |
| Z | 3 | 14 | 2 (1.5-4.5) | 4 (2-8) | .4426 | 0 (0-3) | 1.5 (0-5) | .5564 | 0 (0-6.5) | 2.5 (0-10.5) | .5566 |

Note: A—Intestinal infectious diseases; C—neoplasms; D—diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism; E—endocrine, nutritional and metabolic diseases; G—diseases of the nervous system; H—diseases of the eye and adnexa and diseases of the ear and mastoid process; I—diseases of the circulatory system; J—diseases of the respiratory system; K—diseases of the digestive system; L—diseases of the skin and subcutaneous tissue; M—diseases of the musculoskeletal system and connective tissue; N—diseases of the genitourinary system; R—symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified; S and T—injury, poisoning and certain other consequences of external causes; U—codes for special purposes; Z—factors influencing health status and contact with health services.

**Table S3. Median numbers of serious, monitor-closely, and minor pDDIs per record in the T-List and the P-List in patients depending on primary diagnosis category established during the medical encounter.**

| Clinical entity | Number of EHRs, *n* | | Serious pDDIs, median (IQR) | | *P*-value | Monitor-closely pDDIs, median (IQR) | | *P*-value | Minor pDDIs, median (IQR) | | *P*-value |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | T-List | P-List | T-List | P-List | | T-List | P-List | | T-List | P-List | |
| A | 2 | 3 | 2 (1-3) | 0 (0-1) | .7469 | 20 (9.75-29.25) | 0 (0-15) | .7469 | 5.5 (2.75-8.25) | 0 (0-2) | .7469 |
| C | 6 | 11 | 0 (0-0) | 0 (0-0) | .7878 | 0 (0-0) | 0 (0-0.5) | .7354 | 0 (0-0) | 0 (0-0) | .2184 |
| D | 5 | 9 | 0 (0-0) | 0 (0-1) | .6709 | 2 (1-3) | 0 (0-1) | .2844 | 0 (0-0) | 0 (0-0) | .2330 |
| E | 35 | 38 | 0 (0-0) | 0 (0-0) | .2403 | 1 (0-4) | 0 (0-3) | .3920 | 0 (0-0) | 0 (0-0) | .8679 |
| G | 6 | 16 | 0 (0-1) | 0 (0-0) | .1247 | 1.5 (0.25-4.25) | 0 (0-0.5) | .0742 | 0 (0-2.25) | 0 (0-0) | .1401 |
| H | 1 | 14 | 0 (0-0) | 0 (0-0) | - | 7 (7-7) | 0 (0-0.75) | - | 0 (0-0) | 0 (0-0) | - |
| I | 292 | 536 | 0 (0-1) | 1 (0-1) | **.0001** | 4 (0-8) | 5 (2-8) | .1033 | 0 (0-1) | 0 (0-1) | .9340 |
| J | 45 | 97 | 0 (0-1) | 0 (0-0) | .0703 | 1 (0-5) | 0 (0-2) | .0635 | 0 (0-1) | 0 (0-0) | .1072 |
| K | 15 | 41 | 0 (0-1) | 0 (0-0) | **.0261** | 0 (0-3.5) | 0 (0-1) | .1839 | 0 (0-0) | 0 (0-0) | .1679 |
| L | 2 | 5 | 0 (0-0) | 0 (0-0) | - | 2 (1-3) | 0 (0-0) | .2059 | 0.5 (0.25-0.75) | 0 (0-0) | .2059 |
| M | 33 | 60 | 0 (0-0) | 0 (0-0) | .7537 | 0 (0-3) | 0 (0-1) | .4857 | 0 (0-0) | 0 (0-1) | .0778 |
| N | 18 | 36 | 0 (0-0) | 0 (0-0) | **.0224** | 1 (0-5.75) | 0 (0-0) | **.0046** | 0 (0-0) | 0 (0-0) | .4619 |
| Q | 1 | 1 | 0 (0-0) | 0 (0-0) | - | 3 (3-3) | 6 (6-6) | - | 0 (0-0) | 0 (0-0) | - |
| R | 1 | 4 | 0 (0-0) | 1 (0-2.25) | - | 12 (12-12) | 6 (0-12.25) | - | 0 (0-0) | 0.5 (0-1.25) | - |
| S and T | 1 | 4 | 1 (1-1) | 0 (0-0) | - | 18 (18-18) | 0 (0-0.25) | - | 4 (4-4) | 0 (0-0) | - |
| U07.1 | 12 | 11 | 0 (0-0) | 0 (0-0) | .6685 | 9 (3.5-11.5) | 0 (0-2) | **.0087** | 2 (0.75-3.5) | 0 (0-0.5) | **.0463** |
| U (other than U07.1) | 1 | 1 | 0 (0-0) | 1 (1-1) | - | 0 (0-0) | 4 (4-4) | - | 0 (0-0) | 0 (0-0) | - |
| Z | 3 | 14 | 0 (0-1) | 0 (0-0) | .7987 | 0 (0-2.5) | 1 (0-3.75) | .5559 | 0 (0-0) | 0 (0-0.75) | .3513 |

Note: A—Intestinal infectious diseases; C—neoplasms; D—diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism; E—endocrine, nutritional and metabolic diseases; G—diseases of the nervous system; H—diseases of the eye and adnexa and diseases of the ear and mastoid process; I—diseases of the circulatory system; J—diseases of the respiratory system; K—diseases of the digestive system; L—diseases of the skin and subcutaneous tissue; M—diseases of the musculoskeletal system and connective tissue; N—diseases of the genitourinary system; R—symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified; S and T—injury, poisoning and certain other consequences of external causes; U—codes for special purposes; Z—factors influencing health status and contact with health services.

**Table S4.** Drug combinations resulting in contraindicated potential drug–drug interactions in the list of taken drugs in patients with cardiovascular diseases according to data derived from the electronic health records ($n$ = 1030) established in 2018–2023.

| Drug combinations | *n* | Potential contraindicated drug-drug interactions (T-list) |
|---|---|---|
| indapamide + sotalol | 2 | indapamide and sotalol both increase QTc interval. Contraindicated |
| amitriptyline + indapamide | 1 | amitriptyline and indapamide both increase QTc interval. Contraindicated |
| carbamazepine + linezolid | 1 | carbamazepine increases toxicity of linezolid by unknown mechanism. Contraindicated. D/C MAO inhibitor 2 weeks before |

**Table S5.** Drug combinations resulting in serious potential drug–drug interactions in the list of taken medications in patients with cardiovascular diseases according to data derived from the electronic health records ($n$ = 1030) established in 2018–2023.

| Drug combinations | *n* | Potential serious drug-drug interactions (T-list) |
|---|---|---|
| aspirin + lisinopril | 36 | aspirin, lisinopril. pharmacodynamic antagonism. Avoid or Use Alternate Drug. Coadministration may result in a significant decrease in renal function. NSAIDs may diminish the antihypertensive effect of ACE inhibitors. The mechanism of these interactions is likely related to the ability of NSAIDs to reduce the synthesis of vasodilating renal prostaglandins |
| aspirin + perindopril | 25 | aspirin, perindopril. pharmacodynamic antagonism. Avoid or Use Alternate Drug. Coadministration may result in a significant decrease in renal function. NSAIDs may diminish the antihypertensive effect of ACE inhibitors. The mechanism of these interactions is likely related to the ability of NSAIDs to reduce the synthesis of vasodilating renal prostaglandins |
| clopidogrel + omeprazole | 24 | omeprazole decreases effects of clopidogrel by affecting hepatic enzyme CYP2C19 metabolism. Avoid or Use Alternate Drug. Clopidogrel efficacy may be reduced by drugs that inhibit CYP2C19. Inhibition of platelet aggregation by clopidogrel is entirely due to an active metabolite. Clopidogrel is metabolized to this active metabolite in part by CYP2C19 |
| aspirin + enalapril * | 18 | aspirin, enalapril. pharmacodynamic antagonism. Avoid or Use Alternate Drug. Coadministration may result in a significant decrease in renal function. NSAIDs may diminish the antihypertensive effect of ACE inhibitors. The mechanism of these interactions is likely related to the ability of NSAIDs to reduce the synthesis of vasodilating renal prostaglandins |
| bisoprolol + digoxin | 15 | bisoprolol increases effects of digoxin by pharmacodynamic synergism. Use Caution/Monitor. Enhanced bradycardia |
| aspirin + fosinopril | 10 | aspirin, fosinopril. pharmacodynamic antagonism. Avoid or Use Alternate Drug. Coadministration may result in a significant decrease in renal function. NSAIDs may diminish the antihypertensive effect of ACE inhibitors. The mechanism of these interactions is likely related to the ability of NSAIDs to reduce the synthesis of vasodilating renal prostaglandins |
| digoxin + omeprazole | 10 | omeprazole will increase the level or effect of digoxin by increasing gastric pH. Applies only to oral form of both agents. Avoid or Use Alternate Drug |
| apixaban + clopidogrel | 8 | clopidogrel and apixaban both increase anticoagulation. Avoid or Use Alternate Drug |
| digoxin + metoprolol | 8 | digoxin increases toxicity of metoprolol by unspecified interaction mechanism. Avoid or Use Alternate Drug. Can increase risk of bradycardia |
| potassium + spironolactone | 8 | spironolactone and potassium [chloride] both increase serum potassium. Avoid or Use Alternate Drug |
| bisoprolol + metoprolol | 7 | bisoprolol and metoprolol both increase anti-hypertensive channel blocking. Avoid or Use Alternate Drug |
| amiodarone + digoxin | 4 | amiodarone will increase the level or effect of digoxin by P-glycoprotein (MDR1) efflux transporter. Avoid or Use Alternate Drug. Amiodarone increases PO digoxin serum concentrations by ~70% and IV digoxin by ~17%; measure digoxin levels before initiating amiodarone and reduce PO digoxin dose by 30-50%; decrease IV digoxin dose by 15-30% |
| | | amiodarone will increase the level or effect of digoxin by basic (cationic) drug competition for renal tubular clearance. Avoid or Use Alternate Drug. Amiodarone increases PO digoxin serum |

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|---|---|---|
| | | concentrations by ~70% and IV digoxin by ~17%; measure digoxin levels before initiating amiodarone and reduce PO digoxin dose by 30-50%; decrease IV digoxin dose by 15-30% |
| ceftriaxone + enoxaparin | 4 | ceftriaxone increases effects of enoxaparin by anticoagulation. Avoid or Use Alternate Drug. cephalosporins may decrease prothrombin activity |
| ceftriaxone + heparin | 4 | ceftriaxone will increase the level or effect of heparin by anticoagulation. Avoid or Use Alternate Drug. cephalosporins may decrease prothrombin activity |
| aspirin + captopril * | 3 | aspirin, captopril. pharmacodynamic antagonism. Avoid or Use Alternate Drug. Coadministration may result in a significant decrease in renal function. NSAIDs may diminish the antihypertensive effect of ACE inhibitors. The mechanism of these interactions is likely related to the ability of NSAIDs to reduce the synthesis of vasodilating renal prostaglandins |
| clopidogrel + morphine | 3 | morphine will decrease the level or effect of clopidogrel by Other (see comment). Avoid or Use Alternate Drug. coadministration of opioid agonists delay and reduce absorption of clopidogrel, presumably because of slowed gastric emptying, resulting in reduced exposure to its metabolites; consider use of parenteral antiplatelet agents in acute coronary syndrome patients requiring coadministration of morphine or other opioid agonists |
| ketorolac + lisinopril | 3 | ketorolac, lisinopril. pharmacodynamic antagonism. Avoid or Use Alternate Drug. Coadministration may result in a significant decrease in renal function. NSAIDs may diminish the antihypertensive effect of ACE inhibitors. The mechanism of these interactions is likely related to the ability of NSAIDs to reduce the synthesis of vasodilating renal prostaglandins |
| amikacin + furosemide | 2 | furosemide, amikacin. Either increases toxicity of the other by Mechanism: pharmacodynamic synergism. Avoid or Use Alternate Drug. Increased risk of ototoxicity and nephrotoxicity |
| apixaban + heparin | 2 | heparin and apixaban both increase anticoagulation. Avoid or Use Alternate Drug |
| captopril + losartan | 2 | losartan, captopril. Either increases toxicity of the other by pharmacodynamic synergism. Avoid or Use Alternate Drug. Dual blockade of renin-angiotensin system increases risks of hypotension, hyperkalemia, and renal impairment |
| carbamazepine + omeprazole | 2 | carbamazepine will decrease the level or effect of omeprazole by affecting hepatic enzyme CYP2C19 metabolism. Avoid or Use Alternate Drug |
| clopidogrel + rabeprazole | 2 | rabeprazole decreases effects of clopidogrel by affecting hepatic enzyme CYP2C19 metabolism. Avoid or Use Alternate Drug. Clopidogrel efficacy may be reduced by drugs that inhibit CYP2C19. Inhibition of platelet aggregation by clopidogrel is entirely due to an active metabolite. Clopidogrel is metabolized to this active metabolite in part by CYP2C19 |
| dabigatran + enoxaparin | 2 | dabigatran and enoxaparin both increase anticoagulation. Avoid or Use Alternate Drug. Caution is advised, both drugs have the potential to cause bleeding. Concomitant use may increase risk of bleeding |
| diclofenac + enalapril | 2 | diclofenac, enalapril. pharmacodynamic antagonism. Avoid or Use Alternate Drug. Coadministration may result in a significant decrease in renal function. NSAIDs may diminish the antihypertensive effect of ACE inhibitors. The mechanism of these interactions is likely related to the ability of NSAIDs to reduce the synthesis of vasodilating renal prostaglandins |
| fluconazole + ondansetron | 2 | fluconazole and ondansetron both increase QTc interval. Avoid or Use Alternate Drug. Avoid with congenital long QT syndrome; ECG monitoring recommended with concomitant medications that prolong QT interval, electrolyte abnormalities, CHF, or bradyarrhythmias. Combination may increase ondansetron levels |

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|---|---|---|
| levofloxacin + sodium bicarbonate | 2 | sodium bicarbonate decreases levels of levofloxacin by inhibition of GI absorption. Applies only to oral form of both agents. Avoid or Use Alternate Drug. Separate by 2 hours |
| amiodarone + escitalopram | 1 | escitalopram increases toxicity of amiodarone by QTc interval. Avoid or Use Alternate Drug |
| amiodarone + indapamide | 1 | amiodarone and indapamide both increase QTc interval. Avoid or Use Alternate Drug |
| apixaban + rivaroxaban | 1 | rivaroxaban and apixaban both increase anticoagulation. Avoid or Use Alternate Drug |
| apixaban + warfarin | 1 | apixaban increases effects of warfarin by anticoagulation. Avoid or Use Alternate Drug. Avoid combined use once INR is established in the desired therapeutic range |
| aspirin + ketorolac | 1 | aspirin, ketorolac. Either increases toxicity of the other by pharmacodynamic synergism. Contraindicated |
| bisoprolol + nebivolol | 1 | bisoprolol and nebivolol both increase anti-hypertensive channel blocking. Avoid or Use Alternate Drug |
| bisoprolol + verapamil | 1 | bisoprolol and verapamil both increase anti-hypertensive channel blocking. Modify Therapy/Monitor Closely |
| captopril + diclofenac | 1 | captopril, diclofenac. Either increases toxicity of the other by Other (see comment). Use Caution/Monitor. Comment: May result in renal function deterioration, particularly in elderly or volume depleted individuals |
| captopril + ketorolac | 1 | captopril, ketorolac. Either increases toxicity of the other by Other (see comment). Use Caution/Monitor. Comment: May result in renal function deterioration, particularly in elderly or volume depleted individuals |
| captopril + telmisartan | 1 | telmisartan, captopril. Either increases toxicity of the other by pharmacodynamic synergism. Avoid or Use Alternate Drug. Dual blockade of renin-angiotensin system increases risks of hypotension, hyperkalemia, and renal impairment |
| carbamazepine + prednisolone | 1 | carbamazepine will decrease the level or effect of prednisolone by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Avoid or Use Alternate Drug |
| ceftriaxone + fondaparinux | 1 | ceftriaxone increases effects of fondaparinux by anticoagulation. Avoid or Use Alternate Drug. cephalosporins may decrease prothrombin activity |
| clarithromycin + dexamethasone | 1 | clarithromycin will increase the level or effect of dexamethasone by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Avoid or Use Alternate Drug |
| clarithromycin + enoxaparin | 1 | clarithromycin increases effects of enoxaparin by decreasing metabolism. Avoid or Use Alternate Drug |
| clopidogrel + fondaparinux | 1 | fondaparinux, clopidogrel. Either increases effects of the other by pharmacodynamic synergism. Contraindicated. Enhanced risk of hemorrhage |
| diclofenac + fosinopril | 1 | diclofenac, fosinopril. pharmacodynamic antagonism. Avoid or Use Alternate Drug. Coadministration may result in a significant decrease in renal function. NSAIDs may diminish the antihypertensive effect of ACE inhibitors. The mechanism of these interactions is likely related to the ability of NSAIDs to reduce the synthesis of vasodilating renal prostaglandins |
| diclofenac + ketorolac | 1 | diclofenac, ketorolac. Either increases toxicity of the other by pharmacodynamic synergism. Contraindicated |
| diclofenac + lisinopril | 1 | diclofenac, lisinopril. pharmacodynamic antagonism. Avoid or Use Alternate Drug. Coadministration may result in a significant decrease in renal function. NSAIDs may diminish the antihypertensive effect of ACE inhibitors. The mechanism of these interactions is likely related to the ability of NSAIDs to reduce the synthesis of vasodilating renal prostaglandins |

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|---|---|---|
| diclofenac + methotrexate | 1 | diclofenac increases levels of methotrexate by decreasing renal clearance. Avoid or Use Alternate Drug. Concomitant administration of NSAIDs with high dose methotrexate has been reported to elevate and prolong serum methotrexate levels, resulting in deaths from severe hematologic and GI toxicity. NSAIDs may reduce tubular secretion of methotrexate and enhance toxicity |
| enalapril + ketorolac | 1 | enalapril, ketorolac. Either increases toxicity of the other by Other (see comment). Use Caution/Monitor. Comment: May result in renal function deterioration, particularly in elderly or volume depleted individuals |
| enalapril + losartan | 1 | losartan, enalapril. Either increases toxicity of the other by pharmacodynamic synergism. Avoid or Use Alternate Drug. Dual blockade of renin-angiotensin system increases risks of hypotension, hyperkalemia, and renal impairment |
| enoxaparin + heparin | 1 | enoxaparin and heparin both increase anticoagulation. Avoid or Use Alternate Drug |
| eplerenone + potassium | 1 | potassium chloride, eplerenone. Mechanism: pharmacodynamic synergism. Contraindicated. Hyperkalemia |
| formoterol + indapamide | 1 | formoterol and indapamide both increase QTc interval. Avoid or Use Alternate Drug |
| fosinopril + telmisartan | 1 | telmisartan, fosinopril. Either increases toxicity of the other by pharmacodynamic synergism. Avoid or Use Alternate Drug. Dual blockade of renin-angiotensin system increases risks of hypotension, hyperkalemia, and renal impairment |
| heparin + warfarin | 1 | heparin increases effects of warfarin by anticoagulation. Avoid or Use Alternate Drug. Avoid combined use once INR is established in the desired therapeutic range |
| ketorolac + meloxicam | 1 | ketorolac and meloxicam both increase anticoagulation. Use Caution/Monitor |
| lisinopril + losartan | 2 | losartan, lisinopril. Either increases toxicity of the other by pharmacodynamic synergism. Avoid or Use Alternate Drug. Dual blockade of renin-angiotensin system increases risks of hypotension, hyperkalemia, and renal impairment |
| lisinopril + meloxicam | 1 | lisinopril, meloxicam. Either increases toxicity of the other by Other (see comment). Use Caution/Monitor. Comment: May result in renal function deterioration, particularly in elderly or volume depleted individuals |
| lisinopril + valsartan | 1 | valsartan, lisinopril. Either increases toxicity of the other by pharmacodynamic synergism. Avoid or Use Alternate Drug. Dual blockade of renin-angiotensin system increases risks of hypotension, hyperkalemia, and renal impairment |
| metoprolol + nebivolol | 1 | metoprolol and nebivolol both increase anti-hypertensive channel blocking. Avoid or Use Alternate Drug |
| mifepristone + quinine | 1 | mifepristone will increase the level or effect of quinine by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Avoid or Use Alternate Drug |
| propranolol + sotalol | 1 | propranolol and sotalol both increase anti-hypertensive channel blocking. Avoid or Use Alternate Drug |

Note: Impact of drug–drug interactions associated with the combinations “aspirin + captopril” and “aspirin + enalapril” may be considered insignificant due to the use of low-dose aspirin in the majority of cases. Administration of aspirin at doses less than 300 mg per day has little effect on the effectiveness of captopril and enalapril. Administration of aspirin in higher doses reduces the effectiveness of captopril and enalapril.

**Table S6.** Drug combinations resulting in potential monitor-closely drug–drug interactions in the list of taken medications in patients with cardiovascular diseases according to data derived from the electronic health records ($n$ = 1030) established in 2018–2023.

| Drug combinations | n | Potential monitor-closely drug-drug interactions (T-list) |
|---|---|---|
| aspirin + bisoprolol | 282 | aspirin decreases effects of bisoprolol by pharmacodynamic antagonism. Use Caution/Monitor. Long term (>1 wk) NSAID use. NSAIDs decrease prostaglandin synthesis |
| aspirin + losartan | 120 | aspirin decreases effects of losartan by pharmacodynamic antagonism. Modify Therapy/Monitor Closely. NSAIDs decrease synthesis of vasodilating renal prostaglandins, and thus affect fluid homeostasis and may diminish antihypertensive effect |
| aspirin + spironolactone | 120 | aspirin decreases effects of spironolactone by unspecified interaction mechanism. Use Caution/Monitor. When used concomitantly, spironolactone dose may need to be titrated to higher maintenance dose and the patient should be observed closely to determine if the desired effect is obtained |
| aspirin + metoprolol | 88 | aspirin decreases effects of metoprolol by pharmacodynamic antagonism. Use Caution/Monitor. Long term (>1 wk) NSAID use. NSAIDs decrease prostaglandin synthesis |
| bisoprolol + losartan | 72 | bisoprolol, losartan. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of fetal compromise if given during pregnancy |
| bisoprolol + torsemide | 70 | bisoprolol increases and torsemide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| spironolactone + torsemide | 69 | spironolactone increases and torsemide decreases serum potassium. Effect of interaction is not clear, use caution. Modify Therapy/Monitor Closely |
| bisoprolol + spironolactone | 64 | bisoprolol and spironolactone both increase serum potassium. Modify Therapy/Monitor Closely |
| digoxin + spironolactone | 57 | spironolactone, digoxin. Mechanism: decreasing renal clearance. Use Caution/Monitor. False digoxin assay results may be obtained |
| | | spironolactone increases levels of digoxin by Other (see comment). Use Caution/Monitor. Comment: Spironolactone may cause false elevation of digoxin assay |
| | | spironolactone and digoxin both increase serum potassium. Modify Therapy/Monitor Closely |
| aspirin + torsemide | 56 | aspirin increases and torsemide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| aspirin + clopidogrel | 53 | aspirin, clopidogrel. Either increases toxicity of the other by pharmacodynamic synergism. Use Caution/Monitor. The need for simultaneous use of low-dose aspirin and anticoagulant or antiplatelet agents are common for patients with cardiovascular disease; monitor closely |
| amlodipine + bisoprolol | 51 | bisoprolol, amlodipine. Either increases effects of the other by pharmacodynamic synergism. Use Caution/Monitor. Both drugs lower blood pressure |
| aspirin + lisinopril | 48 | lisinopril, aspirin. Either increases toxicity of the other by Other (see comment). Use Caution/Monitor. Comment: May result in renal function deterioration, particularly with high dose aspirin, in elderly or volume depleted individuals |
| amiodarone + atorvastatin | 42 | amiodarone will increase the level or effect of atorvastatin by P-glycoprotein (MDR1) efflux transporter. Use Caution/Monitor |

| | | |
|---|---|---|
| aspirin + perindopril | 40 | perindopril, aspirin. Either increases toxicity of the other by Other (see comment). Use Caution/Monitor. Comment: May result in renal function deterioration, particularly with high doses of aspirin,in elderly or volume depleted individuals |
| furosemide + spironolactone | 38 | spironolactone increases and furosemide decreases serum potassium. Effect of interaction is not clear, use caution. Modify Therapy/Monitor Closely |
| aspirin + nitroglycerin | 36 | aspirin increases effects of nitroglycerin sublingual by additive vasodilation. Use Caution/Monitor. Vasodilatory and hemodynamic effects of NTG may be enhanced by coadministration with aspirin (additive effect desirable for emergent treatment) |
| amiodarone + bisoprolol | 34 | amiodarone, bisoprolol. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of cardiotoxicity with bradycardia |
| amiodarone + losartan | 32 | amiodarone will increase the level or effect of losartan by affecting hepatic enzyme CYP2C9/10 metabolism. Use Caution/Monitor. May inhibit the conversion of losartan to its active metabolite E-3174. Importance of interaction not established; monitor individual therapeutic response to determine losartan dosage |
| aspirin + captopril * | 32 | captopril, aspirin. Either increases toxicity of the other by Other (see comment). Use Caution/Monitor. Comment: May result in renal function deterioration, particularly with high dose aspirin, elderly or volume depleted individuals |
| aspirin + indapamide | 32 | aspirin increases and indapamide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| bisoprolol + digoxin | 32 | bisoprolol increases effects of digoxin by pharmacodynamic synergism. Use Caution/Monitor. Enhanced bradycardia |
| aspirin + heparin | 30 | aspirin, heparin. Either increases toxicity of the other by anticoagulation. Use Caution/Monitor. The need for simultaneous use of low-dose aspirin and anticoagulant or antiplatelet agents are common for patients with cardiovascular disease; monitor closely |
| aspirin + furosemide | 29 | aspirin increases and furosemide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| | | digoxin increases and torsemide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| losartan + torsemide | 28 | losartan increases and torsemide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| bisoprolol + indapamide | 27 | bisoprolol increases and indapamide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| lisinopril + spironolactone | 26 | lisinopril, spironolactone. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of hyperkalemia |
| aspirin + ticagrelor | 25 | aspirin, ticagrelor. Other (see comment). Use Caution/Monitor. Comment: Maintenance doses of aspirin above 100 mg decreases effectiveness of ticagrelor. Therefore, after the initial loading dose of aspirin (usually 325 mg), use ticagrelor with a maintenance dose of aspirin of 75-100 mg |
| lisinopril + torsemide | 25 | lisinopril, torsemide. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of acute hypotension, renal insufficiency |
| aspirin + telmisartan | 24 | aspirin decreases effects of telmisartan by pharmacodynamic antagonism. Modify Therapy/Monitor Closely. NSAIDs decrease synthesis of vasodilating renal prostaglandins, and thus affect fluid homeostasis and may diminish antihypertensive effect |

| | | |
|---|---|---|
| bisoprolol + furosemide | 24 | bisoprolol increases and furosemide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| losartan + metoprolol | 24 | losartan and metoprolol both increase serum potassium. Use Caution/Monitor |
| aspirin + enalapril * | 22 | enalapril, aspirin. Either increases toxicity of the other by Other (see comment). Use Caution/Monitor. Comment: May result in renal function deterioration, particularly with high dose aspirin, in elderly or volume depleted individuals |
| aspirin + enoxaparin | 22 | aspirin, enoxaparin. Either increases toxicity of the other by pharmacodynamic synergism. Use Caution/Monitor. The need for simultaneous use of low-dose aspirin and anticoagulant or antiplatelet agents are common for patients with cardiovascular disease; monitor closely |
| metoprolol + spironolactone | 22 | metoprolol and spironolactone both increase serum potassium. Modify Therapy/Monitor Closely |
| perindopril + torsemide | 22 | perindopril, torsemide. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of acute hypotension, renal insufficiency |
| losartan + spironolactone | 21 | losartan and spironolactone both increase serum potassium. Modify Therapy/Monitor Closely |
| amiodarone + rivaroxaban | 19 | amiodarone increases levels of rivaroxaban by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Use Caution/Monitor. Patients with renal impairment receiving rivaroxaban with drugs that are combined P-gp and weak or moderate CYP3A4 inhibitors may have significant increases in exposure compared with patients with normal renal function and no inhibitor use, since both pathways of rivaroxaban elimination are affected. Since these increases may increase bleeding risk, use rivaroxaban in this situation only if the potential benefit justifies the potential risk |
| aspirin + insulin | 19 | aspirin increases effects of insulin detemir by pharmacodynamic synergism. Modify Therapy/Monitor Closely. Coadministration of insulin with high doses of salicylates (3 g/day or more) may increase risk for hypoglycemia. Insulin dose adjustment and increased frequency of glucose monitoring may be required |
| metformin + torsemide | 19 | torsemide decreases effects of metformin by pharmacodynamic antagonism. Use Caution/Monitor |
| digoxin + furosemide | 18 | digoxin increases and furosemide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| digoxin + metoprolol | 18 | metoprolol increases effects of digoxin by pharmacodynamic synergism. Use Caution/Monitor. Enhanced bradycardia |
| | | metoprolol and digoxin both increase serum potassium. Use Caution/Monitor |
| amlodipine + nitroglycerin | 17 | amlodipine, nitroglycerin sublingual. Either increases toxicity of the other by additive vasodilation. Modify Therapy/Monitor Closely. Marked orthostatic hypotension reported with concomitant use |
| metoprolol + torsemide | 17 | metoprolol increases and torsemide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| atorvastatin + valsartan | 16 | atorvastatin will increase the level or effect of valsartan by Other (see comment). Use Caution/Monitor. The results from an in vitro study with human liver tissue indicate that valsartan is a substrate of the hepatic uptake transporter OATP1B1; coadministration with OATP1B1 inhibitors may increase valsartan systemic exposure |

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|---|---|---|
| bisoprolol + telmisartan | 16 | bisoprolol, telmisartan. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of fetal compromise if given during pregnancy |
| losartan + omeprazole | 16 | omeprazole will increase the level or effect of losartan by affecting hepatic enzyme CYP2C9/10 metabolism. Use Caution/Monitor. May inhibit the conversion of losartan to its active metabolite E-3174. Importance of interaction not established; monitor individual therapeutic response to determine losartan dosage |
| aspirin + rivaroxaban | 15 | aspirin, rivaroxaban. Either increases toxicity of the other by anticoagulation. Use Caution/Monitor. Both drugs have the potential to cause bleeding. The need for simultaneous use of low-dose aspirin (<100 mg/day) with anticoagulants are common for patients with cardiovascular disease, but may result in increased bleeding; monitor closely. Promptly evaluate any signs or symptoms of blood loss if treated concomitantly with low-dose aspirin. Avoid coadministration with chronic use of higher dose aspirin |
| captopril + torsemide | 15 | captopril, torsemide. Either increases toxicity of the other by Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of acute hypotension, renal insufficiency. Monitor blood pressure and renal function |
| clopidogrel + rivaroxaban | 15 | rivaroxaban, clopidogrel. Other (see comment). Use Caution/Monitor. Comment: Avoid concurrent administration of clopidogrel with rivaroxaban unless the benefit outweighs the risk of increased bleeding |
| aspirin + azilsartan | 14 | aspirin, azilsartan. Either increases toxicity of the other by Other (see comment). Use Caution/Monitor. Comment: May result in renal function deterioration, particularly in elderly or volume depleted individuals |
| | | aspirin decreases effects of azilsartan by pharmacodynamic antagonism. Modify Therapy/Monitor Closely. NSAIDs decrease synthesis of vasodilating renal prostaglandins, and thus affect fluid homeostasis and may diminish antihypertensive effect |
| aspirin + fosinopril | 14 | fosinopril, aspirin. Either increases toxicity of the other by Other (see comment). Use Caution/Monitor. Comment: May result in renal function deterioration, particularly with high dose aspirin, in elderly or volume depleted individuals |
| furosemide + torsemide | 14 | furosemide and torsemide both decrease serum potassium. Use Caution/Monitor |
| enalapril + spironolactone | 13 | enalapril, spironolactone. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of hyperkalemia |
| fosinopril + torsemide | 13 | fosinopril, torsemide. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of acute hypotension, renal insufficiency |
| aspirin + candesartan | 12 | aspirin decreases effects of candesartan by pharmacodynamic antagonism. Modify Therapy/Monitor Closely. NSAIDs decrease synthesis of vasodilating renal prostaglandins, and thus affect fluid homeostasis and may diminish antihypertensive effect |
| aspirin + hydrochlorothiazide | 12 | aspirin increases and hydrochlorothiazide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| aspirin + valsartan | 12 | aspirin decreases effects of valsartan by pharmacodynamic antagonism. Modify Therapy/Monitor Closely. NSAIDs decrease synthesis of vasodilating renal prostaglandins, and thus affect fluid homeostasis and may diminish antihypertensive effect |
| atorvastatin + dexamethasone | 12 | atorvastatin will increase the level or effect of dexamethasone by P-glycoprotein (MDR1) efflux transporter. Use Caution/Monitor |

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| enalapril + furosemide | 12 | enalapril, furosemide. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of acute hypotension, renal insufficiency |
| eplerenone + perindopril | 12 | perindopril, eplerenone. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of hyperkalemia |
| lisinopril + metformin | 12 | lisinopril increases toxicity of metformin by unspecified interaction mechanism. Use Caution/Monitor. Increases risk for hypoglycemia and lactic acidosis |
| perindopril + spironolactone | 12 | perindopril, spironolactone. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of hyperkalemia |
| bisoprolol + hydrochlorothiazide | 11 | bisoprolol increases and hydrochlorothiazide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| enoxaparin + spironolactone | 11 | spironolactone, enoxaparin. Either increases toxicity of the other by serum potassium. Use Caution/Monitor. Both drugs may increase serum potassium levels |
| furosemide + metoprolol | 11 | metoprolol increases and furosemide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| rosuvastatin + warfarin | 11 | rosuvastatin increases effects of warfarin by anticoagulation. Use Caution/Monitor |
| amiodarone + metoprolol | 10 | amiodarone will increase the level or effect of metoprolol by affecting hepatic enzyme CYP2D6 metabolism. Use Caution/Monitor. Monitor cardiac function carefully and observe for signs of bradycardia or heart block when amiodarone and a beta adrenergic blocker are coadministered. Amiodarone should be used with caution in patients receiving a beta adrenergic blocker, particularly if there is suspicion of underlying dysfunction of the sinus node, such as bradycardia or sick sinus syndrome, or if there is partial AV block |
| amiodarone + metoprolol | 10 | amiodarone, metoprolol. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of cardiotoxicity with bradycardia |
| amlodipine + metformin | 10 | amlodipine decreases effects of metformin by pharmacodynamic antagonism. Use Caution/Monitor. Patient should be closely observed for loss of blood glucose control; when drugs are withdrawn from a patient receiving metformin, patient should be observed closely for hypoglycemia |
| aspirin + carvedilol | 10 | aspirin decreases effects of carvedilol by pharmacodynamic antagonism. Use Caution/Monitor. Long term (>1 wk) NSAID use. NSAIDs decrease prostaglandin synthesis |
| aspirin + digoxin | 10 | aspirin and digoxin both increase serum potassium. Use Caution/Monitor |
| atorvastatin + digoxin | 10 | atorvastatin will increase the level or effect of digoxin by P-glycoprotein (MDR1) efflux transporter. Use Caution/Monitor |
| bisoprolol + candesartan | 10 | bisoprolol, candesartan. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of fetal compromise if given during pregnancy |
| bisoprolol + potassium | 10 | bisoprolol and potassium chloride both increase serum potassium. Modify Therapy/Monitor Closely |
| digoxin + omeprazole | 10 | omeprazole will increase the level or effect of digoxin by increasing gastric pH. Applies only to oral form of both agents. Avoid or Use Alternate Drug |
| digoxin + omeprazole | 10 | omeprazole increases toxicity of digoxin by Other (see comment). Use Caution/Monitor. Comment: Prolonged use of PPIs may cause hypomagnesemia and increase risk for digoxin toxicity |

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| aspirin + potassium | 9 | aspirin and potassium chloride both increase serum potassium. Modify Therapy/Monitor Closely |
| aspirin + sacubitril/valsartan | 9 | aspirin decreases effects of sacubitril/valsartan by pharmacodynamic antagonism. Modify Therapy/Monitor Closely. NSAIDs decrease synthesis of vasodilating renal prostaglandins, and thus affect fluid homeostasis and may diminish antihypertensive effect |
| atorvastatin + dabigatran | 9 | atorvastatin will increase the level or effect of dabigatran by P-glycoprotein (MDR1) efflux transporter. Use Caution/Monitor. Atrial fibrillation: Avoid coadministering dabigatran with P-gp inhibitors if CrCl <30 mL/min. DVT/PE treatment: Avoid coadministering dabigatran with P-gp inhibitors if CrCl <50 mL/min |
| budesonide + verapamil | 9 | budesonide will decrease the level or effect of verapamil by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Use Caution/Monitor |
| captopril + indapamide | 9 | indapamide, captopril. Either increases effects of the other by pharmacodynamic synergism. Use Caution/Monitor. Both drugs lower blood pressure. Increased risk of nephrotoxicity. Monitor blood pressure and renal function |
| clopidogrel + pantoprazole | 9 | pantoprazole decreases effects of clopidogrel by affecting hepatic enzyme CYP2C19 metabolism. Use Caution/Monitor. Clopidogrel efficacy may be reduced by drugs that inhibit CYP2C19. Inhibition of platelet aggregation by clopidogrel is entirely due to the active clopidogrel metabolite. Clopidogrel is metabolized in part by CYP2C19. Pantoprazole prescribing information state that coadministration with clopidogrel had no clinically important effect on exposure to clopidogrel active metabolite; no dose adjustment of clopidogrel is required |
| enalapril + insulin | 9 | enalapril increases effects of insulin NPH by pharmacodynamic synergism. Use Caution/Monitor. |
| | | enalapril increases effects of insulin detemir by pharmacodynamic synergism. Use Caution/Monitor |
| furosemide + losartan | 9 | losartan increases and furosemide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| furosemide + potassium | 9 | potassium increases and furosemide decreases serum potassium. Effect of interaction is not clear, use caution. Modify Therapy/Monitor Closely |
| acetazolamide + aspirin | 8 | acetazolamide, aspirin. Mechanism: passive renal tubular reabsorption due to increased pH. Use Caution/Monitor. Salicylate levels increased at moderate doses; risk of CNS toxicity. Salicylate levels decreased at large doses (d/t increased renal excretion of unchanged salicylic acid) |
| | | acetazolamide, aspirin. Either increases levels of the other by Other (see comment). Use Caution/Monitor. Comment: Carbonic anhydrase inhibitors (CAIs) and salicylates inhibit each other's renal tubular secretion, resulting in increased plasma levels. CAIs also shift salicylates from plasma to the CNS, leading to potential neurotoxicity |
| amiodarone + warfarin | 8 | amiodarone will increase the level or effect of warfarin by affecting hepatic enzyme CYP2C9/10 metabolism. Modify Therapy/Monitor Closely. Coadministration increases INR by 100% after 3-4 days. Reduce warfarin dose by one-third to one-half and monitor INR |
| apixaban + aspirin | 8 | aspirin and apixaban both increase anticoagulation. Modify Therapy/Monitor Closely. Both drugs have the potential to cause bleeding. The need for simultaneous use of low-dose aspirin (<100 mg/day) with anticoagulants are common for patients with cardiovascular disease, but may result in increased bleeding; monitor closely. Promptly evaluate any signs or symptoms of |

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| | | blood loss if treated concomitantly with low-dose aspiriin. Avoid coadministration with chronic use of higher dose aspirin. In 1 trial (APPRAISE-2), therapy was terminated because of significantly increased bleeding when apixaban was administered with dual antiplatelet therapy (eg, aspirin plus clopidogrel) compared with single antiplatelet treatment |
| aspirin + warfarin | 8 | aspirin increases effects of warfarin by anticoagulation. Modify Therapy/Monitor Closely. Avoid coadministration of chronic high-dose aspirin. Aspirin's antiplatelet properties may increase anticoagulation effect of warfarin. The need for simultaneous use of low-dose aspirin and warfarin is common for patients with cardiovascular disease |
| atorvastatin + nifedipine | 8 | nifedipine will increase the level or effect of atorvastatin by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Use Caution/Monitor |
| | | nifedipine will decrease the level or effect of atorvastatin by P-glycoprotein (MDR1) efflux transporter. Use Caution/Monitor |
| bisoprolol + felodipine | 8 | bisoprolol and felodipine both increase anti-hypertensive channel blocking. Modify Therapy/Monitor Closely |
| bisoprolol + valsartan | 8 | bisoprolol, valsartan. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of fetal compromise if given during pregnancy |
| clopidogrel + heparin | 8 | heparin, clopidogrel. Either increases effects of the other by pharmacodynamic synergism. Modify Therapy/Monitor Closely. Enhanced risk of hemorrhage; additive effects are intended when both drugs are prescribed as indicated for ACS |
| enalapril + metformin | 8 | enalapril increases toxicity of metformin by unspecified interaction mechanism. Use Caution/Monitor. Increases risk for hypoglycemia and lactic acidosis |
| enalapril + torsemide | 8 | enalapril, torsemide. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of acute hypotension, renal insufficiency |
| indapamide + metoprolol | 8 | metoprolol increases and indapamide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| insulin + lisinopril | 8 | lisinopril increases effects of insulin detemir by pharmacodynamic synergism. Use Caution/Monitor |
| insulin + metformin | 8 | metformin, insulin regular human. Either increases effects of the other by pharmacodynamic synergism. Use Caution/Monitor. Antidiabetic agents are often used in combination; dosage adjustments may be required when initiating or discontinuing antidiabetic agents |
| losartan + warfarin | 8 | losartan will increase the level or effect of warfarin by affecting hepatic enzyme CYP2C9/10 metabolism. Use Caution/Monitor |
| amiodarone + metformin | 7 | amiodarone will increase the level or effect of metformin by basic (cationic) drug competition for renal tubular clearance. Use Caution/Monitor |
| aspirin + prednisolone | 7 | aspirin, prednisolone. Either increases toxicity of the other by pharmacodynamic synergism. Use Caution/Monitor. Increased risk of GI ulceration |
| bisoprolol + metoprolol | 7 | bisoprolol and metoprolol both increase serum potassium. Use Caution/Monitor |
| captopril + spironolactone | 7 | captopril, spironolactone. Either increases toxicity of the other by Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Both drugs lower blood pressure. Risk of hyperkalemia. Monitor blood pressure and potassium |

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| clopidogrel + enoxaparin | 7 | enoxaparin, clopidogrel. Either increases effects of the other by pharmacodynamic synergism. Modify Therapy/Monitor Closely. Enhanced risk of hemorrhage; additive effects are intended when both drugs are prescribed as indicated for ACS |
| dexamethasone + enoxaparin | 7 | dexamethasone, enoxaparin. Other (see comment). Use Caution/Monitor. Comment: Corticosteroids may decrease anticoagulant effects by increasing blood coagulability; conversely, they may impair vascular integrity, thus increasing bleeding risk. Monitor INR closely |
| fosinopril + spironolactone | 7 | fosinopril, spironolactone. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of hyperkalemia |
| indapamide + spironolactone | 7 | spironolactone increases and indapamide decreases serum potassium. Effect of interaction is not clear, use caution. Modify Therapy/Monitor Closely |
| indapamide + torsemide | 7 | torsemide and indapamide both decrease serum potassium. Use Caution/Monitor |
| omeprazole + warfarin | 7 | omeprazole will increase the level or effect of warfarin by Other (see comment). Use Caution/Monitor. Warfarin's less potent R-enantiomer is metabolized in part by CYP3A4 (and also CYP1A2 and CYP2C19). Monitor INR more frequently if coadministered with inhibitors of these isoenzymes and adjust warfarin dose if needed |
| amiodarone + dexamethasone | 6 | amiodarone will increase the level or effect of dexamethasone by P-glycoprotein (MDR1) efflux transporter. Use Caution/Monitor |
| amiodarone + nebivolol | 6 | amiodarone will increase the level or effect of nebivolol by affecting hepatic enzyme CYP2D6 metabolism. Use Caution/Monitor. Monitor cardiac function carefully and observe for signs of bradycardia or heart block when amiodarone and a beta adrenergic blocker are coadministered. Amiodarone should be used with caution in patients receiving a beta adrenergic blocker, particularly if there is suspicion of underlying dysfunction of the sinus node, such as bradycardia or sick sinus syndrome, or if there is partial AV block |
| amiodarone + nebivolol | 6 | amiodarone, nebivolol. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of cardiotoxicity with bradycardia |
| aspirin + sotalol | 6 | aspirin decreases effects of sotalol by pharmacodynamic antagonism. Use Caution/Monitor. Long term (>1 wk) NSAID use. NSAIDs decrease prostaglandin synthesis |
| atorvastatin + budesonide | 6 | atorvastatin will increase the level or effect of budesonide by P-glycoprotein (MDR1) efflux transporter. Use Caution/Monitor |
| atorvastatin + ranolazine | 6 | ranolazine will increase the level or effect of atorvastatin by P-glycoprotein (MDR1) efflux transporter. Use Caution/Monitor |
| | | ranolazine increases toxicity of atorvastatin by Other (see comment). Modify Therapy/Monitor Closely. Comment: OATP1B1 inhibitors may increase risk of myopathy |
| atorvastatin + sacubitril/valsartan | 6 | atorvastatin will increase the level or effect of sacubitril/valsartan by Other (see comment). Use Caution/Monitor. The results from an in vitro study with human liver tissue indicate that valsartan is a substrate of the hepatic uptake transporter OATP1B1; coadministration with OATP1B1 inhibitors may increase valsartan systemic exposure |
| bisoprolol + formoterol | 6 | bisoprolol decreases effects of formoterol by pharmacodynamic antagonism. Use Caution/Monitor |
| | | bisoprolol increases and formoterol decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |

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| bisoprolol + meloxicam | 6 | bisoprolol and meloxicam both increase serum potassium. Use Caution/Monitor |
| bisoprolol + sacubitril/valsartan | 6 | bisoprolol, sacubitril/valsartan. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of fetal compromise if given during pregnancy |
| budesonide + omeprazole | 6 | omeprazole decreases effects of budesonide by increasing gastric pH. Applies only to oral form of both agents. Modify Therapy/Monitor Closely. Enteric-coated budesonide dissolves at pH >5.5. Also, dissolution of extended-release budesonide tablets is pH dependent. Coadministration with drugs that increase gastric pH may cause these budesonide products to prematurely dissolve, and possibly affect release properties and absorption of the drug in the duodenum |
| empagliflozin + torsemide | 6 | empagliflozin, torsemide. Either increases effects of the other by pharmacodynamic synergism. Use Caution/Monitor. Coadministration of empagliflozin with diuretics results in increased urine volume and frequency of voids, which might enhance the potential for volume depletion |
| indapamide + losartan | 6 | losartan increases and indapamide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| insulin + losartan | 6 | losartan increases effects of insulin glargine by unspecified interaction mechanism. Use Caution/Monitor. Concomitant use of insulin and ARBs may require insulin dosage adjustment and increased glucose monitoring |
| metformin + perindopril | 6 | perindopril increases toxicity of metformin by unspecified interaction mechanism. Use Caution/Monitor. Increases risk for hypoglycemia and lactic acidosis |
| metoprolol + sacubitril/valsartan | 6 | metoprolol, sacubitril/valsartan. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of fetal compromise if given during pregnancy |
| potassium + torsemide | 6 | potassium chloride increases and torsemide decreases serum potassium. Effect of interaction is not clear, use caution. Modify Therapy/ Monitor Closely |
| amiodarone + captopril | 5 | amiodarone, captopril. Either increases effects of the other by pharmacodynamic synergism. Use Caution/Monitor. Both drugs lower blood pressure. Monitor blood pressure |
| amlodipine + sotalol | 5 | sotalol and amlodipine both increase anti-hypertensive channel blocking. Modify Therapy/Monitor Closely |
| aspirin + chlorthalidone | 5 | aspirin increases and chlorthalidone decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| atorvastatin + prednisolone | 5 | atorvastatin will increase the level or effect of prednisolone by P-glycoprotein (MDR1) efflux transporter. Use Caution/Monitor |
| digoxin + enalapril | 5 | enalapril increases levels of digoxin by unspecified interaction mechanism. Use Caution/Monitor |
| digoxin + potassium | 5 | potassium chloride and digoxin both increase serum potassium. Modify Therapy/Monitor Closely |
| empagliflozin + spironolactone | 5 | empagliflozin, spironolactone. Either increases effects of the other by pharmacodynamic synergism. Use Caution/Monitor. Coadministration of empagliflozin with diuretics results in increased urine volume and frequency of voids, which might enhance the potential for volume depletion |
| enalapril + enoxaparin | 5 | enoxaparin increases toxicity of enalapril by Other (see comment). Use Caution/Monitor. Comment: Low molecular weight heparins may suppress adrenal aldosterone secretion, which can potentially cause hyperkalemia |

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| enoxaparin + losartan | 5 | enoxaparin increases toxicity of losartan by Other (see comment). Use Caution/Monitor. Comment: Low molecular weight heparins may suppress adrenal aldosterone secretion, which can potentially cause hyperkalemia |
| furosemide + lisinopril | 5 | lisinopril, furosemide. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of acute hypotension, renal insufficiency |
| heparin + lisinopril | 5 | heparin increases toxicity of lisinopril by Other (see comment). Use Caution/Monitor. Comment: Low molecular weight heparins may suppress adrenal aldosterone secretion, which can potentially cause hyperkalemia |
| Indapamide + losartan | 5 | losartan increases and indapamide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| insulin+ metformin | 5 | metformin, insulin aspart. Either increases effects of the other by pharmacodynamic synergism. Use Caution/Monitor. Antidiabetic agents are often used in combination; dosage adjustments may be required when initiating or discontinuing antidiabetic agents |
| | | metformin, insulin glargine. Either increases effects of the other by pharmacodynamic synergism. Use Caution/Monitor. Antidiabetic agents are often used in combination; do sage adjustments may be required when initiating or discontinuing antidiabetic agents |
| ipratropium + tiotropium | 5 | ipratropium and tiotropium both decrease cholinergic effects/transmission. Use Caution/Monitor. Due to the poor systemic absorption of ipratropium, interaction unlikely at regularly recommended dosages |
| levofloxacin + prednisolone | 5 | prednisolone and levofloxacin both increase Other (see comment). Use Caution/Monitor. Coadministration of quinolone antibiotics and corticosteroids may increase risk of tendon rupture |
| metoprolol + nifedipine | 5 | metoprolol and nifedipine both increase anti-hypertensive channel blocking. Modify Therapy/Monitor Closely |
| amiodarone + tamsulosin | 4 | amiodarone increases levels of tamsulosin by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Use Caution/Monitor. Dose reduction may be needed for coadministered drugs that are predominantly metabolized by CYP3A |
| | | amiodarone increases levels of tamsulosin by affecting hepatic enzyme CYP2D6 metabolism. Use Caution/Monitor |
| amlodipine + carvedilol | 4 | carvedilol and amlodipine both increase anti-hypertensive channel blocking. Modify Therapy/Monitor Closely |
| amlodipine + nebivolol | 4 | nebivolol, amlodipine. Either increases effects of the other by pharmacodynamic synergism. Use Caution/Monitor. Both drugs lower blood pressure |
| amoxicillin + aspirin | 4 | amoxicillin, aspirin. Either increases levels of the other by plasma protein binding competition. Use Caution/Monitor |
| | | amoxicillin, aspirin. Either increases levels of the other by decreasing renal clearance. Use Caution/Monitor |
| aspirin + dexamethasone | 4 | aspirin, dexamethasone. Either increases toxicity of the other by pharmacodynamic synergism. Use Caution/Monitor. Increased risk of GI ulceration |
| aspirin + diclofenac | 4 | aspirin and diclofenac both increase anticoagulation. Use Caution/Monitor |
| | | aspirin and diclofenac both increase serum potassium. Use Caution/Monitor |

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| aspirin + doxazosin | 4 | aspirin decreases effects of doxazosin by pharmacodynamic antagonism. Use Caution/Monitor. NSAIDs decrease prostaglandin synthesis |
| aspirin + ketorolac | 4 | aspirin and ketorolac both increase anticoagulation. Use Caution/Monitor |
| | | aspirin and ketorolac both increase serum potassium. Use Caution/Monitor |
| aspirin + meloxicam | 4 | aspirin and meloxicam both increase anticoagulation. Use Caution/Monitor |
| | | aspirin and meloxicam both increase serum potassium. Use Caution/Monitor |
| atorvastatin + telmisartan | 4 | telmisartan increases toxicity of atorvastatin by Other (see comment). Use Caution/Monitor. Comment: OATP1B1 inhibitors may increase risk of myopathy |
| atorvastatin + verapamil | 4 | verapamil will increase the level or effect of atorvastatin by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Use Caution/Monitor |
| | | verapamil will increase the level or effect of atorvastatin by P-glycoprotein (MDR1) efflux transporter. Use Caution/Monitor |
| bisoprolol + diclofenac | 4 | bisoprolol and diclofenac both increase serum potassium. Use Caution/Monitor |
| bisoprolol + ketorolac | 4 | bisoprolol and ketorolac both increase serum potassium. Use Caution/Monitor |
| bisoprolol + nifedipine | 4 | bisoprolol, nifedipine. Either decreases effects of the other by pharmacodynamic synergism. Use Caution/Monitor. Both drugs lower blood pressure |
| calcium carbonate + metoprolol | 4 | calcium carbonate decreases effects of metoprolol by unspecified interaction mechanism. Use Caution/Monitor |
| | | calcium carbonate decreases levels of metoprolol by inhibition of GI absorption. Applies only to oral form of both agents. Use Caution/Monitor. Separate by 2 hours |
| candesartan + torsemide | 4 | candesartan increases and torsemide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| carvedilol + losartan | 4 | carvedilol, losartan. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of fetal compromise if given during pregnancy |
| clopidogrel + ticagrelor | 4 | ticagrelor, clopidogrel. Either increases effects of the other by Other (see comment). Use Caution/Monitor. Comment: Increased risk of bleeding during concomitant use of medications that increase potential for bleeding |
| clopidogrel + warfarin | 4 | clopidogrel, warfarin. Either increases effects of the other by pharmacodynamic synergism. Modify Therapy/Monitor Closely. Drugs with antiplatelet properties may increase anticoagulation effect of warfarin |
| dapagliflozin + insulin | 4 | dapagliflozin, insulin aspart. Either increases effects of the other by pharmacodynamic synergism. Use Caution/Monitor. Antidiabetic agents are often used in combination; dosage adjustments may be required when initiating or discontinuing antidiabetic agents |
| | | dapagliflozin, insulin detemir. Either increases effects of the other by pharmacodynamic synergism. Use Caution/Monitor. Antidiabetic agents are often used in combination; dosage adjustments may be required when initiating or discontinuing antidiabetic agents |
| digoxin + perindopril | 4 | perindopril increases levels of digoxin by unspecified interaction mechanism. Use Caution/Monitor |
| enalapril + potassium | 4 | enalapril increases levels of potassium chloride by decreasing elimination. Use Caution/Monitor. Risk of hyperkalemia |
| eplerenone + fosinopril | 4 | fosinopril, eplerenone. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of hyperkalemia |

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| eplerenone + losartan | 4 | losartan, eplerenone. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of hyperkalemia |
| eplerenone + sacubitril/valsartan | 4 | sacubitril/valsartan, eplerenone. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of hyperkalemia |
| formoterol + furosemide | 4 | formoterol and furosemide both decrease serum potassium. Use Caution/Monitor |
| ivabradine + metoprolol | 4 | ivabradine, metoprolol. Either increases effects of the other by pharmacodynamic synergism. Modify Therapy/Monitor Closely. Most patients receiving ivabradine will also be treated with a beta-blocker. The risk of bradycardia increases with coadministration of drugs that slow heart rate (eg, digoxin, amiodarone, beta-blockers). Monitor heart rate in patients taking ivabradine with other negative chronotropes |
| losartan + nebivolol | 4 | losartan and nebivolol both increase serum potassium. Use Caution/Monitor |
| losartan + sotalol | 4 | losartan and sotalol both increase serum potassium. Use Caution/Monitor |
| metoprolol + valsartan | 4 | metoprolol, valsartan. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of fetal compromise if given during pregnancy |
| sacubitril/valsartan + sotalol | 4 | sacubitril/valsartan and sotalol both increase serum potassium. Use Caution/Monitor |
| sacubitril/valsartan + torsemide | 4 | sacubitril/valsartan increases and torsemide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| sotalol + telmisartan | 4 | sotalol, telmisartan. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of fetal compromise if given during pregnancy |
| amiodarone + carvedilol | 3 | amiodarone will increase the level or effect of carvedilol by affecting hepatic enzyme CYP2C9/10 metabolism. Use Caution/Monitor |
| | | amiodarone will increase the level or effect of carvedilol by affecting hepatic enzyme CYP2D6 metabolism. Use Caution/Monitor. Monitor for signs of bradycardia or heart block when amiodarone and a beta adrenergic blocker are coadministered. Amiodarone should be used with caution in patients receiving a beta adrenergic blocker, particularly if there is suspicion of underlying dysfunction of the sinus node, such as bradycardia or sick sinus syndrome, or if there is partial AV block |
| | | amiodarone, carvedilol. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of cardiotoxicity with bradycardia |
| amiodarone + dabigatran | 3 | amiodarone will increase the level or effect of dabigatran by P-glycoprotein (MDR1) efflux transporter. Use Caution/Monitor. Atrial fibrillation: Avoid coadministering dabigatran with P-gp inhibitors if CrCl <30 mL/min. DVT/PE treatment: Avoid coadministering dabigatran with P-gp inhibitors if CrCl <50 mL/min |
| aspirin + dabigatran | 3 | dabigatran and aspirin both increase anticoagulation. Modify Therapy/Monitor Closely. Both drugs have the potential to cause bleeding. The need for simultaneous use of low-dose aspirin (<100 mg/day) with anticoagulants are common for patients with cardiovascular disease, but may result in increased bleeding; monitor closely. Promptly evaluate any signs or symptoms of blood loss if treated concomitantly with low-dose aspirin. Avoid coadministration with chronic use of higher dose aspirin |
| aspirin + formoterol | 3 | aspirin increases and formoterol decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |

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| aspirin + olmesartan | 3 | aspirin decreases effects of olmesartan by pharmacodynamic antagonism. Modify Therapy/Monitor Closely. NSAIDs decrease synthesis of vasodilating renal prostaglandins, and thus affect fluid homeostasis and may diminish antihypertensive effect |
| bisoprolol + sodium bicarbonate | 3 | sodium bicarbonate decreases levels of bisoprolol by inhibition of GI absorption. Applies only to oral form of both agents. Use Caution/Monitor. Separate by 2 hours |
| budesonide + dexamethasone | 3 | budesonide will decrease the level or effect of dexamethasone by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Use Caution/Monitor |
| captopril + chlorthalidone | 3 | captopril, chlorthalidone. Either increases toxicity of the other by pharmacodynamic synergism. Use Caution/ Monitor. Both drugs lower blood pressure. Increased risk of nephrotoxicity. Monitor blood pressure and renal function |
| captopril + furosemide | 3 | captopril, furosemide. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of acute hypotension, renal insufficiency |
| carvedilol + torsemide | 3 | carvedilol increases and torsemide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| clopidogrel + felodipine | 3 | felodipine decreases effects of clopidogrel by decreasing metabolism. Use Caution/Monitor. Cytochrome P450 2C19 inhibitors decrease the conversion of clopidogrel to its active form |
| dexamethasone + heparin | 3 | dexamethasone, heparin. Other (see comment). Use Caution/Monitor. Comment: Corticosteroids may decrease anticoagulant effects by increasing blood coagulability; conversely, they may impair vascular integrity, thus increasing bleeding risk. Monitor INR closely |
| dexamethasone + verapamil | 3 | dexamethasone will decrease the level or effect of verapamil by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Use Caution/Monitor |
| digoxin + losartan | 3 | losartan and digoxin both increase serum potassium. Use Caution/Monitor |
| digoxin + metformin | 3 | digoxin, metformin. Either increases levels of the other by basic (cationic) drug competition for renal tubular clearance. Use Caution/Monitor. Measure serum digoxin concentrations before initiating metformin. Monitor patients who take both metformin and digoxin for possible digoxin toxicity and lactic acidosis. Reduce the digoxin and/or metformin dose as necessary |
| empagliflozin + insulin | 3 | empagliflozin, insulin aspart. Either increases effects of the other by pharmacodynamic synergism. Modify Therapy/Monitor Closely. Consider a lower dose of insulin or insulin secretagogue to avoid hypoglycemia when coadministered with SGLT2 inhibitors |
| enoxaparin + fosinopril | 3 | enoxaparin increases toxicity of fosinopril by Other (see comment). Use Caution/Monitor. Comment: Low molecular weight heparins may suppress adrenal aldosterone secretion, which can potentially cause hyperkalemia |
| enoxaparin + lisinopril | 3 | enoxaparin increases toxicity of lisinopril by Other (see comment). Use Caution/Monitor. Comment: Low molecular weight heparins may suppress adrenal aldosterone secretion, which can potentially cause hyperkalemia |
| enoxaparin + rivaroxaban | 3 | rivaroxaban, enoxaparin. Either increases effects of the other by anticoagulation. Use Caution/Monitor. Avoid concurrent use of rivaroxaban with other anticoagulants due to increased bleeding risk other than during therapeutic transition periods where patients should be observed closely. Monitor for signs/symptoms of blood loss |
| eplerenone + losartan | 3 | losartan, eplerenone. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of hyperkalemia |

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| ferrous sulfate + omeprazole | 3 | omeprazole will decrease the level or effect of ferrous sulfate by increasing gastric pH. Applies only to oral form of both agents. Use Caution/Monitor |
| formoterol + spironolactone | 3 | spironolactone increases and formoterol decreases serum potassium. Effect of interaction is not clear, use caution. Modify Therapy/Monitor Closely |
| fosinopril + metformin | 3 | fosinopril increases toxicity of metformin by unspecified interaction mechanism. Use Caution/Monitor. Increases risk for hypoglycemia and lactic acidosis |
| furosemide + perindopril | 3 | perindopril, furosemide. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of acute hypotension, renal insufficiency |
| heparin + rivaroxaban | 3 | rivaroxaban, heparin. Either increases effects of the other by anticoagulation. Use Caution/Monitor. Avoid concurrent use of rivaroxaban with other anticoagulants due to increased bleeding risk other than during therapeutic transition periods where patients should be observed closely. Monitor for signs/symptoms of blood loss |
| heparin + spironolactone | 3 | spironolactone, heparin. Either increases toxicity of the other by serum potassium. Use Caution/Monitor. Both drugs may increase serum potassium levels |
| heparin + ticagrelor | 3 | ticagrelor, heparin. Either increases effects of the other by anticoagulation. Use Caution/Monitor. Increased risk of bleeding during concomitant use of medications that increase potential for bleeding |
| ibuprofen + losartan | 3 | ibuprofen decreases effects of losartan by pharmacodynamic antagonism. Modify Therapy/Monitor Closely. NSAIDs decrease synthesis of vasodilating renal prostaglandins, and thus affect fluid homeostasis and may diminish antihypertensive effect |
| indomethacin + losartan | 3 | indomethacin decreases effects of losartan by pharmacodynamic antagonism. Modify Therapy/Monitor Closely. NSAIDs decrease synthesis of vasodilating renal prostaglandins, and thus affect fluid homeostasis and may diminish antihypertensive effect |
| ketorolac + lisinopril | 3 | ketorolac, lisinopril. pharmacodynamic antagonism. Avoid or Use Alternate Drug. Coadministration may result in a significant decrease in renal function. NSAIDs may diminish the antihypertensive effect of ACE inhibitors. The mechanism of these interactions is likely related to the ability of NSAIDs to reduce the synthesis of vasodilating renal prostaglandins |
| lisinopril + potassium | 3 | lisinopril increases levels of potassium chloride by decreasing elimination. Use Caution/Monitor. Risk of hyperkalemia |
| losartan + potassium | 3 | losartan and potassium chloride both increase serum potassium. Use Caution/Monitor |
| metoprolol + potassium | 3 | metoprolol and potassium acid phosphate both increase serum potassium. Modify Therapy/Monitor Closely |
| sacubitril/valsartan + spironolactone | 3 | sacubitril/valsartan and spironolactone both increase serum potassium. Modify Therapy/Monitor Closely |
| sotalol + torsemide | 3 | sotalol increases and torsemide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| torsemide + valsartan | 3 | valsartan increases and torsemide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| aceclofenac + aspirin | 2 | aceclofenac and aspirin both increase anticoagulation. Use Caution/Monitor |
| | | aceclofenac and aspirin both increase serum potassium. Use Caution/Monitor |
| aceclofenac + bisoprolol | 2 | aceclofenac decreases effects of bisoprolol by pharmacodynamic antagonism. Use Caution/Monitor. Long term (>1 wk) NSAID use. NSAIDs decrease prostaglandin synthesis |

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| amiodarone + budesonide | 2 | amiodarone will increase the level or effect of budesonide by P-glycoprotein (MDR1) efflux transporter. Use Caution/Monitor |
| amiodarone + hydrochlorothiazide | 2 | amiodarone will increase the level or effect of hydrochlorothiazide by basic (cationic) drug competition for renal tubular clearance. Use Caution/Monitor |
| amitriptyline + tramadol | 2 | amitriptyline and tramadol both increase serotonin levels. Modify Therapy/Monitor Closely |
| ampicillin + spironolactone | 2 | ampicillin increases effects of spironolactone by unspecified interaction mechanism. Use Caution/Monitor. Hyperkalemia |
| aspirin + betaxolol | 2 | aspirin decreases effects of betaxolol by pharmacodynamic antagonism. Use Caution/Monitor. Long term (>1 wk) NSAID use. NSAIDs decrease prostaglandin synthesis |
| aspirin + ibuprofen | 2 | aspirin and ibuprofen both increase anticoagulation. Use Caution/ Monitor |
| | | aspirin and ibuprofen both increase serum potassium. Use Caution/ Monitor |
| aspirin + ketoprofen | 2 | aspirin and ketoprofen both increase serum potassium. Use Caution/Monitor |
| | | aspirin and ketoprofen both increase anticoagulation. Use Caution/Monitor |
| aspirin + nebivolol | 2 | aspirin decreases effects of nebivolol by pharmacodynamic antagonism. Use Caution/Monitor. Long term (>1 wk) NSAID use. NSAIDs decrease prostaglandin synthesis |
| aspirin + prasugrel | 2 | aspirin, prasugrel. Either increases toxicity of the other by pharmacodynamic synergism. Use Caution/Monitor. The need for simultaneous use of low-dose aspirin and anticoagulant or antiplatelet agents are common for patients with cardiovascular disease; monitor closely |
| aspirin + ramipril | 2 | aspirin, ramipril. pharmacodynamic antagonism. Avoid or Use Alternate Drug. Coadministration may result in a significant decrease in renal function. NSAIDs may diminish the antihypertensive effect of ACE inhibitors. The mechanism of these interactions is likely related to the ability of NSAIDs to reduce the synthesis of vasodilating renal prostaglandins |
| aspirin + timolol | 2 | timolol and aspirin both increase serum potassium. Use Caution/ Monitor |
| atorvastatin + fluconazole | 2 | fluconazole will increase the level or effect of atorvastatin by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Use Caution/Monitor |
| azilsartan + meloxicam | 2 | meloxicam, azilsartan. Either increases toxicity of the other by Other (see comment). Use Caution/Monitor. Comment: May result in renal function deterioration, particularly in elderly or volume depleted individuals |
| | | meloxicam decreases effects of azilsartan by pharmacodynamic antagonism. Modify Therapy/Monitor Closely. NSAIDs decrease synthesis of vasodilating renal prostaglandins, and thus affect fluid homeostasis and may diminish antihypertensive effect |
| betaxolol + olmesartan | 2 | betaxolol, olmesartan. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of fetal compromise if given during pregnancy |
| bisoprolol + calcium carbonate | 2 | calcium carbonate decreases effects of bisoprolol by unspecified interaction mechanism. Use Caution/Monitor |
| | | calcium carbonate decreases levels of bisoprolol by inhibition of GI absorption. Applies only to oral form of both agents. Use Caution/Monitor. Separate by 2 hours |
| bisoprolol + chlorthalidone | 2 | bisoprolol increases and chlorthalidone decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| bisoprolol + ibuprofen | 2 | bisoprolol and ibuprofen both increase serum potassium. Use Caution/Monitor |
| bisoprolol + ketoprofen | 2 | bisoprolol and ketoprofen both increase serum potassium. Use Caution/Monitor |
| bisoprolol + lornoxicam | 2 | bisoprolol and lornoxicam both increase serum potassium. Use Caution/Monitor |

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| calcium carbonate + nifedipine | 2 | calcium carbonate decreases effects of nifedipine by pharmacodynamic antagonism. Use Caution/Monitor |
| canagliflozin + glimepiride | 2 | glimepiride, canagliflozin. Either increases effects of the other by pharmacodynamic synergism. Modify Therapy/Monitor Closely. Consider a lower dose of insulin or insulin secretagogue to avoid hypoglycemia when coadministered with canagliflozin |
| canagliflozin + lisinopril | 2 | lisinopril and canagliflozin both increase serum potassium. Use Caution/Monitor |
| canagliflozin + spironolactone | 2 | spironolactone and canagliflozin both increase serum potassium. Use Caution/Monitor |
| captopril + eplerenone | 2 | captopril, eplerenone. Either increases toxicity of the other by Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of hyperkalemia. Monitor potassium |
| captopril + potassium | 2 | captopril increases levels of potassium chloride by decreasing elimination. Use Caution/Monitor. Risk of hyperkalemia |
| | | potassium chloride increases toxicity of captopril by Mechanism: unspecified interaction mechanism. Modify Therapy/Monitor Closely. Both drugs increase potassium. Monitor potassium |
| carbamazepine + enalapril | 2 | enalapril increases levels of carbamazepine by decreasing metabolism. Use Caution/Monitor |
| carbamazepine + omeprazole | 2 | carbamazepine will decrease the level or effect of omeprazole by affecting hepatic enzyme CYP2C19 metabolism. Avoid or Use Alternate Drug |
| | | carbamazepine will decrease the level or effect of omeprazole by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Use Caution/Monitor |
| carvedilol + spironolactone | 2 | carvedilol and spironolactone both increase serum potassium. Modify Therapy/Monitor Closely |
| cefotaxime + warfarin | 2 | cefotaxime increases effects of warfarin by unspecified interaction mechanism. Use Caution/Monitor |
| celecoxib + meloxicam | 2 | celecoxib and meloxicam both increase anticoagulation. Use Caution/Monitor |
| | | celecoxib and meloxicam both increase serum potassium. Use Caution/Monitor |
| chlorthalidone + metoprolol | 2 | metoprolol increases and chlorthalidone decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| clopidogrel + dexamethasone | 2 | dexamethasone will increase the level or effect of clopidogrel by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Use Caution/Monitor. CYP3A4 inducers may increase the metabolism of clopidogrel to its active metabolite. Monitor patients for potential increase in antiplatelet effects when CYP3A4 inducers are used in combination with clopidogrel |
| dabigatran + clopidogrel | 2 | dabigatran, clopidogrel. Either increases effects of the other by pharmacodynamic synergism. Use Caution/Monitor. Both drugs have the potential to cause bleeding. Concomitant use may increase risk of bleeding |
| dabigatran + rivaroxaban | 2 | rivaroxaban, dabigatran. Either increases effects of the other by anticoagulation. Use Caution/Monitor. Avoid concurrent use of rivaroxaban with other anticoagulants due to increased bleeding risk other than during therapeutic transition periods where patients should be observed closely. Monitor for signs/symptoms of blood loss |
| dexamethasone + metronidazole | 2 | metronidazole will increase the level or effect of dexamethasone by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Use Caution/Monitor |

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| diclofenac + enalapril | 2 | enalapril, diclofenac. Either increases toxicity of the other by Other (see comment). Use Caution/Monitor. Comment: May result in renal function deterioration, particularly in elderly or volume depleted individuals |
| diclofenac + ketoprofen | 2 | diclofenac and ketoprofen both increase anticoagulation. Use Caution/Monitor |
| | | diclofenac and ketoprofen both increase serum potassium. Use Caution/Monitor |
| | | diclofenac will increase the level or effect of ketoprofen by acidic (anionic) drug competition for renal tubular clearance. Minor/Significance Unknown |
| diclofenac + ketorolac | 2 | diclofenac, ketorolac. Either increases toxicity of the other by pharmacodynamic synergism. Contraindicated |
| | | diclofenac and ketorolac both increase anticoagulation. Use Caution/Monitor |
| | | diclofenac and ketorolac both increase serum potassium. Use Caution/Monitor |
| diclofenac + lornoxicam | 2 | diclofenac and lornoxicam both increase anticoagulation. Use Caution/Monitor |
| | | diclofenac and lornoxicam both increase serum potassium. Use Caution/Monitor |
| diclofenac + meloxicam | 2 | diclofenac and meloxicam both increase anticoagulation. Use Caution/Monitor |
| | | diclofenac and meloxicam both increase serum potassium. Use Caution/Monitor |
| diclofenac + sotalol | 2 | diclofenac decreases effects of sotalol by pharmacodynamic antagonism. Use Caution/Monitor. Long term (>1 wk) NSAID use. NSAIDs decrease prostaglandin synthesis |
| digoxin + hydrochlorothiazide | 2 | digoxin will increase the level or effect of hydrochlorothiazide by basic (cationic) drug competition for renal tubular clearance. Use Caution/Monitor |
| digoxin + hydrochlorothiazide | 2 | digoxin increases and hydrochlorothiazide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| digoxin + indapamide | 2 | digoxin increases and indapamide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| digoxin + lisinopril | 2 | lisinopril increases levels of digoxin by unspecified interaction mechanism. Use Caution/Monitor |
| doxazosin + metoprolol | 2 | doxazosin and metoprolol both increase anti-hypertensive channel blocking. Modify Therapy/Monitor Closely |
| doxazosin + nifedipine | 2 | doxazosin and nifedipine both increase anti-hypertensive channel blocking. Use Caution/Monitor |
| empagliflozin + glimepiride | 2 | empagliflozin, glimepiride. Either increases effects of the other by pharmacodynamic synergism. Modify Therapy/Monitor Closely. Consider a lower dose of insulin or insulin secretagogue to avoid hypoglycemia when coadministered with SGLT2 inhibitors |
| enalapril + heparin | 2 | heparin increases toxicity of enalapril by Other (see comment). Use Caution/Monitor. Comment: Low molecular weight heparins may suppress adrenal aldosterone secretion, which can potentially cause hyperkalemia |
| enoxaparin + ketorolac | 2 | enoxaparin and ketorolac both increase anticoagulation. Modify Therapy/Monitor Closely |
| felodipine + metformin | 2 | felodipine decreases effects of metformin by pharmacodynamic antagonism. Use Caution/Monitor. Patient should be closely observed for loss of blood glucose control; when drugs are withdrawn from a patient receiving metformin, patient should be observed closely for hypoglycemia |

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| felodipine + nitroglycerin | 2 | felodipine, nitroglycerin sublingual. Either increases toxicity of the other by additive vasodilation. Modify Therapy/Monitor Closely. Marked orthostatic hypotension reported with concomitant use |
| fluconazole + omeprazole | 2 | fluconazole will increase the level or effect of omeprazole by affecting hepatic enzyme CYP2C19 metabolism. Use Caution/Monitor |
| fluconazole + sulfamethoxazole | 2 | fluconazole will increase the level or effect of sulfamethoxazole by affecting hepatic enzyme CYP2C9/10 metabolism. Minor/Significance Unknown |
| fluconazole + trimethoprim | 2 | fluconazole and trimethoprim both increase QTc interval. Modify Therapy/Monitor Closely |
| furosemide + sacubitril/valsartan | 2 | sacubitril/valsartan increases and furosemide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| glimepiride + lisinopril | 2 | lisinopril increases effects of glimepiride by pharmacodynamic synergism. Use Caution/Monitor |
| heparin + losartan | 2 | heparin increases toxicity of losartan by Other (see comment). Use Caution/Monitor. Comment: Low molecular weight heparins may suppress adrenal aldosterone secretion, which can potentially cause hyperkalemia |
| heparin + prednisolone | 2 | prednisolone, heparin. Other (see comment). Use Caution/Monitor. Comment: Corticosteroids may decrease anticoagulant effects by increasing blood coagulability; conversely, they may impair vascular integrity, thus increasing bleeding risk. Monitor INR closely |
| hydrochlorothiazide + metoprolol | 2 | hydrochlorothiazide, metoprolol. Either increases toxicity of the other by Other (see comment). Modify Therapy/Monitor Closely. Comment: May cause idiosyncratic reaction, resulting in acute transient myopia and acute angle-closure glaucoma, which can lead to permanent vision loss |
| hydrochlorothiazide + telmisartan | 2 | telmisartan increases and hydrochlorothiazide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| hydrochlorothiazide + torsemide | 2 | torsemide and hydrochlorothiazide both decrease serum potassium. Use Caution/Monitor |
| indapamide + potassium | 2 | potassium chloride increases and indapamide decreases serum potassium. Effect of interaction is not clear, use caution. Modify Therapy/Monitor Closely |
| indapamide + sotalol | 2 | sotalol increases and indapamide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| insulin + levofloxacin | 2 | levofloxacin increases effects of insulin detemir by pharmacodynamic synergism. Use Caution/Monitor. Quinolone antibiotic administration may result in hyper- or hypoglycemia. Gatifloxacin is most likely to produce dysglycemia; moxifloxacin is least likely |
| ivabradine + bisoprolol | 2 | ivabradine, bisoprolol. Either increases effects of the other by pharmacodynamic synergism. Modify Therapy/Monitor Closely. Most patients receiving ivabradine will also be treated with a beta-blocker. The risk of bradycardia increases with coadministration of drugs that slow heart rate (eg, digoxin, amiodarone, beta-blockers). Monitor heart rate in patients taking ivabradine with other negative chronotropes |
| ketoprofen + meloxicam | 2 | ketoprofen and meloxicam both increase anticoagulation. Use Caution/Monitor |
| | | ketoprofen and meloxicam both increase serum potassium. Use Caution/Monitor |
| ketoprofen + sotalol | 2 | ketoprofen decreases effects of sotalol by pharmacodynamic antagonism. Use Caution/Monitor. Long term (>1 wk) NSAID use. NSAIDs decrease prostaglandin synthesis |

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| ketorolac + meloxicam | 2 | ketorolac and meloxicam both increase anticoagulation. Use Caution/Monitor |
| | | ketorolac and meloxicam both increase serum potassium. Use Caution/Monitor |
| ketorolac + nebivolol | 2 | ketorolac decreases effects of nebivolol by pharmacodynamic antagonism. Use Caution/Monitor. Long term (>1 wk) NSAID use. NSAIDs decrease prostaglandin synthesis |
| levothyroxine + metformin | 2 | levothyroxine decreases effects of metformin by pharmacodynamic antagonism. Use Caution/Monitor. Patient should be closely observed for loss of blood glucose control; when drugs are withdrawn from a patient receiving metformin, patient should be observed closely for hypoglycemia |
| meloxicam + sotalol | 2 | meloxicam decreases effects of sotalol by pharmacodynamic antagonism. Use Caution/Monitor. Long term (>1 wk) NSAID use. NSAIDs decrease prostaglandin synthesis |
| metoprolol + ranolazine | 2 | ranolazine will increase the level or effect of metoprolol by affecting hepatic enzyme CYP2D6 metabolism. Use Caution/Monitor |
| metoprolol + telmisartan | 2 | metoprolol, telmisartan. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of fetal compromise if given during pregnancy |
| nifedipine + nitroglycerin | 2 | nifedipine, nitroglycerin sublingual. Either increases toxicity of the other by additive vasodilation. Modify Therapy/ Monitor Closely. Marked orthostatic hypotension reported with concomitant use |
| perindopril + potassium | 2 | perindopril increases levels of potassium chloride by decreasing elimination. Use Caution/Monitor. Risk of hyperkalemia |
| phenylephrine + xylometazoline | 2 | phenylephrine and xylometazoline both decrease sedation. Use Caution/Monitor |
| | | phenylephrine and xylometazoline both increase sympathetic (adrenergic) effects, including increased blood pressure and heart rate. Use Caution/Monitor |
| sotalol + valsartan | 2 | sotalol, valsartan. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of fetal compromise if given during pregnancy |
| spironolactone + valsartan | 2 | valsartan and spironolactone both increase serum potassium. Modify Therapy/Monitor Closely |
| telmisartan + torsemide | 2 | telmisartan increases and torsemide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| aceclofenac + indapamide | 1 | aceclofenac increases and indapamide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| allopurinol + calcium carbonate | 1 | calcium carbonate decreases levels of allopurinol by inhibition of GI absorption. Applies only to oral form of both agents. Use Caution/Monitor. Separate by 2 hours |
| amikacin + digoxin | 1 | amikacin will increase the level or effect of digoxin by altering intestinal flora. Applies only to oral form of both agents. Use Caution/Monitor |
| amikacin + vancomycin | 1 | amikacin and vancomycin both increase nephrotoxicity and/or ototoxicity. Use Caution/Monitor |
| amiodarone + atenolol | 1 | amiodarone, atenolol. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of cardiotoxicity with bradycardia |
| amiodarone + metronidazole | 1 | metronidazole will increase the level or effect of amiodarone by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Use Caution/Monitor |
| amitriptyline + atorvastatin | 1 | atorvastatin will increase the level or effect of amitriptyline by P-glycoprotein (MDR1) efflux transporter. Use Caution/Monitor |

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| amitriptyline + carbamazepine | 1 | carbamazepine will decrease the level or effect of amitriptyline by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Use Caution/Monitor |
| amitriptyline + gabapentin | 1 | gabapentin, amitriptyline. Either increases effects of the other by pharmacodynamic synergism. Modify Therapy/Monitor Closely. Coadministration of CNS depressants can result in serious, life-threatening, and fatal respiratory depression. Use lowest dose possible and monitor for respiratory depression and sedation |
| amlodipine + betaxolol | 1 | betaxolol, amlodipine. Either increases effects of the other by pharmacodynamic synergism. Use Caution/Monitor. Both drugs lower blood pressure |
| amlodipine + clarithromycin | 1 | clarithromycin will increase the level or effect of amlodipine by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Use Caution/Monitor. Increased effect of calcium channel blockers may lead to hypotension, edema, decreased HR, and acute kidney injury due to reduced renal blood flow |
| amlodipine + doxazosin | 1 | doxazosin and amlodipine both increase anti-hypertensive channel blocking. Use Caution/Monitor |
| amlodipine + magnesium supplement | 1 | magnesium supplement, amlodipine. Either increases toxicity of the other by pharmacodynamic synergism. Use Caution/Monitor. Calcium channel blockers may increase toxic effects of magnesium; magnesium may increase hypotensive effects of calcium channel blockers |
| ampicillin + aspirin | 1 | ampicillin, aspirin. Either increases levels of the other by plasma protein binding competition. Use Caution/Monitor |
| ampicillin + omeprazole | 1 | omeprazole will decrease the level or effect of ampicillin by increasing gastric pH. Applies only to oral form of both agents. Use Caution/Monitor |
| aspirin + escitalopram | 1 | escitalopram, aspirin. Either increases toxicity of the other by pharmacodynamic synergism. Use Caution/Monitor. Increased risk of upper GI bleeding. SSRIs inhib. serotonin uptake by platelets |
| aspirin + fondaparinux | 1 | fondaparinux and aspirin both increase anticoagulation. Modify Therapy/Monitor Closely |
| atenolol + chlorthalidone | 1 | atenolol increases and chlorthalidone decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| atorvastatin + metronidazole | 1 | metronidazole will increase the level or effect of atorvastatin by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Use Caution/Monitor |
| azithromycin + atorvastatin | 1 | azithromycin will increase the level or effect of atorvastatin by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Use Caution/Monitor. If this combination is used, closely monitor for evidence of atorvastatin toxicity (eg, muscle aches or pains, renal dysfunction) |
| azithromycin + sodium bicarbonate | 1 | sodium bicarbonate decreases levels of azithromycin by inhibition of GI absorption. Applies only to oral form of both agents. Use Caution/Monitor. Separate by 2 hours |
| azithromycin + warfarin | 1 | azithromycin increases toxicity of warfarin by anticoagulation. Use Caution/Monitor. Postmarketing reports have suggested that concomitant administration of azithromycin may potentiate effects of oral warfarin but the interaction does not appear to alter prothrombin time |
| bisoprolol + doxazosin | 1 | doxazosin and bisoprolol both increase anti-hypertensive channel blocking. Modify Therapy/ Monitor Closely |
| bisoprolol + insulin | 1 | bisoprolol, insulin degludec. Other (see comment). Modify Therapy/Monitor Closely. Comment: Beta-blockers may either increase or decrease the blood glucose lowering effect of insulin; beta-blockers can prolong hypoglycemia (interference with glycogenolysis) or cause hyperglycemia (insulin secretion inhibited) |

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| bisoprolol + nebivolol | 1 | bisoprolol and nebivolol both increase anti-hypertensive channel blocking. Avoid or Use Alternate Drug |
| bisoprolol + timolol | 1 | bisoprolol and timolol both increase serum potassium. Use Caution/ Monitor |
| bisoprolol + verapamil | 1 | bisoprolol and verapamil both increase anti-hypertensive channel blocking. Modify Therapy/Monitor Closely |
| budesonide + clarithromycin | 1 | clarithromycin will increase the level or effect of budesonide by P-glycoprotein (MDR1) efflux transporter. Use Caution/ Monitor |
| budesonide + clopidogrel | 1 | budesonide will increase the level or effect of clopidogrel by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Use Caution/Monitor. CYP3A4 inducers may increase the metabolism of clopidogrel to its active metabolite. Monitor patients for potential increase in antiplatelet effects when CYP3A4 inducers are used in combination with clopidogrel |
| budesonide + enoxaparin | 1 | budesonide, enoxaparin. Other (see comment). Use Caution/Monitor. Comment: Corticosteroids may decrease anticoagulant effects by increasing blood coagulability; conversely, they may impair vascular integrity, thus increasing bleeding risk. Monitor INR closely |
| budesonide + esomeprazole | 1 | esomeprazole decreases effects of budesonide by increasing gastric pH. Applies only to oral form of both agents. Modify Therapy/Monitor Closely. Enteric-coated budesonide dissolves at pH >5.5. Also, dissolution of extended-release budesonide tablets is pH dependent. Coadministration with drugs that increase gastric pH may cause these budesonide products to prematurely dissolve, and possibly affect release properties and absorption of the drug in the duodenum |
| budesonide + heparin | 1 | budesonide, heparin. Other (see comment). Use Caution/Monitor. Comment: Corticosteroids may decrease anticoagulant effects by increasing blood coagulability; conversely, they may impair vascular integrity, thus increasing bleeding risk. Monitor INR closely |
| budesonide + ketorolac | 1 | ketorolac, budesonide. Either increases toxicity of the other by pharmacodynamic synergism. Use Caution/Monitor. Increased risk of GI ulceration |
| budesonide + theophylline | 1 | budesonide will decrease the level or effect of theophylline by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Use Caution/Monitor |
| calcium carbonate + captopril | 1 | calcium carbonate decreases effects of captopril by unspecified interaction mechanism. Use Caution/Monitor. Calcium carbonate may decrease absorption of captopril |
| calcium carbonate + celecoxib | 1 | calcium carbonate decreases levels of celecoxib by inhibition of GI absorption. Applies only to oral form of both agents. Use Caution/Monitor. Separate by 2 hours |
| calcium carbonate + levothyroxine | 1 | calcium carbonate decreases levels of levothyroxine by inhibition of GI absorption. Applies only to oral form of both agents. Use Caution/Monitor. Separate administration by 4 hours |
| calcium carbonate + ramipril | 1 | calcium carbonate decreases effects of ramipril by unspecified interaction mechanism. Use Caution/Monitor |
| calcium carbonate + rosuvastatin | 1 | calcium carbonate decreases levels of rosuvastatin by inhibition of GI absorption. Applies only to oral form of both agents. Use Caution/Monitor. Separate by 2 hours |
| calcium carbonate + vitamin D | 1 | vitamin D, calcium carbonate. Other (see comment). Use Caution/Monitor. Comment: The concurrent use of vitamin D with calcium salts is generally beneficial; in some patients this combination may result in hypercalcemia |
| calcium gluconate + levothyroxine | 1 | calcium gluconate decreases levels of levothyroxine by inhibition of GI absorption. Applies only to oral form of both agents. Use Caution/Monitor. Separate administration by 4 hours |

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| candesartan + eplerenone | 1 | candesartan, eplerenone. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of hyperkalemia |
| candesartan + indapamide | 1 | candesartan increases and indapamide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| candesartan + insulin | 1 | candesartan increases effects of insulin detemir by unspecified interaction mechanism. Use Caution/Monitor. Concomitant use of insulin and ARBs may require insulin dosage adjustment and increased glucose monitoring |
| candesartan + spironolactone | 1 | candesartan and spironolactone both increase serum potassium. Modify Therapy/Monitor Closely |
| captopril + diclofenac | 1 | captopril, diclofenac. Either increases toxicity of the other by Other (see comment). Use Caution/Monitor. Comment: May result in renal function deterioration, particularly in elderly or volume depleted individuals |
| captopril + isosorbide dinitrate | 1 | isosorbide dinitrate, captopril. Either increases effects of the other by pharmacodynamic synergism. Use Caution/Monitor. Both drugs lower blood pressure. Monitor blood pressure |
| captopril + ketoprofen | 1 | captopril, ketoprofen. Either increases toxicity of the other by Other (see comment). Use Caution/Monitor. Comment: May result in renal function deterioration, particularly in elderly or volume depleted individuals |
| captopril + ketorolac | 1 | captopril, ketorolac. Either increases toxicity of the other by Other (see comment). Use Caution/Monitor. Comment: May result in renal function deterioration, particularly in elderly or volume depleted individuals |
| captopril + meloxicam | 1 | captopril, meloxicam. Either increases toxicity of the other by Other (see comment). Use Caution/Monitor. Comment: May result in renal function deterioration, particularly in elderly or volume depleted individuals |
| captopril + metformin | 1 | captopril increases toxicity of metformin by unspecified interaction mechanism. Use Caution/ Monitor. Increases risk for hypoglycemia and lactic acidosis |
| captopril + pentoxifylline | 1 | pentoxifylline, captopril. Either increases effects of the other by pharmacodynamic synergism. Use Caution/Monitor. Both drugs lower blood pressure. Monitor blood pressure |
| carbamazepine + heparin | 1 | carbamazepine decreases levels of heparin by increasing metabolism. Use Caution/Monitor |
| carbamazepine + linezolid | 1 | carbamazepine decreases levels of linezolid by increasing metabolism. Use Caution/Monitor |
| carbamazepine + rivaroxaban | 1 | carbamazepine decreases levels of rivaroxaban by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Use Caution/Monitor. Avoid concomitant use of rivaroxaban with drugs that are combined P-gp and strong CYP3A4 inducers. Consider increasing the rivaroxaban dose if these drugs must be coadministered |
| carvedilol + hydrochlorothiazide | 1 | carvedilol increases and hydrochlorothiazide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/ Monitor |
| carvedilol + indapamide | 1 | carvedilol increases and indapamide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| carvedilol + nifedipine | 1 | carvedilol and nifedipine both increase anti-hypertensive channel blocking. Modify Therapy/Monitor Closely |
| celecoxib + heparin | 1 | heparin and celecoxib both increase anticoagulation. Modify Therapy/Monitor Closely |

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| celecoxib + indapamide | 1 | celecoxib increases and indapamide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| celecoxib + lisinopril | 1 | lisinopril, celecoxib. Either increases toxicity of the other by Other (see comment). Use Caution/Monitor. Comment: May result in renal function deterioration, particularly in elderly or volume depleted individuals |
| celecoxib + rivaroxaban | 1 | rivaroxaban, celecoxib. Other (see comment). Use Caution/Monitor. Comment: NSAIDs are known to increase bleeding. Bleeding risk may be increased when NSAIDs are used concomitantly with rivaroxaban. Monitor for signs/symptoms of blood loss |
| chlorthalidone + meloxicam | 1 | chlorthalidone will increase the level or effect of meloxicam by acidic (anionic) drug competition for renal tubular clearance. Minor/Significance Unknown |
| ciprofloxacin + diclofenac | 1 | diclofenac, ciprofloxacin. Other (see comment). Modify Therapy/Monitor Closely. Comment: Mechanism: unknown. Increased risk of CNS stimulation and seizures with high doses of fluoroquinolones |
| ciprofloxacin + omeprazole | 1 | omeprazole will decrease the level or effect of ciprofloxacin by unknown mechanism. Use Caution/Monitor. Absorption of the ciprofloxacin ER tablet was slightly diminished (20%) when coadministered with omeprazole |
| clarithromycin + dexamethasone | 1 | clarithromycin will increase the level or effect of dexamethasone by P-glycoprotein (MDR1) efflux transporter. Use Caution/Monitor |
| clopidogrel + diclofenac | 1 | clopidogrel, diclofenac. Either increases effects of the other by pharmacodynamic synergism. Modify Therapy/Monitor Closely. Clopidogrel and NSAIDs both inhibit platelet aggregation |
| clopidogrel + verapamil | 1 | verapamil will decrease the level or effect of clopidogrel by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Use Caution/Monitor. Inhibition of CYP3A4 will reduce clopidogrel bioactivation |
| dapagliflozin + glimepiride | 1 | glimepiride, dapagliflozin. Either increases effects of the other by pharmacodynamic synergism. Modify Therapy/Monitor Closely. Consider a lower dose of insulin or insulin secretagogue to avoid hypoglycemia when coadministered with dapagliflozin |
| dexamethasone + fluconazole | 1 | fluconazole will increase the level or effect of dexamethasone by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Use Caution/Monitor |
| dexamethasone + levofloxacin | 1 | dexamethasone and levofloxacin both increase Other (see comment). Use Caution/Monitor. Coadministration of quinolone antibiotics and corticosteroids may increase risk of tendon rupture |
| dexamethasone + rivaroxaban | 1 | dexamethasone decreases levels of rivaroxaban by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Use Caution/Monitor. Avoid concomitant use of rivaroxaban with drugs that are combined P-gp and strong CYP3A4 inducers. Consider increasing the rivaroxaban dose if these drugs must be coadministered |
| dexamethasone + theophylline | 1 | dexamethasone will decrease the level or effect of theophylline by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Use Caution/Monitor |
| diclofenac + enoxaparin | 1 | enoxaparin and diclofenac both increase anticoagulation. Modify Therapy/Monitor Closely |
| diclofenac + fosinopril | 1 | diclofenac, fosinopril. pharmacodynamic antagonism. Avoid or Use Alternate Drug. Coadministration may result in a significant decrease in renal function. NSAIDs may diminish the antihypertensive effect of ACE inhibitors. The mechanism of these interactions is likely related to the ability of NSAIDs to reduce the synthesis of vasodilating renal prostaglandins |

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| diclofenac + lisinopril | 1 | diclofenac, lisinopril. pharmacodynamic antagonism. Avoid or Use Alternate Drug. Coadministration may result in a significant decrease in renal function. NSAIDs may diminish the antihypertensive effect of ACE inhibitors. The mechanism of these interactions is likely related to the ability of NSAIDs to reduce the synthesis of vasodilating renal prostaglandins |
| diclofenac + prednisolone | 1 | diclofenac, prednisolone. Either increases toxicity of the other by pharmacodynamic synergism. Use Caution/Monitor. Increased risk of GI ulceration |
| digoxin + esomeprazole | 1 | esomeprazole increases toxicity of digoxin by Other (see comment). Use Caution/Monitor. Comment: Prolonged use of PPIs may cause hypomagnesemia and increase risk for digoxin toxicity |
| digoxin + felodipine | 1 | felodipine will increase the level or effect of digoxin by P-glycoprotein (MDR1) efflux transporter. Use Caution/Monitor |
| digoxin + fosinopril | 1 | felodipine will increase the level or effect of digoxin by P-glycoprotein (MDR1) efflux transporter. Use Caution/Monitor |
| digoxin + levofloxacin | 1 | levofloxacin will increase the level or effect of digoxin by altering intestinal flora. Applies only to oral form of both agents. Use Caution/Monitor |
| digoxin + meloxicam | 1 | meloxicam and digoxin both increase serum potassium. Use Caution/Monitor |
| digoxin + memantine | 1 | digoxin will increase the level or effect of memantine by basic (cationic) drug competition for renal tubular clearance. Use Caution/Monitor |
| digoxin + metoclopramide | 1 | metoclopramide decreases levels of digoxin by inhibition of GI absorption. Applies only to oral form of both agents. Use Caution/Monitor |
| digoxin + moxifloxacin | 1 | moxifloxacin will increase the level or effect of digoxin by altering intestinal flora. Applies only to oral form of both agents. Use Caution/Monitor |
| digoxin + sacubitril/valsartan | 1 | sacubitril/valsartan and digoxin both increase serum potassium. Use Caution/Monitor |
| digoxin + salmeterol | 1 | digoxin increases and salmeterol decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| digoxin + valsartan | 1 | valsartan will increase the level or effect of digoxin by decreasing renal clearance. Use Caution/Monitor. Monitor digoxin levels closely when coadministered with drugs that may decrease glomerular filtration or tubular secretion |
| digoxin + vancomycin | 1 | vancomycin will increase the level or effect of digoxin by altering intestinal flora. Applies only to oral form of both agents. Use Caution/Monitor |
| diltiazem + magnesium supplement | 1 | magnesium supplement, diltiazem. Either increases toxicity of the other by pharmacodynamic synergism. Use Caution/Monitor. Calcium channel blockers may increase toxic effects of magnesium; magnesium may increase hypotensive effects of calcium channel blockers |
| diphenhydramine + tamsulosin | 1 | diphenhydramine increases levels of tamsulosin by affecting hepatic enzyme CYP2D6 metabolism. Use Caution/Monitor |
| doxazosin + lisinopril | 1 | lisinopril, doxazosin. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Exaggerated first dose hypotensive response |
| doxazosin + perindopril | 1 | perindopril, doxazosin. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Exaggerated first dose hypotensive response |

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| dulaglutide + metformin | 1 | dulaglutide, metformin. Either increases effects of the other by pharmacodynamic synergism. Use Caution/Monitor. Antidiabetic agents are often used in combination; dosage adjustments may be required when initiating or discontinuing antidiabetic agents |
| enalapril + eplerenone | 1 | enalapril, eplerenone. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of hyperkalemia |
| enalapril + ketorolac | 1 | enalapril, ketorolac. Either increases toxicity of the other by Other (see comment). Use Caution/Monitor. Comment: May result in renal function deterioration, particularly in elderly or volume depleted individuals |
| enalapril + meloxicam | 1 | enalapril, meloxicam. Either increases toxicity of the other by Other (see comment). Use Caution/Monitor. Comment: May result in renal function deterioration, particularly in elderly or volume depleted individuals |
| enalapril + sodium bicarbonate | 1 | sodium bicarbonate decreases effects of enalapril by unspecified interaction mechanism. Use Caution/Monitor |
| enoxaparin + prednisolone | 1 | prednisolone, enoxaparin. Other (see comment). Use Caution/Monitor. Comment: Corticosteroids may decrease anticoagulant effects by increasing blood coagulability; conversely, they may impair vascular integrity, thus increasing bleeding risk. Monitor INR closely |
| enoxaparin + sacubitril/valsartan | 1 | enoxaparin increases toxicity of sacubitril/valsartan by Other (see comment). Use Caution/Monitor. Comment: Low molecular weight heparins may suppress adrenal aldosterone secretion, which can potentially cause hyperkalemia |
| enoxaparin + ticagrelor | 1 | ticagrelor, enoxaparin. Either increases effects of the other by anticoagulation. Use Caution/Monitor. Increased risk of bleeding during concomitant use of medications that increase potential for bleeding |
| eplerenone + lisinopril | 1 | lisinopril, eplerenone. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of hyperkalemia |
| eplerenone + ramipril | 1 | ramipril, eplerenone. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of hyperkalemia |
| eplerenone + verapamil | 1 | verapamil will increase the level or effect of eplerenone by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Use Caution/Monitor. Plasma concentrations and pharmacologic or toxic effects of eplerenone may be increased by verapamil |
| escitalopram + omeprazole | 1 | omeprazole will increase the level or effect of escitalopram by affecting hepatic enzyme CYP2C19 metabolism. Use Caution/Monitor |
| felodipine + metoprolol | 1 | metoprolol and felodipine both increase anti-hypertensive channel blocking. Modify Therapy/Monitor Closely |
| ferrous sulfate + pantoprazole | 1 | pantoprazole will decrease the level or effect of ferrous sulfate by increasing gastric pH. Applies only to oral form of both agents. Use Caution/Monitor |
| fluconazole + levofloxacin | 1 | fluconazole and levofloxacin both increase QTc interval. Modify Therapy/Monitor Closely |
| fluconazole + rivaroxaban | 1 | fluconazole increases levels of rivaroxaban by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Use Caution/Monitor. Patients with renal impairment receiving rivaroxaban with moderate CYP3A4 inhibitors may have significant increases in exposure compared with patients with normal renal function and no inhibitor use; increased may increase bleeding risk |

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| formoterol + indapamide | 1 | formoterol and indapamide both decrease serum potassium. Use Caution/Monitor |
| formoterol + moxonidine | 1 | moxonidine increases and formoterol decreases sedation. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| fosinopril + furosemide | 1 | fosinopril, furosemide. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of acute hypotension, renal insufficiency |
| fosinopril + heparin | 1 | heparin increases toxicity of fosinopril by Other (see comment). Use Caution/Monitor. Comment: Low molecular weight heparins may suppress adrenal aldosterone secretion, which can potentially cause hyperkalemia |
| furosemide + insulin | 1 | furosemide decreases effects of insulin degludec by Other (see comment). Use Caution/Monitor. Comment: Diuretics may cause hyperglycemia and glycosuria in patients with diabetes mellitus, possibly by diuretic-induced hypokalemia |
| furosemide + lisinopril | 1 | lisinopril, furosemide. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of acute hypotension, renal insufficiency |
| gentamicin + ketorolac | 1 | ketorolac increases and gentamicin decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| heparin + meloxicam | 1 | heparin and meloxicam both increase anticoagulation. Modify Therapy/Monitor Closely |
| heparin + perindopril | 1 | heparin increases toxicity of perindopril by Other (see comment). Use Caution/Monitor. Comment: Low molecular weight heparins may suppress adrenal aldosterone secretion, which can potentially cause hyperkalemia |
| heparin + telmisartan | 1 | heparin increases toxicity of telmisartan by Other (see comment). Use Caution/Monitor. Comment: Low molecular weight heparins may suppress adrenal aldosterone secretion, which can potentially cause hyperkalemia |
| heparin + valsartan | 1 | heparin increases toxicity of valsartan by Other (see comment). Use Caution/Monitor. Comment: Low molecular weight heparins may suppress adrenal aldosterone secretion, which can potentially cause hyperkalemia |
| hydrochlorothiazide + losartan | 1 | losartan increases and hydrochlorothiazide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| hydrochlorothiazide + potassium | 1 | potassium chloride increases and hydrochlorothiazide decreases serum potassium. Effect of interaction is not clear, use caution. Modify Therapy/Monitor Closely |
| hydrochlorothiazide + sotalol | 1 | sotalol increases and hydrochlorothiazide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| hydrochlorothiazide + spironolactone | 1 | spironolactone increases and hydrochlorothiazide decreases serum potassium. Effect of interaction is not clear, use caution. Modify Therapy/Monitor Closely |
| ibuprofen + torsemide | 1 | ibuprofen increases and torsemide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| ibuprofen + warfarin | 1 | ibuprofen, warfarin. Either increases effects of the other by pharmacodynamic synergism. Modify Therapy/Monitor Closely. Drugs with antiplatelet properties may increase anticoagulation effect of warfarin |
| indapamide + ketorolac | 1 | ibuprofen, warfarin. Either increases effects of the other by pharmacodynamic synergism. Modify Therapy/Monitor Closely. Drugs with antiplatelet properties may increase anticoagulation effect of warfarin |

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| indapamide + timolol | 1 | timolol increases and indapamide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/ Monitor |
| indapamide + valsartan | 1 | valsartan increases and indapamide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| insulin + perindopril | 1 | perindopril increases effects of insulin aspart by pharmacodynamic synergism. Use Caution/Monitor |
| insulin + telmisartan | 1 | telmisartan increases effects of insulin aspart by unspecified interaction mechanism. Use Caution/Monitor. Concomitant use of insulin and ARBs may require insulin dosage adjustment and increased glucose monitoring |
| insulin + torsemide | 1 | torsemide decreases effects of insulin degludec by Other (see comment). Use Caution/Monitor. Comment: Diuretics may cause hyperglycemia and glycosuria in patients with diabetes mellitus, possibly by diuretic-induced hpokalemia |
| ketoprofen + ramipril | 1 | ramipril, ketoprofen. Either increases toxicity of the other by Other (see comment). Use Caution/Monitor. Comment: May result in renal function deterioration, particularly in elderly or volume depleted individuals |
| ketorolac + levofloxacin | 1 | levofloxacin, ketorolac. Other (see comment). Modify Therapy/Monitor Closely. Comment: Risk of CNS stimulation/seizure. Mechanism: Displacement of GABA from receptors in brain |
| ketorolac + prednisolone | 1 | ketorolac, prednisolone. Either increases toxicity of the other by pharmacodynamic synergism. Use Caution/Monitor. Increased risk of GI ulceration |
| ketorolac + rivaroxaban | 1 | rivaroxaban, ketorolac. Other (see comment). Use Caution/Monitor. Comment: NSAIDs are known to increase bleeding. Bleeding risk may be increased when NSAIDs are used concomitantly with rivaroxaban. Monitor for signs/symptoms of blood loss |
| levocarnitine + warfarin | 1 | levocarnitine increases effects of warfarin by unspecified interaction mechanism. Use Caution/Monitor |
| levofloxacin + magnesium sulfate | 1 | magnesium sulfate decreases levels of levofloxacin by inhibition of GI absorption. Applies only to oral form of both agents. Use Caution/Monitor. Separate by 2 hours |
| levofloxacin + moxifloxacin | 1 | levofloxacin and moxifloxacin both increase QTc interval. Modify Therapy/Monitor Closely |
| levothyroxine + magnesium supplement | 1 | magnesium supplement will decrease the level or effect of levothyroxine by Other (see comment). Modify Therapy/Monitor Closely. Drug may adsorb to magnesium; may decrease absorption by the intestinal tract; applies to oral forms; may separate administration of drugs by 4 hr |
| levothyroxine + warfarin | 1 | levothyroxine increases effects of warfarin by unspecified interaction mechanism. Use Caution/Monitor |
| lisinopril + meloxicam | 1 | lisinopril, meloxicam. Either increases toxicity of the other by Other (see comment). Use Caution/Monitor. Comment: May result in renal function deterioration, particularly in elderly or volume depleted individuals |
| losartan + lornoxicam | 1 | losartan and lornoxicam both increase serum potassium. Use Caution/Monitor |
| losartan + sacubitril/valsartan | 1 | losartan and sacubitril/valsartan both increase serum potassium. Use Caution/Monitor |
| losartan + tizanidine | 1 | tizanidine increases effects of losartan by pharmacodynamic synergism. Use Caution/Monitor. Risk of hypotension |

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| magnesium supplement + nifedipine | 1 | magnesium supplement, nifedipine. Either increases toxicity of the other by Other (see comment). Use Caution/Monitor. Comment: Calcium channel blockers may increase toxic effects of magnesium; magnesium may increase hypotensive effects of calcium channel blockers |
| magnesium supplement + potassium | 1 | magnesium supplement will decrease the level or effect of potassium phosphate by Other (see comment). Modify Therapy/Monitor Closely. Drug may form a chelate with divalent cations; may decrease absorption by the intestinal tract; applies to oral forms; separate administration of drugs to avoid interaction |
| meloxicam + torsemide | 1 | meloxicam increases and torsemide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| meloxicam + warfarin | 1 | meloxicam, warfarin. Either increases effects of the other by pharmacodynamic synergism. Modify Therapy/Monitor Closely. Drugs with antiplatelet properties may increase anticoagulation effect of warfarin |
| metformin + nifedipine | 1 | nifedipine decreases effects of metformin by pharmacodynamic antagonism. Use Caution/Monitor. Patient should be closely observed for loss of blood glucose control; when drugs are withdrawn from a patient receiving metformin, patient should be observed closely for hypoglycemia |
| metformin + ramipril | 1 | ramipril increases toxicity of metformin by unspecified interaction mechanism. Use Caution/Monitor. Increases risk for hypoglycemia and lactic acidosis |
| methotrexate + omeprazole | 1 | omeprazole increases levels of methotrexate by decreasing renal clearance. Use Caution/Monitor. Temporary withdrawal of PPI may be considered in some patients |
| metoprolol + nebivolol | 1 | metoprolol and nebivolol both increase anti-hypertensive channel blocking. Avoid or Use Alternate Drug |
| mifepristone + quinine | 1 | mifepristone, quinine. QTc interval. Modify Therapy/Monitor Closely. Use alternatives if available |
| moxifloxacin + prednisolone | 1 | prednisolone and moxifloxacin both increase Other (see comment). Use Caution/Monitor. Coadministration of quinolone antibiotics and corticosteroids may increase risk of tendon rupture |
| neostigmine + pyridostigmine | 1 | neostigmine and pyridostigmine both increase cholinergic effects/transmission. Use Caution/Monitor |
| nifedipine + sotalol | 1 | sotalol and nifedipine both increase anti-hypertensive channel blocking. Modify Therapy/Monitor Closely |
| nitroglycerin + verapamil | 1 | verapamil, nitroglycerin sublingual. Either increases toxicity of the other by additive vasodilation. Modify Therapy/Monitor Closely. Marked orthostatic hypotension reported with concomitant use |
| pentoxifylline + warfarin | 1 | pentoxifylline increases effects of warfarin by anticoagulation. Use Caution/Monitor |
| potassium + telmisartan | 1 | telmisartan and potassium chloride both increase serum potassium. Use Caution/Monitor |
| propranolol + sotalol | 1 | propranolol and sotalol both increase serum potassium. Use Caution/Monitor |
| rivaroxaban + saw palmetto | 1 | saw palmetto increases toxicity of rivaroxaban by unspecified interaction mechanism. Use Caution/Monitor. May increase risk of bleeding |
| rivaroxaban + verapamil | 1 | verapamil increases levels of rivaroxaban by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Use Caution/Monitor. Verapamil also inhibits P-gp activity, which can further increase rivaroxaban serum levels; since both pathways of rivaroxaban elimination are affected, |

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| | | patients with renal impairment receiving rivaroxaban with drugs that are combined P-gp and moderate CYP3A4 inhibitors may increase exposure compared to patients with normal renal function; monitor for bleeding |
| salmeterol + spironolactone | 1 | spironolactone increases and salmeterol decreases serum potassium. Effect of interaction is not clear, use caution. Modify Therapy/Monitor Closely |
| salmeterol + torsemide | 1 | salmeterol and torsemide both decrease serum potassium. Use Caution/Monitor |

Note: Impact of drug–drug interactions associated with the combinations “aspirin + captopril” and “aspirin + enalapril” may be considered insignificant due to the use of low-dose aspirin in the majority of cases. Administration of aspirin at doses less than 300 mg per day has little effect on the effectiveness of captopril and enalapril. Administration of aspirin in higher doses reduces the effectiveness of captopril and enalapril.

**Table S7.** Drug combinations resulting in potential minor drug–drug interactions in the list of taken medications in patients with cardiovascular diseases according to data derived from the electronic health records ($n$ = 1030) established in 2018–2023.

| Drug combinations | n | Potential minor drug-drug interactions (T-list) |
|---|---|---|
| aspirin + furosemide | 25 | aspirin decreases effects of furosemide by pharmacodynamic antagonism. Minor/Significance Unknown. NSAIDs decrease prostaglandin synthesis |
| clopidogrel + torsemide | 22 | clopidogrel increases levels of torsemide by decreasing metabolism. Minor/Significance Unknown |
| magnesium hydroxide + spironolactone | 21 | spironolactone increases levels of magnesium hydroxide by decreasing renal clearance. Minor/Significance Unknown |
| magnesium hydroxide + torsemide | 20 | torsemide decreases levels of magnesium hydroxide by increasing renal clearance. Minor/Significance Unknown |
| aspirin + indapamide | 18 | indapamide will increase the level or effect of aspirin by acidic (anionic) drug competition for renal tubular clearance. Minor/Significance Unknown |
| aspirin + eplerenone | 10 | aspirin decreases effects of eplerenone by pharmacodynamic antagonism. Minor/Significance Unknown. NSAIDs decrease prostaglandin synthesis |
| dexamethasone + omeprazole | 10 | dexamethasone will decrease the level or effect of omeprazole by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Minor/Significance Unknown |
| ascorbic acid + aspirin | 9 | ascorbic acid will increase the level or effect of aspirin by acidic (anionic) drug competition for renal tubular clearance. Minor/Significance Unknown |
| ascorbic acid + aspirin | 9 | ascorbic acid increases levels of aspirin by decreasing renal clearance. Minor/Significance Unknown |
| aspirin + hydrochlorothiazide | 9 | hydrochlorothiazide will increase the level or effect of aspirin by acidic (anionic) drug competition for renal tubular clearance. Minor/Significance Unknown |
| aspirin + prednisolone | 7 | prednisolone decreases levels of aspirin by increasing renal clearance. Minor/Significance Unknown |
| ceftriaxone + furosemide | 7 | ceftriaxone increases toxicity of furosemide by pharmacodynamic synergism. Minor/Significance Unknown. Increased risk of nephrotoxicity |
| furosemide + magnesium hydroxide | 7 | furosemide decreases levels of magnesium hydroxide by increasing renal clearance. Minor/Significance Unknown |
| furosemide + prednisolone | 7 | prednisolone, furosemide. Mechanism: pharmacodynamic synergism. Minor/Significance Unknown. Risk of hypokalemia, especially with strong glucocorticoid activity |
| hydrochlorothiazide + magnesium hydroxide | 7 | hydrochlorothiazide decreases levels of magnesium hydroxide by increasing renal clearance. Minor/Significance Unknown |
| indapamide + magnesium hydroxide | 7 | indapamide decreases levels of magnesium hydroxide by increasing renal clearance. Minor/Significance Unknown |
| indapamide + metformin | 7 | indapamide decreases effects of metformin by pharmacodynamic antagonism. Minor/Significance Unknown. Thiazide dosage >50 mg/day may increase blood glucose |
| furosemide + metformin | 6 | furosemide increases levels of metformin by unspecified interaction mechanism. Minor/Significance Unknown. Patient should be closely observed for loss of blood glucose control; when drugs are withdrawn from a patient receiving metformin, patient should be observed closely for hypoglycemia |

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| acetaminophen + enoxaparin | 5 | acetaminophen increases effects of enoxaparin by unknown mechanism. Minor/Significance Unknown |
| budesonide + furosemide | 5 | budesonide, furosemide. Mechanism: pharmacodynamic synergism. Minor/Significance Unknown. Risk of hypokalemia, especially with strong glucocorticoid activity |
| dexamethasone + torsemide | 5 | dexamethasone, torsemide. Mechanism: pharmacodynamic synergism. Minor/Significance Unknown. Risk of hypokalemia, especially with strong glucocorticoid activity |
| prednisolone + torsemide | 5 | prednisolone, torsemide. Mechanism: pharmacodynamic synergism. Minor/Significance Unknown. Risk of hypokalemia, especially with strong glucocorticoid activity |
| acetaminophen + heparin | 4 | acetaminophen increases effects of heparin by unknown mechanism. Minor/Significance Unknown |
| acetazolamide + aspirin | 4 | aspirin will decrease the level or effect of acetazolamide by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Minor/Significance Unknown |
| acetazolamide + omeprazole | 4 | acetazolamide will increase the level or effect of omeprazole by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Minor/Significance Unknown |
| aspirin + dexamethasone | 4 | dexamethasone decreases levels of aspirin by increasing renal clearance. Minor/Significance Unknown |
| cyanocobalamin + omeprazole | 4 | omeprazole decreases levels of cyanocobalamin by inhibition of GI absorption. Applies only to oral form of both agents. Minor/Significance Unknown |
| dexamethasone + furosemide | 4 | dexamethasone, furosemide. Mechanism: pharmacodynamic synergism. Minor/Significance Unknown. Risk of hypokalemia, especially with strong glucocorticoid activity |
| dexamethasone + insulin | 4 | dexamethasone decreases effects of insulin regular human by pharmacodynamic antagonism. Minor/Significance Unknown |
| | | dexamethasone decreases effects of insulin lispro by pharmacodynamic antagonism. Minor/Significance Unknown |
| | | dexamethasone decreases effects of insulin detemir by pharmacodynamic antagonism. Minor/Significance Unknown |
| acetazolamide + rivaroxaban | 3 | acetazolamide will increase the level or effect of rivaroxaban by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Minor/Significance Unknown |
| aspirin + chlorthalidone | 3 | chlorthalidone will increase the level or effect of aspirin by acidic (anionic) drug competition for renal tubular clearance. Minor/Significance Unknown |
| aspirin + verapamil | 3 | verapamil increases effects of aspirin by unknown mechanism. Minor/Significance Unknown. Enhanced antiplatelet activity |
| chlorthalidone + magnesium hydroxide | 3 | chlorthalidone decreases levels of magnesium hydroxide by increasing renal clearance. Minor/Significance Unknown |
| digoxin + magnesium hydroxide | 3 | digoxin decreases levels of magnesium hydroxide by increasing renal clearance. Minor/Significance Unknown |
| insulin + potassium | 3 | potassium chloride increases effects of insulin aspart by pharmacodynamic synergism. Minor/Significance Unknown. Interaction especially seen in the treatment of hypokalemia |
| acetazolamide + atorvastatin | 2 | acetazolamide will increase the level or effect of atorvastatin by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Minor/Significance Unknown |
| acetazolamide + budesonide | 2 | acetazolamide will increase the level or effect of budesonide by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Minor/Significance Unknown |

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| amikacin + aspirin | 2 | aspirin increases levels of amikacin by decreasing renal clearance. Minor/Significance Unknown. Interaction mainly occurs in preterm infants |
| amlodipine + dexamethasone | 2 | dexamethasone will decrease the level or effect of amlodipine by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Minor/Significance Unknown |
| aspirin + cyanocobalamin | 2 | aspirin decreases levels of cyanocobalamin by inhibition of GI absorption. Applies only to oral form of both agents. Minor/Significance Unknown |
| aspirin + diclofenac | 2 | aspirin and diclofenac both increase anticoagulation. Use Caution/Monitor |
| aspirin + ketorolac | 2 | aspirin will increase the level or effect of ketorolac by acidic (anionic) drug competition for renal tubular clearance. Minor/Significance Unknown |
| carbamazepine + omeprazole | 2 | omeprazole increases levels of carbamazepine by decreasing metabolism. Minor/Significance Unknown. Monitor plasma levels when used concomitantly |
| cyclophosphamide + ondansetron | 2 | cyclophosphamide will increase the level or effect of ondansetron by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Minor/Significance Unknown |
| cyclophosphamide + trimethoprim | 2 | cyclophosphamide will increase the level or effect of trimethoprim by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Minor/Significance Unknown |
| dexamethasone + indapamide | 2 | dexamethasone, indapamide. Mechanism: pharmacodynamic synergism. Minor/Significance Unknown. Risk of hypokalemia, especially with strong glucocorticoid activity |
| dextrose + magnesium sulfate | 2 | dextrose decreases levels of magnesium sulfate by increasing renal clearance. Minor/Significance Unknown |
| fluconazole + sulfamethoxazole | 2 | fluconazole will increase the level or effect of sulfamethoxazole by affecting hepatic enzyme CYP2C9/10 metabolism. Minor/Significance Unknown |
| furosemide + magnesium sulfate | 2 | furosemide decreases levels of magnesium sulfate by increasing renal clearance. Minor/Significance Unknown |
| indapamide + magnesium sulfate | 2 | indapamide decreases levels of magnesium sulfate by increasing renal clearance. Minor/Significance Unknown |
| insulin + prednisolone | 2 | prednisolone decreases effects of insulin aspart by pharmacodynamic antagonism. Minor/Significance Unknown |
| magnesium sulfate + spironolactone | 2 | spironolactone increases levels of magnesium sulfate by decreasing renal clearance. Minor/Significance Unknown |
| metformin + potassium | 2 | potassium chloride increases effects of metformin by pharmacodynamic synergism. Minor/Significance Unknown. Interaction especially seen in the treatment of hypokalemia |
| acetaminophen + metronidazole | 1 | metronidazole will increase the level or effect of acetaminophen by affecting hepatic enzyme CYP2E1 metabolism. Minor/Significance Unknown |
| acetazolamide + amiodarone | 1 | acetazolamide will increase the level or effect of amiodarone by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Minor/Significance Unknown |
| acetazolamide + dexamethasone | 1 | acetazolamide will increase the level or effect of dexamethasone by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Minor/Significance Unknown |
| acetazolamide + isosorbide dinitrate | 1 | acetazolamide will increase the level or effect of isosorbide dinitrate by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Minor/Significance Unknown |
| acetazolamide + losartan | 1 | acetazolamide will increase the level or effect of losartan by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Minor/Significance Unknown |

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| acyclovir + indapamide | 1 | indapamide will increase the level or effect of acyclovir by acidic (anionic) drug competition for renal tubular clearance. Minor/Significance Unknown |
| amikacin + magnesium hydroxide | 1 | amikacin decreases levels of magnesium hydroxide by increasing renal clearance. Minor/Significance Unknown |
| amiodarone + diclofenac | 1 | amiodarone will increase the level or effect of diclofenac by affecting hepatic enzyme CYP2C9/10 metabolism. Minor/Significance Unknown |
| amitriptyline + carbamazepine | 1 | carbamazepine decreases levels of amitriptyline by increasing metabolism. Minor/Significance Unknown |
| amoxicillin + clarithromycin | 1 | clarithromycin decreases effects of amoxicillin by pharmacodynamic antagonism. Minor/Significance Unknown |
| aspirin + calcium carbonate | 1 | calcium carbonate, aspirin. Mechanism: passive renal tubular reabsorption due to increased pH. Minor/ Significance Unknown. Salicylate levels increased at moderate doses; salicylate levels decreased at large doses (d/ t increased renal excretion of unchanged salicylic acid) |
| aspirin + folic acid | 1 | aspirin decreases levels of folic acid by inhibition of GI absorption. Applies only to oral form of both agents. Minor/Significance Unknown |
| aspirin + meloxicam | 1 | aspirin will increase the level or effect of meloxicam by acidic (anionic) drug competition for renal tubular clearance. Minor/Significance Unknown |
| aspirin + sodium bicarbonate | 1 | sodium bicarbonate, aspirin. Mechanism: passive renal tubular reabsorption due to increased pH. Minor/Significance Unknown. Salicylate levels increased at moderate doses; salicylate levels decreased at large doses (d/t increased renal excretion of unchanged salicylic acid) |
| aspirin + vancomycin | 1 | aspirin increases levels of vancomycin by decreasing renal clearance. Minor/Significance Unknown. Interaction mainly occurs in neonates |
| atorvastatin + cyclophosphamide | 1 | cyclophosphamide will increase the level or effect of atorvastatin by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Minor/Significance Unknown |
| budesonide + indapamide | 1 | budesonide, indapamide. Mechanism: pharmacodynamic synergism. Minor/Significance Unknown. Risk of hypokalemia, especially with strong glucocorticoid activity |
| budesonide + insulin | 1 | budesonide decreases effects of insulin aspart by pharmacodynamic antagonism. Minor/Significance Unknown |
| budesonide + metformin | 1 | budesonide decreases effects of metformin by pharmacodynamic antagonism. Minor/Significance Unknown |
| calcium gluconate + torsemide | 1 | torsemide decreases levels of calcium gluconate by increasing renal clearance. Minor/Significance Unknown |
| carvedilol + omeprazole | 1 | omeprazole will increase the level or effect of carvedilol by affecting hepatic enzyme CYP2C9/10 metabolism. Minor/Significance Unknown |
| chlorthalidone + metformin | 1 | chlorthalidone decreases effects of metformin by pharmacodynamic antagonism. Minor/Significance Unknown. Thiazide dosage >50 mg/day may increase blood glucose |
| clarithromycin + dexamethasone | 1 | dexamethasone will decrease the level or effect of clarithromycin by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Minor/Significance Unknown |
| cyanocobalamin + metformin | 1 | metformin decreases levels of cyanocobalamin by unspecified interaction mechanism. Minor/Significance Unknown. It may take several years of metformin therapy to develop vitamin B12 deficiency |

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| dexamethasone + eplerenone | 1 | dexamethasone will decrease the level or effect of eplerenone by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Minor/Significance Unknown |
| dexamethasone + esomeprazole | 1 | dexamethasone will decrease the level or effect of esomeprazole by increasing metabolism. Minor/Significance Unknown |
| dexamethasone + metformin | 1 | dexamethasone decreases effects of metformin by pharmacodynamic antagonism. Minor/Significance Unknown |
| dextrose + magnesium hydroxide | 1 | dextrose decreases levels of magnesium hydroxide by increasing renal clearance. Minor/Significance Unknown |
| diclofenac + ketoprofen | 1 | diclofenac will increase the level or effect of ketoprofen by acidic (anionic) drug competition for renal tubular clearance. Minor/Significance Unknown |
| diclofenac + ketorolac | 1 | diclofenac will increase the level or effect of ketorolac by acidic (anionic) drug competition for renal tubular clearance. Minor/Significance Unknown |
| diclofenac + meloxicam | 1 | diclofenac will increase the level or effect of meloxicam by acidic (anionic) drug competition for renal tubular clearance. Minor/Significance Unknown |
| diclofenac + metronidazole | 1 | metronidazole will increase the level or effect of diclofenac by affecting hepatic enzyme CYP2C9/10 metabolism. Minor/Significance Unknown |
| diclofenac topical + diclofenac | 1 | diclofenac topical, diclofenac. Either increases effects of the other by pharmacodynamic synergism. Minor/Significance Unknown. Although low, there is systemic exposure to diclofenac topical; theoretically, concomitant administration with systemic NSAIDS or aspirin may result in increased NSAID adverse effects |
| diclofenac topical + ketoprofen | 1 | diclofenac topical, ketoprofen. Either increases effects of the other by pharmacodynamic synergism. Minor/Significance Unknown. Although low, there is systemic exposure to diclofenac topical; theoretically, concomitant administration with systemic NSAIDS or aspirin may result in increased NSAID adverse effects |
| | | diclofenac topical, meloxicam. Either increases effects of the other by pharmacodynamic synergism. Minor/Significance Unknown. Although low, there is systemic exposure to diclofenac topical; theoretically, concomitant administration with systemic NSAIDS or aspirin may result in increased NSAID adverse effects |
| digoxin + magnesium sulfate | 1 | digoxin decreases levels of magnesium sulfate by increasing renal clearance. Minor/Significance Unknown |
| eplerenone + metronidazole | 1 | metronidazole will increase the level or effect of eplerenone by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Minor/Significance Unknown |
| esomeprazole + levothyroxine | 1 | esomeprazole decreases levels of levothyroxine by increasing gastric pH. Applies only to oral form of both agents. Minor/Significance Unknown. Conflicting evidence regarding this interaction exists |
| folic acid + torsemide | 1 | torsemide decreases levels of folic acid by increasing renal clearance. Minor/Significance Unknown |
| formoterol + indapamide | 1 | formoterol, indapamide. Mechanism: pharmacodynamic synergism. Minor/Significance Unknown. Hypokalemia |
| gentamicin + ketorolac | 1 | ketorolac increases levels of gentamicin by decreasing renal clearance. Minor/Significance Unknown. Interaction mainly occurs in preterm infants |

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| hydrochlorothiazide + insulin | 1 | hydrochlorothiazide decreases effects of insulin aspart by pharmacodynamic antagonism. Minor/Significance Unknown. Thiazide dosage >50 mg/day may increase blood glucose |
| indapamide + insulin | 1 | indapamide decreases effects of insulin glargine by pharmacodynamic antagonism. Minor/Significance Unknown. Thiazide dosage >50 mg/day may increase blood glucose |
| indapamide + ketorolac | 1 | indapamide will increase the level or effect of aspirin by acidic (anionic) drug competition for renal tubular clearance. Minor/Significance Unknown |
| indapamide + vildagliptin | 1 | indapamide decreases effects of vildagliptin by pharmacodynamic antagonism. Minor/Significance Unknown. Thiazide dosage >50 mg/day may increase blood glucose |
| ketoprofen + meloxicam | 1 | ketoprofen will increase the level or effect of meloxicam by acidic (anionic) drug competition for renal tubular clearance. Minor/Significance Unknown |
| ketorolac + meloxicam | 1 | ketorolac will increase the level or effect of meloxicam by acidic (anionic) drug competition for renal tubular clearance. Minor/Significance Unknown |
| levothyroxine + omeprazole | 1 | omeprazole decreases levels of levothyroxine by increasing gastric pH. Applies only to oral form of both agents. Minor/Significance Unknown. Conflicting evidence regarding this interaction exists |
| lisinopril + spironolactone | 1 | lisinopril, spironolactone. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of hyperkalemia |
| magnesium sulfate + torsemide | 1 | torsemide decreases levels of magnesium sulfate by increasing renal clearance. Minor/Significance Unknown |
| metformin + nifedipine | 1 | nifedipine increases levels of metformin by enhancing GI absorption. Applies only to oral form of both agents. Minor/Significance Unknown |
| metformin + prednisolone | 1 | prednisolone decreases effects of metformin by pharmacodynamic antagonism. Minor/Significance Unknown |
| omeprazole + theophylline | 1 | omeprazole increases toxicity of theophylline by Other (see comment). Minor/Significance Unknown. Comment: Prolonged use of proton pump inhibitors can cause hypochlorhydria, which in turn causes peristalsis in small intestine to increase and peristalsis in the proximal colon to decrease; monitor for toxicity |
| pyridoxine + theophylline | 1 | theophylline decreases levels of pyridoxine by altering metabolism. Minor/Significance Unknown |

**Table S8.** Drug combinations resulting in potential contraindicated drug–drug interactions in the list of prescribed medications in patients with cardiovascular diseases according to data derived from the electronic health records (*n* = 1030) established in 2018–2023.

| Drug combinations | n | Potential contraindicated drug-drug interactions (P-list) |
|---|---|---|
| captopril + sacubitril/valsartan | 10 | sacubitril/valsartan, captopril. Either increases toxicity of the other by Other (see comment). Contraindicated. Comment: Coadministration of neprilysin inhibitors (eg, sacubitril) with ACE inhibitors may increase angioedema risk; do not administer ACE inhibitors within 36 hr of switching to or from sacubitril/valsartan |
| amitriptyline + indapamide | 1 | amitriptyline and indapamide both increase QTc interval. Contraindicated |
| apixaban + carbamazepine | 1 | carbamazepine will decrease the level or effect of apixaban by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Contraindicated. Reduces anticoagulant effect by decreasing apixaban systemic exposure |
| lisinopril + sacubitril/valsartan | 1 | sacubitril/valsartan, lisinopril. Either increases toxicity of the other by Other (see comment). Contraindicated. Comment: Coadministration of neprilysin inhibitors (eg, sacubitril) with ACE inhibitors may increase angioedema risk; do not administer ACE inhibitors within 36 hr of switching to or from sacubitril/valsartan |

**Table S9.** Drug combinations resulting in potential serious drug–drug interactions in the list of prescribed medications in patients with cardiovascular diseases according to data derived from the electronic health records ($n$ = 1030) established in 2018–2023.

| Drug combinations | n | Potential serious drug-drug interactions (P-list) |
|---|---|---|
| aspirin + captopril * | 84 | aspirin, captopril. pharmacodynamic antagonism. Avoid or Use Alternate Drug. Coadministration may result in a significant decrease in renal function. NSAIDs may diminish the antihypertensive effect of ACE inhibitors. The mechanism of these interactions is likely related to the ability of NSAIDs to reduce the synthesis of vasodilating renal prostaglandins |
| aspirin + perindopril | 74 | aspirin, perindopril. pharmacodynamic antagonism. Avoid or Use Alternate Drug. Coadministration may result in a significant decrease in renal function. NSAIDs may diminish the antihypertensive effect of ACE inhibitors. The mechanism of these interactions is likely related to the ability of NSAIDs to reduce the synthesis of vasodilating renal prostaglandins |
| aspirin + lisinopril | 58 | aspirin, lisinopril. pharmacodynamic antagonism. Avoid or Use Alternate Drug. Coadministration may result in a significant decrease in renal function. NSAIDs may diminish the antihypertensive effect of ACE inhibitors. The mechanism of these interactions is likely related to the ability of NSAIDs to reduce the synthesis of vasodilating renal prostaglandins |
| clopidogrel + omeprazole | 41 | omeprazole decreases effects of clopidogrel by affecting hepatic enzyme CYP2C19 metabolism. Avoid or Use Alternate Drug. Clopidogrel efficacy may be reduced by drugs that inhibit CYP2C19. Inhibition of platelet aggregation by clopidogrel is entirely due to an active metabolite. Clopidogrel is metabolized to this active metabolite in part by CYP2C19 |
| aspirin + fosinopril | 28 | aspirin, fosinopril. pharmacodynamic antagonism. Avoid or Use Alternate Drug. Coadministration may result in a significant decrease in renal function. NSAIDs may diminish the antihypertensive effect of ACE inhibitors. The mechanism of these interactions is likely related to the ability of NSAIDs to reduce the synthesis of vasodilating renal prostaglandins |
| aspirin + enalapril * | 20 | aspirin, enalapril. pharmacodynamic antagonism. Avoid or Use Alternate Drug. Coadministration may result in a significant decrease in renal function. NSAIDs may diminish the antihypertensive effect of ACE inhibitors. The mechanism of these interactions is likely related to the ability of NSAIDs to reduce the synthesis of vasodilating renal prostaglandins |
| apixaban + clopidogrel | 18 | clopidogrel and apixaban both increase anticoagulation. Avoid or Use Alternate Drug |
| bisoprolol + digoxin | 16 | bisoprolol increases effects of digoxin by pharmacodynamic synergism. Use Caution/Monitor. Enhanced bradycardia |
| captopril + losartan | 15 | losartan, captopril. Either increases toxicity of the other by pharmacodynamic synergism. Avoid or Use Alternate Drug. Dual blockade of renin-angiotensin system increases risks of hypotension, hyperkalemia, and renal impairment |
| captopril + sacubitril/valsartan | 10 | sacubitril/valsartan, captopril. Either increases toxicity of the other by pharmacodynamic synergism. Avoid or Use Alternate Drug. Dual blockade of renin-angiotensin system increases risks of hypotension, hyperkalemia, and renal impairment |
| digoxin + metoprolol | 9 | digoxin increases toxicity of metoprolol by unspecified interaction mechanism. Avoid or Use Alternate Drug. Can increase risk of bradycardia |
| allopurinol + captopril | 8 | captopril increases toxicity of allopurinol by Mechanism: unspecified interaction mechanism. Avoid or Use Alternate Drug. May increase risk for allergic or hypersensitivity reactions to |

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| | | allopurinol Monitor for symptoms of hypersensitivty reactions if both drugs must be used together |
| amiodarone + indapamide | 6 | amiodarone and indapamide both increase QTc interval. Avoid or Use Alternate Drug |
| aspirin + ramipril | 6 | aspirin, ramipril. pharmacodynamic antagonism. Avoid or Use Alternate Drug. Coadministration may result in a significant decrease in renal function. NSAIDs may diminish the antihypertensive effect of ACE inhibitors. The mechanism of these interactions is likely related to the ability of NSAIDs to reduce the synthesis of vasodilating renal prostaglandins |
| azilsartan + captopril | 5 | azilsartan, captopril. Either increases toxicity of the other by pharmacodynamic synergism. Avoid or Use Alternate Drug. Dual blockade of renin-angiotensin system increases risks of hypotension, hyperkalemia, and renal impairment |
| captopril + valsartan | 5 | sacubitril/valsartan, captopril. Either increases toxicity of the other by pharmacodynamic synergism. Avoid or Use Alternate Drug. Dual blockade of renin-angiotensin system increases risks of hypotension, hyperkalemia, and renal impairment |
| atorvastatin + fenofibrate | 4 | fenofibrate, atorvastatin. Either increases effects of the other by pharmacodynamic synergism. Avoid or Use Alternate Drug. Fenofibrate may further increase risk for rhabdomyolysis when added to optimal statin regimen to further decrease TG and increase HDLs |
| digoxin + omeprazole | 4 | omeprazole will increase the level or effect of digoxin by increasing gastric pH. Applies only to oral form of both agents. Avoid or Use Alternate Drug |
| allopurinol + perindopril | 3 | perindopril, allopurinol. Mechanism: unknown. Avoid or Use Alternate Drug. Risk of anaphylaxis, Stevens Johnson syndrome |
| amlodipine + nifedipine | 3 | amlodipine and nifedipine both increase anti-hypertensive channel blocking. Use Caution/Monitor |
| atorvastatin + carbamazepine | 3 | carbamazepine will decrease the level or effect of atorvastatin by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Avoid or Use Alternate Drug |
| atorvastatin + clarithromycin | 3 | clarithromycin will increase the level or effect of atorvastatin by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Avoid or Use Alternate Drug. Do not exceed atorvastatin dose of 20 mg/day when coadministered with clarithromycin |
| carbamazepine + omeprazole | 3 | carbamazepine will decrease the level or effect of omeprazole by affecting hepatic enzyme CYP2C19 metabolism. Avoid or Use Alternate Drug |
| clopidogrel + esomeprazole | 3 | esomeprazole decreases effects of clopidogrel by affecting hepatic enzyme CYP2C19 metabolism. Avoid or Use Alternate Drug. Clopidogrel efficacy may be reduced by drugs that inhibit CYP2C19. Inhibition of platelet aggregation by clopidogrel is entirely due to an active metabolite. Clopidogrel is metabolized to this active metabolite in part by CYP2C19 |
| digoxin + pantoprazole | 3 | pantoprazole will increase the level or effect of digoxin by increasing gastric pH. Applies only to oral form of both agents. Avoid or Use Alternate Drug |
| amiodarone + clarithromycin | 2 | amiodarone and clarithromycin both increase QTc interval. Avoid or Use Alternate Drug |
| aspirin + ibuprofen | 2 | ibuprofen increases toxicity of aspirin by anticoagulation. Avoid or Use Alternate Drug. increases risk of bleeding |
| | | ibuprofen decreases effects of aspirin by Other (see comment). Avoid or Use Alternate Drug. Comment: Ibuprofen decreases the antiplatelet effects of low-dose aspirin by blocking the active |

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| | | site of platelet cyclooxygenase. Administer ibuprofen 8 h before aspirin or at least 2-4 h after aspirin. The effect of other NSAIDs on aspirin is not established |
| candesartan + captopril | 2 | candesartan, captopril. Either increases toxicity of the other by pharmacodynamic synergism. Avoid or Use Alternate Drug. Dual blockade of renin-angiotensin system increases risks of hypotension, hyperkalemia, and renal impairment |
| captopril + ketoprofen | 2 | ketoprofen, captopril. pharmacodynamic antagonism. Avoid or Use Alternate Drug. Coadministration may result in a significant decrease in renal function. NSAIDs may diminish the antihypertensive effect of ACE inhibitors. The mechanism of these interactions is likely related to the ability of NSAIDs to reduce the synthesis of vasodilating renal prostaglandins |
| celecoxib + lisinopril | 2 | celecoxib, lisinopril. pharmacodynamic antagonism. Avoid or Use Alternate Drug. Coadministration may result in a significant decrease in renal function. NSAIDs may diminish the antihypertensive effect of ACE inhibitors. The mechanism of these interactions is likely related to the ability of NSAIDs to reduce the synthesis of vasodilating renal prostaglandins |
| clopidogrel + fondaparinux | 2 | fondaparinux, clopidogrel. Either increases effects of the other by pharmacodynamic synergism. Contraindicated. Enhanced risk of hemorrhage |
| digoxin + esomeprazole | 2 | esomeprazole will increase the level or effect of digoxin by increasing gastric pH. Applies only to oral form of both agents. Avoid or Use Alternate Drug |
| eplerenone + spironolactone | 2 | spironolactone, eplerenone. Mechanism: pharmacodynamic synergism. Contraindicated. Hyperkalemia |
| fenofibrate + rosuvastatin | 2 | fenofibrate, rosuvastatin. Either increases effects of the other by pharmacodynamic synergism. Avoid or Use Alternate Drug. Fenofibrate may further increase risk for rhabdomyolysis when added to optimal statin regimen to further decrease TG and increase HDLs |
| lisinopril + losartan | 2 | losartan, lisinopril. Either increases toxicity of the other by pharmacodynamic synergism. Avoid or Use Alternate Drug. Dual blockade of renin-angiotensin system increases risks of hypotension, hyperkalemia, and renal impairment |
| allopurinol + enalapril | 1 | enalapril, allopurinol. Mechanism: unknown. Avoid or Use Alternate Drug. Risk of anaphylaxis, Stevens Johnson syndrome |
| allopurinol + warfarin | 1 | allopurinol increases effects of warfarin by anticoagulation. Avoid or Use Alternate Drug |
| aluminum hydroxide + digoxin | 1 | aluminum hydroxide will increase the level or effect of digoxin by increasing gastric pH. Applies only to oral form of both agents. Avoid or Use Alternate Drug |
| amlodipine + simvastatin | 1 | amlodipine increases levels of simvastatin by Other (see comment). Avoid or Use Alternate Drug. Comment: Benefits of combination therapy should be carefully weighed against the potential risks of combination. Potential for increased risk of myopathy/rhabdomyolysis. Limit simvastatin dose to no more than 20 mg/day when used concurrently |
| apixaban + ketoprofen | 1 | ketoprofen and apixaban both increase anticoagulation. Avoid or Use Alternate Drug |
| aspirin + ketorolac | 1 | aspirin, ketorolac. Either increases toxicity of the other by pharmacodynamic synergism. Contraindicated |
| bisoprolol + timolol | 1 | bisoprolol and timolol both increase anti-hypertensive channel blocking. Avoid or Use Alternate Drug |
| bisoprolol + verapamil | 1 | verapamil, bisoprolol. Either increases toxicity of the other by unspecified interaction mechanism. Avoid or Use Alternate Drug. Can increase risk of bradycardia |

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| budesonide + clarithromycin | 1 | clarithromycin will increase the level or effect of budesonide by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Avoid or Use Alternate Drug |
| budesonide + pneumococcal vaccine polyvalent | 1 | budesonide decreases effects of pneumococcal vaccine polyvalent by pharmacodynamic antagonism. Contraindicated. Corticosteroids also increase risk of infection with concomitant live vaccines |
| captopril + ibuprofen | 1 | ibuprofen, captopril. pharmacodynamic antagonism. Avoid or Use Alternate Drug. Coadministration may result in a significant decrease in renal function. NSAIDs may diminish the antihypertensive effect of ACE inhibitors. The mechanism of these interactions is likely related to the ability of NSAIDs to reduce the synthesis of vasodilating renal prostaglandins |
| + meloxicam | 1 | meloxicam, captopril. pharmacodynamic antagonism. Avoid or Use Alternate Drug. Coadministration may result in a significant decrease in renal function. NSAIDs may diminish the antihypertensive effect of ACE inhibitors. The mechanism of these interactions is likely related to the ability of NSAIDs to reduce the synthesis of vasodilating renal prostaglandins |
| captopril + naproxen | 1 | naproxen, captopril. pharmacodynamic antagonism. Avoid or Use Alternate Drug. Coadministration may result in a significant decrease in renal function. NSAIDs may diminish the antihypertensive effect of ACE inhibitors. The mechanism of these interactions is likely related to the ability of NSAIDs to reduce the synthesis of vasodilating renal prostaglandins |
| captopril + olmesartan | 1 | olmesartan, captopril. Either increases toxicity of the other by pharmacodynamic synergism. Avoid or Use Alternate Drug. Dual blockade of renin-angiotensin system increases risks of hypotension, hyperkalemia, and renal impairment |
| captopril + telmisartan | 1 | telmisartan, captopril. Either increases toxicity of the other by pharmacodynamic synergism. Avoid or Use Alternate Drug. Dual blockade of renin-angiotensin system increases risks of hypotension, hyperkalemia, and renal impairment |
| carbamazepine + felodipine | 1 | carbamazepine will decrease the level or effect of felodipine by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Avoid or Use Alternate Drug |
| cilostazol + esomeprazole | 1 | esomeprazole increases toxicity of cilostazol by affecting hepatic enzyme CYP2C19 metabolism. Avoid or Use Alternate Drug. Decrease cilostazol dose by 50%; 3,4-dehydrocilostazol, an active metabolite, increased by 69% as a result of omeprazole inhibition of CYP2C19 |
| clarithromycin + enoxaparin | 1 | clarithromycin increases effects of enoxaparin by decreasing metabolism. Avoid or Use Alternate Drug |
| clopidogrel + rabeprazole | 1 | rabeprazole decreases effects of clopidogrel by affecting hepatic enzyme CYP2C19 metabolism. Avoid or Use Alternate Drug. Clopidogrel efficacy may be reduced by drugs that inhibit CYP2C19. Inhibition of platelet aggregation by clopidogrel is entirely due to an active metabolite. Clopidogrel is metabolized to this active metabolite in part by CYP2C19 |
| dabigatran + heparin | 1 | dabigatran and heparin both increase anticoagulation. Avoid or Use Alternate Drug. Both drugs have the potential to cause bleeding. Concomitant use may increase risk of bleeding |
| digoxin + nebivolol | 1 | digoxin, nebivolol. Either decreases toxicity of the other by unspecified interaction mechanism. Avoid or Use Alternate Drug. Can increase risk of bradycardia |
| digoxin + verapamil | 1 | verapamil increases levels of digoxin by decreasing renal clearance. Avoid or Use Alternate Drug |
| enalapril + meloxicam | 1 | meloxicam, enalapril. pharmacodynamic antagonism. Avoid or Use Alternate Drug. Coadministration may result in a significant decrease in renal function. NSAIDs may diminish |

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| | | the antihypertensive effect of ACE inhibitors. The mechanism of these interactions is likely related to the ability of NSAIDs to reduce the synthesis of vasodilating renal prostaglandins |
| formoterol + indapamide | 1 | formoterol and indapamide both increase QTc interval. Avoid or Use Alternate Drug |
| ibuprofen + lisinopril | 1 | ibuprofen, lisinopril. pharmacodynamic antagonism. Avoid or Use Alternate Drug. Coadministration may result in a significant decrease in renal function. NSAIDs may diminish the antihypertensive effect of ACE inhibitors. The mechanism of these interactions is likely related to the ability of NSAIDs to reduce the synthesis of vasodilating renal prostaglandins |
| ibuprofen + methotrexate | 1 | ibuprofen increases levels of methotrexate by decreasing renal clearance. Avoid or Use Alternate Drug. Concomitant administration of NSAIDs with high dose methotrexate has been reported to elevate and prolong serum methotrexate levels, resulting in deaths from severe hematologic and GI toxicity. NSAIDs may reduce tubular secretion of methotrexate and enhance toxicity |
| ivabradine + ticagrelor | 1 | ticagrelor will increase the level or effect of ivabradine by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Avoid or Use Alternate Drug. Avoid coadministration of ivabradine with moderate CYP3A4 inhibitors |
| ketoprofen + perindopril | 1 | ketoprofen, perindopril. pharmacodynamic antagonism. Avoid or Use Alternate Drug. Coadministration may result in a significant decrease in renal function. NSAIDs may diminish the antihypertensive effect of ACE inhibitors. The mechanism of these interactions is likely related to the ability of NSAIDs to reduce the synthesis of vasodilating renal prostaglandins |
| ketoprofen + ramipril | 1 | ketoprofen, ramipril. pharmacodynamic antagonism. Avoid or Use Alternate Drug. Coadministration may result in a significant decrease in renal function. NSAIDs may diminish the antihypertensive effect of ACE inhibitors. The mechanism of these interactions is likely related to the ability of NSAIDs to reduce the synthesis of vasodilating renal prostaglandins |
| lisinopril + meloxicam | 1 | meloxicam, lisinopril. pharmacodynamic antagonism. Avoid or Use Alternate Drug. Coadministration may result in a significant decrease in renal function. NSAIDs may diminish the antihypertensive effect of ACE inhibitors. The mechanism of these interactions is likely related to the ability of NSAIDs to reduce the synthesis of vasodilating renal prostaglandins |
| lisinopril + sacubitril/valsartan | 1 | sacubitril/valsartan, lisinopril. Either increases toxicity of the other by pharmacodynamic synergism. Avoid or Use Alternate Drug. Dual blockade of renin-angiotensin system increases risks of hypotension, hyperkalemia, and renal impairment |
| lisinopril + valsartan | 1 | valsartan, lisinopril. Either increases toxicity of the other by pharmacodynamic synergism. Avoid or Use Alternate Drug. Dual blockade of renin-angiotensin system increases risks of hypotension, hyperkalemia, and renal impairment |
| losartan + perindopril | 1 | losartan, perindopril. Either increases toxicity of the other by pharmacodynamic synergism. Avoid or Use Alternate Drug. Dual blockade of renin-angiotensin system increases risks of hypotension, hyperkalemia, and renal impairment |
| niacin + rosuvastatin | 1 | niacin, rosuvastatin. Either increases toxicity of the other by pharmacodynamic synergism. Avoid or Use Alternate Drug. Increased risk of rhabdomyolysis (>1 g/day niacin) |

Note: Impact of drug–drug interactions associated with the combinations “aspirin + captopril” and “aspirin + enalapril” may be considered insignificant due to the use of low-dose aspirin in the majority of cases. Administration of aspirin at doses less than 300 mg per day has little effect on the effectiveness of captopril and enalapril. Administration of aspirin in higher doses reduces the effectiveness of captopril and enalapril.

**Table S10.** Drug combinations resulting in potential monitor-closely drug–drug interactions in the list of prescribed medications in patients with cardiovascular diseases according to data derived from the electronic health records ($n$ = 1030) established in 2018–2023.

| Drug combinations | n | Potential monitor-closely drug-drug interactions (P-list) |
|---|---|---|
| aspirin + bisoprolol | 412 | aspirin decreases effects of bisoprolol by pharmacodynamic antagonism. Use Caution/Monitor. Long term (>1 wk) NSAID use. NSAIDs decrease prostaglandin synthesis |
| aspirin + spironolactone | 140 | spironolactone and aspirin both increase serum potassium. Modify Therapy/Monitor Closely |
| aspirin + losartan | 129 | aspirin decreases effects of losartan by pharmacodynamic antagonism. Modify Therapy/Monitor Closely. NSAIDs decrease synthesis of vasodilating renal prostaglandins, and thus affect fluid homeostasis and may diminish antihypertensive effect |
| bisoprolol + torsemide | 117 | bisoprolol increases and torsemide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| aspirin + metoprolol | 112 | aspirin decreases effects of metoprolol by pharmacodynamic antagonism. Use Caution/Monitor. Long term (>1 wk) NSAID use. NSAIDs decrease prostaglandin synthesis |
| aspirin + torsemide | 103 | aspirin increases and torsemide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| spironolactone + torsemide | 94 | spironolactone increases and torsemide decreases serum potassium. Effect of interaction is not clear, use caution. Modify Therapy/Monitor Closely |
| aspirin + captopril * | 84 | captopril, aspirin. Either increases toxicity of the other by Other (see comment). Use Caution/Monitor. Comment: May result in renal function deterioration, particularly with high dose aspirin, elderly or volume depleted individuals |
| aspirin + nitroglycerin | 82 | aspirin increases effects of nitroglycerin sublingual by additive vasodilation. Use Caution/Monitor. Vasodilatory and hemodynamic effects of NTG may be enhanced by coadministration with aspirin (additive effect desirable for emergent treatment) |
| aspirin + perindopril | 78 | perindopril, aspirin. Either increases toxicity of the other by Other (see comment). Use Caution/Monitor. Comment: May result in renal function deterioration, particularly with high doses of aspirin,in elderly or volume depleted individuals |
| bisoprolol + spironolactone | 74 | bisoprolol and spironolactone both increase serum potassium. Modify Therapy/Monitor Closely |
| amiodarone + atorvastatin | 66 | amiodarone will increase the level or effect of atorvastatin by P-glycoprotein (MDR1) efflux transporter. Use Caution/Monitor |
| amlodipine + bisoprolol | 64 | bisoprolol, amlodipine. Either increases effects of the other by pharmacodynamic synergism. Use Caution/Monitor. Both drugs lower blood pressure |
| aspirin + lisinopril | 63 | lisinopril, aspirin. Either increases toxicity of the other by Other (see comment). Use Caution/Monitor. Comment: May result in renal function deterioration, particularly with high dose aspirin, in elderly or volume depleted individuals |
| aspirin + clopidogrel | 61 | aspirin, clopidogrel. Either increases toxicity of the other by pharmacodynamic synergism. Use Caution/Monitor. The need for simultaneous use of low-dose aspirin and anticoagulant or antiplatelet agents are common for patients with cardiovascular disease; monitor closely |
| digoxin + spironolactone | 60 | spironolactone, digoxin. Mechanism: decreasing renal clearance. Use Caution/Monitor. False digoxin assay results may be obtained |

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| captopril + torsemide | 59 | captopril, torsemide. Either increases toxicity of the other by Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of acute hypotension, renal insufficiency. Monitor blood pressure and renal function |
| aspirin + ticagrelor | 58 | aspirin, ticagrelor. Other (see comment). Use Caution/Monitor. Comment: Maintenance doses of aspirin above 100 mg decreases effectiveness of ticagrelor. Therefore, after the initial loading dose of aspirin (usually 325 mg), use ticagrelor with a maintenance dose of aspirin of 75-100 mg |
| bisoprolol + losartan | 58 | bisoprolol, losartan. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of fetal compromise if given during pregnancy |
| atorvastatin + sacubitril/valsartan | 48 | losartan and bisoprolol both increase serum potassium. Use Caution/Monitor |
| amiodarone + bisoprolol | 46 | amiodarone, bisoprolol. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of cardiotoxicity with bradycardia |
| captopril + spironolactone | 45 | captopril, spironolactone. Either increases toxicity of the other by Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Both drugs lower blood pressure. Risk of hyperkalemia. Monitor blood pressure and potassium |
| metoprolol + torsemide | 45 | metoprolol increases and torsemide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| | | perindopril, torsemide. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of acute hypotension, renal insufficiency |
| digoxin + torsemide | 42 | digoxin increases and torsemide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| aspirin + indapamide | 36 | aspirin increases and indapamide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| aspirin + sacubitril/valsartan | 33 | aspirin decreases effects of sacubitril/valsartan by pharmacodynamic antagonism. Modify Therapy/Monitor Closely. NSAIDs decrease synthesis of vasodilating renal prostaglandins, and thus affect fluid homeostasis and may diminish antihypertensive effect |
| perindopril + spironolactone | 33 | perindopril, spironolactone. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of hyperkalemia |
| amlodipine + nitroglycerin | 32 | amlodipine, nitroglycerin sublingual. Either increases toxicity of the other by additive vasodilation. Modify Therapy/Monitor Closely. Marked orthostatic hypotension reported with concomitant use |
| bisoprolol + digoxin | 32 | bisoprolol increases effects of digoxin by pharmacodynamic synergism. Use Caution/Monitor. Enhanced bradycardia |
| bisoprolol + indapamide | 31 | bisoprolol increases and indapamide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| lisinopril + torsemide | 31 | lisinopril, torsemide. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of acute hypotension, renal insufficiency |
| amiodarone + losartan | 30 | amiodarone will increase the level or effect of losartan by affecting hepatic enzyme CYP2C9/10 metabolism. Use Caution/Monitor. May inhibit the conversion of losartan to its active metabolite E-3174. Importance of interaction not established; monitor individual therapeutic response to determine losartan dosage |

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| amiodarone + metoprolol | 30 | amiodarone, metoprolol. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of cardiotoxicity with bradycardia |
| | | amiodarone will increase the level or effect of metoprolol by affecting hepatic enzyme CYP2D6 metabolism. Use Caution/Monitor. Monitor cardiac function carefully and observe for signs of bradycardia or heart block when amiodarone and a beta adrenergic blocker are coadministered. Amiodarone should be used with caution in patients receiving a beta adrenergic blocker, particularly if there is suspicion of underlying dysfunction of the sinus node, such as bradycardia or sick sinus syndrome, or if there is partial AV block |
| aspirin + fosinopril | 30 | fosinopril, aspirin. Either increases toxicity of the other by Other (see comment). Use Caution/Monitor. Comment: May result in renal function deterioration, particularly with high dose aspirin, in elderly or volume depleted individuals |
| losartan + metoprolol | 30 | losartan and metoprolol both increase serum potassium. Use Caution/Monitor |
| metoprolol + spironolactone | 28 | metoprolol and spironolactone both increase serum potassium. Modify Therapy/Monitor Closely |
| aspirin + valsartan | 27 | aspirin decreases effects of valsartan by pharmacodynamic antagonism. Modify Therapy/Monitor Closely. NSAIDs decrease synthesis of vasodilating renal prostaglandins, and thus affect fluid homeostasis and may diminish antihypertensive effect |
| aspirin + valsartan | 27 | valsartan and aspirin both increase serum potassium. Use Caution/Monitor |
| amiodarone + captopril | 25 | amiodarone, captopril. Either increases effects of the other by pharmacodynamic synergism. Use Caution/Monitor. Both drugs lower blood pressure. Monitor blood pressure |
| amiodarone + rivaroxaban | 25 | amiodarone increases levels of rivaroxaban by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Use Caution/Monitor. Patients with renal impairment receiving rivaroxaban with drugs that are combined P-gp and weak or moderate CYP3A4 inhibitors may have significant increases in exposure compared with patients with normal renal function and no inhibitor use, since both pathways of rivaroxaban elimination are affected. Since these increases may increase bleeding risk, use rivaroxaban in this situation only if the potential benefit justifies the potential risk |
| losartan + torsemide | 25 | losartan increases and torsemide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| eplerenone + perindopril | 24 | perindopril, eplerenone. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of hyperkalemia |
| fosinopril + torsemide | 23 | fosinopril, torsemide. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of acute hypotension, renal insufficiency |
| aspirin + enalapril * | 22 | enalapril, aspirin. Either increases toxicity of the other by Other (see comment). Use Caution/Monitor. Comment: May result in renal function deterioration, particularly with high dose aspirin, in elderly or volume depleted individuals |
| aspirin + rivaroxaban | 22 | aspirin, rivaroxaban. Either increases toxicity of the other by anticoagulation. Use Caution/Monitor. Both drugs have the potential to cause bleeding. The need for simultaneous use of low-dose aspirin (<100 mg/day) with anticoagulants are common for patients with cardiovascular disease, but may result in increased bleeding; monitor closely. Promptly evaluate any signs or symptoms of blood loss if treated concomitantly with low-dose aspirin. Avoid coadministration with chronic use of higher dose aspirin |

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| lisinopril + spironolactone | 22 | lisinopril, spironolactone. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of hyperkalemia |
| aspirin + candesartan | 21 | aspirin decreases effects of candesartan by pharmacodynamic antagonism. Modify Therapy/Monitor Closely. NSAIDs decrease synthesis of vasodilating renal prostaglandins, and thus affect fluid homeostasis and may diminish antihypertensive effect |
| aspirin + candesartan | 21 | candesartan and aspirin both increase serum potassium. Use Caution/Monitor |
| sacubitril/valsartan + torsemide | 21 | sacubitril/valsartan increases and torsemide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| atorvastatin + valsartan | 20 | atorvastatin will increase the level or effect of valsartan by Other (see comment). Use Caution/Monitor. The results from an in vitro study with human liver tissue indicate that valsartan is a substrate of the hepatic uptake transporter OATP1B1; coadministration with OATP1B1 inhibitors may increase valsartan systemic exposure |
| | | valsartan increases toxicity of atorvastatin by Other (see comment). Use Caution/Monitor. Comment: OATP1B1 inhibitors may increase risk of myopathy |
| atorvastatin + digoxin | 19 | atorvastatin will increase the level or effect of digoxin by P-glycoprotein (MDR1) efflux transporter. Use Caution/Monitor |
| captopril + eplerenone | 19 | captopril, eplerenone. Either increases toxicity of the other by Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of hyperkalemia. Monitor potassium |
| clopidogrel + pantoprazole | 19 | pantoprazole decreases effects of clopidogrel by affecting hepatic enzyme CYP2C19 metabolism. Use Caution/Monitor. Clopidogrel efficacy may be reduced by drugs that inhibit CYP2C19. Inhibition of platelet aggregation by clopidogrel is entirely due to the active clopidogrel metabolite. Clopidogrel is metabolized in part by CYP2C19. Pantoprazole prescribing information state that coadministration with clopidogrel had no clinically important effect on exposure to clopidogrel active metabolite; no dose adjustment of clopidogrel is required |
| furosemide + spironolactone | 19 | spironolactone increases and furosemide decreases serum potassium. Effect of interaction is not clear, use caution. Modify Therapy/Monitor Closely |
| bisoprolol + telmisartan | 18 | bisoprolol, telmisartan. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of fetal compromise if given during pregnancy |
| | | telmisartan and bisoprolol both increase serum potassium. Use Caution/Monitor |
| digoxin + metoprolol | 18 | metoprolol increases effects of digoxin by pharmacodynamic synergism. Use Caution/Monitor. Enhanced bradycardia |
| | | metoprolol and digoxin both increase serum potassium. Use Caution/Monitor |
| metoprolol + sacubitril/valsartan | 18 | metoprolol, sacubitril/valsartan. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of fetal compromise if given during pregnancy |
| | | sacubitril/valsartan and metoprolol both increase serum potassium. Use Caution/Monitor |
| aspirin + azilsartan | 16 | aspirin, azilsartan. Either increases toxicity of the other by Other (see comment). Use Caution/Monitor. Comment: May result in renal function deterioration, particularly in elderly or volume depleted individuals |
| | | aspirin decreases effects of azilsartan by pharmacodynamic antagonism. Modify Therapy/Monitor Closely. NSAIDs decrease synthesis of vasodilating renal prostaglandins, and thus affect fluid homeostasis and may diminish antihypertensive effect |

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| bisoprolol + sacubitril/valsartan | 16 | bisoprolol, sacubitril/valsartan. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of fetal compromise if given during pregnancy |
| | | sacubitril/valsartan and bisoprolol both increase serum potassium. Use Caution/Monitor |
| clopidogrel + rivaroxaban | 16 | rivaroxaban, clopidogrel. Other (see comment). Use Caution/Monitor. Comment: Avoid concurrent administration of clopidogrel with rivaroxaban unless the benefit outweighs the risk of increased bleeding |
| eplerenone + sacubitril/valsartan | 16 | sacubitril/valsartan, eplerenone. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of hyperkalemia |
| aspirin + furosemide | 15 | aspirin increases and furosemide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| | | aspirin decreases effects of telmisartan by pharmacodynamic antagonism. Modify Therapy/Monitor Closely. NSAIDs decrease synthesis of vasodilating renal prostaglandins, and thus affect fluid homeostasis and may diminish antihypertensive effect |
| | | telmisartan, aspirin. Either increases toxicity of the other by Other (see comment). Use Caution/Monitor. Comment: May result in renal function deterioration, particularly in elderly or volume depleted individuals |
| captopril + indapamide | 15 | indapamide, captopril. Either increases effects of the other by pharmacodynamic synergism. Use Caution/Monitor. Both drugs lower blood pressure. Increased risk of nephrotoxicity. Monitor blood pressure and renal function |
| ipratropium + tiotropium | 15 | ipratropium and tiotropium both decrease cholinergic effects/transmission. Use Caution/Monitor. Due to the poor systemic absorption of ipratropium, interaction unlikely at regularly recommended dosages |
| aspirin + carvedilol | 14 | aspirin decreases effects of carvedilol by pharmacodynamic antagonism. Use Caution/Monitor. Long term (>1 wk) NSAID use. NSAIDs decrease prostaglandin synthesis |
| | | carvedilol and aspirin both increase serum potassium. Use Caution/Monitor |
| aspirin + hydrochlorothiazide | 14 | aspirin increases and hydrochlorothiazide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| aspirin + insulin | 14 | aspirin increases effects of insulin regular human by pharmacodynamic synergism. Modify Therapy/Monitor Closely. Coadministration of insulin with high doses of salicylates (3 g/day or more) may increase risk for hypoglycemia. Insulin dose adjustment and increased frequency of glucose monitoring may be required |
| bisoprolol + candesartan | 14 | bisoprolol, candesartan. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of fetal compromise if given during pregnancy |
| | | candesartan and bisoprolol both increase serum potassium. Use Caution/Monitor |
| rosuvastatin + warfarin | 14 | rosuvastatin increases effects of warfarin by anticoagulation. Use Caution/Monitor |
| atorvastatin + dabigatran | 13 | atorvastatin will increase the level or effect of dabigatran by P-glycoprotein (MDR1) efflux transporter. Use Caution/Monitor. Atrial fibrillation: Avoid coadministering dabigatran with P-gp inhibitors if CrCl <30 mL/min. DVT/PE treatment: Avoid coadministering dabigatran with P-gp inhibitors if CrCl <50 mL/min |
| enalapril + torsemide | 13 | enalapril, torsemide. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of acute hypotension, renal insufficiency |

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| amoxicillin + aspirin | 12 | amoxicillin, aspirin. Either increases levels of the other by plasma protein binding competition. Use Caution/Monitor |
| | | amoxicillin, aspirin. Either increases levels of the other by decreasing renal clearance. Use Caution/Monitor |
| atorvastatin + verapamil | 12 | verapamil will increase the level or effect of atorvastatin by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Use Caution/Monitor |
| | | verapamil will increase the level or effect of atorvastatin by P-glycoprotein (MDR1) efflux transporter. Use Caution/Monitor |
| bisoprolol + formoterol | 12 | bisoprolol decreases effects of formoterol by pharmacodynamic antagonism. Use Caution/Monitor |
| | | bisoprolol increases and formoterol decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| bisoprolol + furosemide | 12 | bisoprolol increases and furosemide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| insulin + metformin | 12 | metformin, insulin glargine. Either increases effects of the other by pharmacodynamic synergism. Use Caution/Monitor. Antidiabetic agents are often used in combination; dosage adjustments may be required when initiating or discontinuing antidiabetic agents |
| losartan + spironolactone | 12 | losartan and spironolactone both increase serum potassium. Modify Therapy/Monitor Closely |
| metformin + torsemide | 12 | torsemide decreases effects of metformin by pharmacodynamic antagonism. Use Caution/Monitor |
| bisoprolol + hydrochlorothiazide | 11 | bisoprolol increases and hydrochlorothiazide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| enalapril + spironolactone | 11 | enalapril, spironolactone. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of hyperkalemia |
| fosinopril + spironolactone | 11 | fosinopril, spironolactone. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of hyperkalemia |
| indapamide + losartan | 11 | losartan increases and indapamide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| lisinopril + metformin | 11 | lisinopril increases toxicity of metformin by unspecified interaction mechanism. Use Caution/Monitor. Increases risk for hypoglycemia and lactic acidosis |
| losartan + omeprazole | 11 | omeprazole will increase the level or effect of losartan by affecting hepatic enzyme CYP2C9/10 metabolism. Use Caution/Monitor. May inhibit the conversion of losartan to its active metabolite E-3174. Importance of interaction not established; monitor individual therapeutic response to determine losartan dosage |
| amlodipine + metformin | 10 | amlodipine decreases effects of metformin by pharmacodynamic antagonism. Use Caution/Monitor. Patient should be closely observed for loss of blood glucose control; when drugs are withdrawn from a patient receiving metformin, patient should be observed closely for hypoglycemia |
| aspirin + heparin | 10 | aspirin, heparin. Either increases toxicity of the other by anticoagulation. Use Caution/Monitor. The need for simultaneous use of low-dose aspirin and anticoagulant or antiplatelet agents are common for patients with cardiovascular disease; monitor closely |
| aspirin + heparin | 10 | heparin and aspirin both increase anticoagulation. Modify Therapy/Monitor Closely |

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| aspirin + nebivolol | 10 | aspirin decreases effects of nebivolol by pharmacodynamic antagonism. Use Caution/Monitor. Long term (>1 wk) NSAID use. NSAIDs decrease prostaglandin synthesis |
| | | nebivolol and aspirin both increase serum potassium. Use Caution/Monitor |
| aspirin + warfarin | 10 | aspirin increases effects of warfarin by anticoagulation. Modify Therapy/Monitor Closely. Avoid coadministration of chronic high-dose aspirin. Aspirin's antiplatelet properties may increase anticoagulation effect of warfarin. The need for simultaneous use of low-dose aspirin and warfarin is common for patients with cardiovascular disease |
| atorvastatin + nifedipine | 10 | nifedipine will decrease the level or effect of atorvastatin by P-glycoprotein (MDR1) efflux transporter. Use Caution/Monitor |
| | | nifedipine will increase the level or effect of atorvastatin by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Use Caution/Monitor |
| bisoprolol + valsartan | 10 | bisoprolol, valsartan. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of fetal compromise if given during pregnancy |
| | | valsartan and bisoprolol both increase serum potassium. Use Caution/Monitor |
| eplerenone + fosinopril | 10 | fosinopril, eplerenone. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of hyperkalemia |
| formoterol + torsemide | 10 | formoterol and torsemide both decrease serum potassium. Use Caution/Monitor |
| indapamide + metoprolol | 10 | metoprolol increases and indapamide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| sacubitril/valsartan + spironolactone | 10 | sacubitril/valsartan and spironolactone both increase serum potassium. Modify Therapy/Monitor Closely |
| amiodarone + warfarin | 9 | amiodarone will increase the level or effect of warfarin by affecting hepatic enzyme CYP2C9/10 metabolism. Modify Therapy/Monitor Closely. Coadministration increases INR by 100% after 3-4 days. Reduce warfarin dose by one-third to one-half and monitor INR |
| apixaban + aspirin | 9 | aspirin and apixaban both increase anticoagulation. Modify Therapy/Monitor Closely. Both drugs have the potential to cause bleeding. The need for simultaneous use of low-dose aspirin (<100 mg/day) with anticoagulants are common for patients with cardiovascular disease, but may result in increased bleeding; monitor closely. Promptly evaluate any signs or symptoms of blood loss if treated concomitantly with low-dose aspiriin. Avoid coadministration with chronic use of higher dose aspirin. In 1 trial (APPRAISE-2), therapy was terminated because of significantly increased bleeding when apixaban was administered with dual antiplatelet therapy (eg, aspirin plus clopidogrel) compared with single antiplatelet treatment |
| bisoprolol + ivabradine | 9 | ivabradine, bisoprolol. Either increases effects of the other by pharmacodynamic synergism. Modify Therapy/Monitor Closely. Most patients receiving ivabradine will also be treated with a beta-blocker. The risk of bradycardia increases with coadministration of drugs that slow heart rate (eg, digoxin, amiodarone, beta-blockers). Monitor heart rate in patients taking ivabradine with other negative chronotropes |
| | | meloxicam decreases effects of bisoprolol by pharmacodynamic antagonism. Use Caution/Monitor. Long term (>1 wk) NSAID use. NSAIDs decrease prostaglandin synthesis |
| | | bisoprolol and meloxicam both increase serum potassium. Use Caution/Monitor |

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| aspirin + enoxaparin | 8 | enoxaparin and aspirin both increase anticoagulation. Use Caution/Monitor. Additive effects are intended when both drugs are prescribed as indicated for unstable angina, non-Q-wave MI, and STEMI |
| | | aspirin, enoxaparin. Either increases toxicity of the other by pharmacodynamic synergism. Use Caution/Monitor. The need for simultaneous use of low-dose aspirin and anticoagulant or antiplatelet agents are common for patients with cardiovascular disease; monitor closely |
| atorvastatin + budesonide | 8 | atorvastatin will increase the level or effect of budesonide by P-glycoprotein (MDR1) efflux transporter. Use Caution/Monitor |
| bisoprolol + felodipine | 8 | bisoprolol and felodipine both increase anti-hypertensive channel blocking. Modify Therapy/Monitor Closely |
| digoxin + furosemide | 8 | furosemide increases effects of digoxin by pharmacodynamic synergism. Use Caution/Monitor. Hypokalemia increases digoxin effects |
| | | digoxin increases and furosemide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| digoxin + perindopril | 8 | perindopril increases levels of digoxin by unspecified interaction mechanism. Use Caution/Monitor |
| formoterol + spironolactone | 8 | spironolactone increases and formoterol decreases serum potassium. Effect of interaction is not clear, use caution. Modify Therapy/Monitor Closely |
| metformin + perindopril | 8 | perindopril increases toxicity of metformin by unspecified interaction mechanism. Use Caution/Monitor. Increases risk for hypoglycemia and lactic acidosis |
| omeprazole + warfarin | 8 | omeprazole will increase the level or effect of warfarin by Other (see comment). Use Caution/Monitor. Warfarin's less potent R-enantiomer is metabolized in part by CYP3A4 (and also CYP1A2 and CYP2C19). Monitor INR more frequently if coadministered with inhibitors of these isoenzymes and adjust warfarin dose if needed |
| aspirin + formoterol | 7 | aspirin increases and formoterol decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| captopril + digoxin | 7 | captopril increases levels of digoxin by unspecified interaction mechanism. Use Caution/Monitor |
| losartan + warfarin | 7 | losartan will increase the level or effect of warfarin by affecting hepatic enzyme CYP2C9/10 metabolism. Use Caution/Monitor |
| spironolactone + valsartan | 7 | valsartan and spironolactone both increase serum potassium. Modify Therapy/Monitor Closely |
| torsemide + valsartan | 7 | valsartan increases and torsemide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| amiodarone + dabigatran | 6 | amiodarone will increase the level or effect of dabigatran by P-glycoprotein (MDR1) efflux transporter. Use Caution/Monitor. Atrial fibrillation: Avoid coadministering dabigatran with P-gp inhibitors if CrCl <30 mL/min. DVT/PE treatment: Avoid coadministering dabigatran with P-gp inhibitors if CrCl <50 mL/min |
| aspirin + chlorthalidone | 6 | aspirin increases and chlorthalidone decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| aspirin + digoxin | 6 | aspirin and digoxin both increase serum potassium. Use Caution/Monitor |

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| aspirin + olmesartan | 6 | olmesartan, aspirin. Either increases toxicity of the other by Other (see comment). Use Caution/Monitor. Comment: May result in renal function deterioration, particularly in elderly or volume depleted individuals |
| | | aspirin decreases effects of olmesartan by pharmacodynamic antagonism. Modify Therapy/Monitor Closely. NSAIDs decrease synthesis of vasodilating renal prostaglandins, and thus affect fluid homeostasis and may diminish antihypertensive effect |
| | | olmesartan and aspirin both increase serum potassium. Use Caution/Monitor |
| aspirin + ramipril | 6 | ramipril, aspirin. Either increases toxicity of the other by Other (see comment). Use Caution/Monitor. Comment: May result in renal function deterioration, particularly with high doses of aspirin, in elderly or volume depleted individuals |
| atorvastatin + ranolazine | 6 | ranolazine will increase the level or effect of atorvastatin by P-glycoprotein (MDR1) efflux transporter. Use Caution/Monitor |
| | | ranolazine increases toxicity of atorvastatin by Other (see comment). Modify Therapy/Monitor Closely. Comment: OATP1B1 inhibitors may increase risk of myopathy |
| bisoprolol + lornoxicam | 6 | lornoxicam decreases effects of bisoprolol by pharmacodynamic antagonism. Use Caution/Monitor. Long term (>1 wk) NSAID use. NSAIDs decrease prostaglandin synthesis |
| | | bisoprolol and lornoxicam both increase serum potassium. Use Caution/Monitor |
| captopril + furosemide | 6 | captopril, furosemide. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of acute hypotension, renal insufficiency |
| eplerenone + lisinopril | 6 | lisinopril, eplerenone. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of hyperkalemia |
| eplerenone + ramipril | 6 | ramipril, eplerenone. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of hyperkalemia |
| ferrous sulfate + omeprazole | 6 | omeprazole will decrease the level or effect of ferrous sulfate by increasing gastric pH. Applies only to oral form of both agents. Use Caution/Monitor |
| hydrochlorothiazide + metoprolol | 6 | hydrochlorothiazide, metoprolol. Either increases toxicity of the other by Other (see comment). Modify Therapy/Monitor Closely. Comment: May cause idiosyncratic reaction, resulting in acute transient myopia and acute angle-closure glaucoma, which can lead to permanent vision loss |
| | | metoprolol increases and hydrochlorothiazide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| indapamide + torsemide | 6 | torsemide and indapamide both decrease serum potassium. Use Caution/Monitor |
| ivabradine + metoprolol | 6 | ivabradine, metoprolol. Either increases effects of the other by pharmacodynamic synergism. Modify Therapy/Monitor Closely. Most patients receiving ivabradine will also be treated with a beta-blocker. The risk of bradycardia increases with coadministration of drugs that slow heart rate (eg, digoxin, amiodarone, beta-blockers). Monitor heart rate in patients taking ivabradine with other negative chronotropes |
| losartan + sotalol | 6 | sotalol, losartan. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of fetal compromise if given during pregnancy |
| | | losartan and sotalol both increase serum potassium. Use Caution/Monitor |
| amiodarone + metformin | 5 | amiodarone will increase the level or effect of metformin by basic (cationic) drug competition for renal tubular clearance. Use Caution/Monitor |

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| aspirin + dabigatran | 5 | dabigatran and aspirin both increase anticoagulation. Modify Therapy/Monitor Closely. Both drugs have the potential to cause bleeding. The need for simultaneous use of low-dose aspirin (<100 mg/day) with anticoagulants are common for patients with cardiovascular disease, but may result in increased bleeding; monitor closely. Promptly evaluate any signs or symptoms of blood loss if treated concomitantly with low-dose aspirin. Avoid coadministration with chronic use of higher dose aspirin |
| candesartan + torsemide | 5 | candesartan increases and torsemide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| captopril + metformin | 5 | captopril increases toxicity of metformin by unspecified interaction mechanism. Use Caution/Monitor. Increases risk for hypoglycemia and lactic acidosis |
| clopidogrel + warfarin | 5 | clopidogrel, warfarin. Either increases effects of the other by pharmacodynamic synergism. Modify Therapy/Monitor Closely. Drugs with antiplatelet properties may increase anticoagulation effect of warfarin |
| digoxin + enalapril | 5 | enalapril increases levels of digoxin by unspecified interaction mechanism. Use Caution/Monitor |
| empagliflozin + torsemide | 5 | empagliflozin, torsemide. Either increases effects of the other by pharmacodynamic synergism. Use Caution/Monitor. Coadministration of empagliflozin with diuretics results in increased urine volume and frequency of voids, which might enhance the potential for volume depletion |
| formoterol + moxonidine | 5 | moxonidine increases and formoterol decreases sedation. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| furosemide + losartan | 5 | losartan increases and furosemide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| insulin + losartan | 5 | losartan increases effects of insulin regular human by unspecified interaction mechanism. Use Caution/Monitor. Concomitant use of insulin and ARBs may require insulin dosage adjustment and increased glucose monitoring |
| aceclofenac + bisoprolol | 4 | aceclofenac decreases effects of bisoprolol by pharmacodynamic antagonism. Use Caution/Monitor. Long term (>1 wk) NSAID use. NSAIDs decrease prostaglandin synthesis |
| | | bisoprolol and aceclofenac both increase serum potassium. Use Caution/Monitor |
| amiodarone + budesonide | 4 | budesonide will decrease the level or effect of amiodarone by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Use Caution/Monitor |
| | | amiodarone will increase the level or effect of budesonide by P-glycoprotein (MDR1) efflux transporter. Use Caution/Monitor |
| amlodipine + carvedilol | 4 | carvedilol and amlodipine both increase anti-hypertensive channel blocking. Modify Therapy/Monitor Closely |
| aspirin + atenolol | 4 | aspirin decreases effects of atenolol by pharmacodynamic antagonism. Use Caution/Monitor. Long term (>1 wk) NSAID use. NSAIDs decrease prostaglandin synthesis |
| aspirin + atenolol | 4 | atenolol and aspirin both increase serum potassium. Use Caution/Monitor |
| aspirin + doxazosin | 4 | aspirin decreases effects of doxazosin by pharmacodynamic antagonism. Use Caution/Monitor. NSAIDs decrease prostaglandin synthesis |
| aspirin + ketoprofen | 4 | aspirin and ketoprofen both increase anticoagulation. Use Caution/Monitor |
| | | aspirin and ketoprofen both increase serum potassium. Use Caution/Monitor |
| aspirin + ketorolac | 4 | aspirin and ketorolac both increase anticoagulation. Use Caution/Monitor |

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| | | aspirin and ketorolac both increase serum potassium. Use Caution/Monitor |
| aspirin + meloxicam | 4 | aspirin and meloxicam both increase anticoagulation. Use Caution/Monitor |
| | | aspirin and meloxicam both increase serum potassium. Use Caution/Monitor |
| aspirin + sotalol | 4 | sotalol and aspirin both increase serum potassium. Use Caution/Monitor |
| | | aspirin decreases effects of sotalol by pharmacodynamic antagonism. Use Caution/Monitor. Long term (>1 wk) NSAID use. NSAIDs decrease prostaglandin synthesis |
| atenolol + sacubitril/valsartan | 4 | atenolol, sacubitril/valsartan. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of fetal compromise if given during pregnancy |
| | | sacubitril/valsartan and atenolol both increase serum potassium. Use Caution/Monitor |
| bisoprolol + chlorthalidone | 4 | bisoprolol increases and chlorthalidone decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| bisoprolol + nifedipine | 4 | bisoprolol, nifedipine. Either decreases effects of the other by pharmacodynamic synergism. Use Caution/Monitor. Both drugs lower blood pressure |
| bisoprolol + olmesartan | 4 | bisoprolol, olmesartan. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of fetal compromise if given during pregnancy |
| | | olmesartan and bisoprolol both increase serum potassium. Use Caution/Monitor |
| calcium carbonate + metoprolol | 4 | calcium carbonate decreases effects of metoprolol by unspecified interaction mechanism. Use Caution/Monitor. |
| | | calcium carbonate decreases levels of metoprolol by inhibition of GI absorption. Applies only to oral form of both agents. Use Caution/Monitor. Separate by 2 hours |
| celecoxib + meloxicam | 4 | calcium carbonate decreases effects of metoprolol by unspecified interaction mechanism. Use Caution/Monitor |
| | | calcium carbonate decreases levels of metoprolol by inhibition of GI absorption. Applies only to oral form of both agents. Use Caution/Monitor. Separate by 2 hours |
| ciprofloxacin + omeprazole | 4 | omeprazole will decrease the level or effect of ciprofloxacin by unknown mechanism. Use Caution/Monitor. Absorption of the ciprofloxacin ER tablet was slightly diminished (20%) when coadministered with omeprazole |
| clopidogrel + ticagrelor | 4 | ticagrelor, clopidogrel. Either increases effects of the other by Other (see comment). Use Caution/Monitor. Comment: Increased risk of bleeding during concomitant use of medications that increase potential for bleeding |
| digoxin + lisinopril | 4 | lisinopril increases levels of digoxin by unspecified interaction mechanism. Use Caution/Monitor |
| digoxin + metformin | 4 | digoxin, metformin. Either increases levels of the other by basic (cationic) drug competition for renal tubular clearance. Use Caution/Monitor. Measure serum digoxin concentrations before initiating metformin. Monitor patients who take both metformin and digoxin for possible digoxin toxicity and lactic acidosis. Reduce the digoxin and/or metformin dose as necessary |
| digoxin + omeprazole | 4 | omeprazole increases toxicity of digoxin by Other (see comment). Use Caution/Monitor. Comment: Prolonged use of PPIs may cause hypomagnesemia and increase risk for digoxin toxicity |
| enalapril + metformin | 4 | enalapril increases toxicity of metformin by unspecified interaction mechanism. Use Caution/Monitor. Increases risk for hypoglycemia and lactic acidosis |

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| enoxaparin + losartan | 4 | enoxaparin increases toxicity of losartan by Other (see comment). Use Caution/Monitor. Comment: Low molecular weight heparins may suppress adrenal aldosterone secretion, which can potentially cause hyperkalemia |
| eplerenone + losartan | 4 | losartan, eplerenone. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of hyperkalemia |
| felodipine + nitroglycerin | 4 | felodipine, nitroglycerin sublingual. Either increases toxicity of the other by additive vasodilation. Modify Therapy/Monitor Closely. Marked orthostatic hypotension reported with concomitant use |
| formoterol + nebivolol | 4 | nebivolol decreases effects of formoterol by pharmacodynamic antagonism. Use Caution/Monitor |
| | | nebivolol increases and formoterol decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| furosemide + torsemide | 4 | furosemide and torsemide both decrease serum potassium. Use Caution/Monitor |
| indapamide + spironolactone | 4 | spironolactone increases and indapamide decreases serum potassium. Effect of interaction is not clear, use caution. Modify Therapy/Monitor Closely |
| ketoprofen + meloxicam | 4 | ketoprofen and meloxicam both increase anticoagulation. Use Caution/Monitor |
| | | ketoprofen and meloxicam both increase serum potassium. Use Caution/Monitor |
| metoprolol + valsartan | 4 | metoprolol, valsartan. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of fetal compromise if given during pregnancy |
| | | valsartan and metoprolol both increase serum potassium. Use Caution/Monitor |
| sotalol + torsemide | 4 | sotalol increases and torsemide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| sotalol + valsartan | 4 | sotalol, valsartan. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of fetal compromise if given during pregnancy |
| | | valsartan and sotalol both increase serum potassium. Use Caution/Monitor |
| amiodarone + carvedilol | 3 | amiodarone will increase the level or effect of carvedilol by affecting hepatic enzyme CYP2C9/10 metabolism. Use Caution/Monitor |
| | | amiodarone will increase the level or effect of carvedilol by affecting hepatic enzyme CYP2D6 metabolism. Use Caution/Monitor. Monitor for signs of bradycardia or heart block when amiodarone and a beta adrenergic blocker are coadministered. Amiodarone should be used with caution in patients receiving a beta adrenergic blocker, particularly if there is suspicion of underlying dysfunction of the sinus node, such as bradycardia or sick sinus syndrome, or if there is partial AV block |
| | | amiodarone, carvedilol. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of cardiotoxicity with bradycardia |
| amlodipine + nifedipine | 3 | amlodipine and nifedipine both increase anti-hypertensive channel blocking. Use Caution/Monitor |
| amlodipine + sotalol | 3 | sotalol and amlodipine both increase anti-hypertensive channel blocking. Modify Therapy/Monitor Closely |
| aspirin + potassium | 3 | aspirin and potassium chloride both increase serum potassium. Modify Therapy/Monitor Closely |

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| atorvastatin + carbamazepine | 3 | carbamazepine increases toxicity of atorvastatin by Other (see comment). Use Caution/Monitor. Comment: OATP1B1 inhibitors may increase risk of myopathy |
| atorvastatin + telmisartan | 3 | telmisartan increases toxicity of atorvastatin by Other (see comment). Use Caution/Monitor. Comment: OATP1B1 inhibitors may increase risk of myopathy |
| bisoprolol + potassium | 3 | bisoprolol and potassium chloride both increase serum potassium. Modify Therapy/Monitor Closely |
| budesonide + clopidogrel | 3 | budesonide will increase the level or effect of clopidogrel by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Use Caution/Monitor. CYP3A4 inducers may increase the metabolism of clopidogrel to its active metabolite. Monitor patients for potential increase in antiplatelet effects when CYP3A4 inducers are used in combination with clopidogrel |
| budesonide + esomeprazole | 3 | esomeprazole decreases effects of budesonide by increasing gastric pH. Applies only to oral form of both agents. Modify Therapy/Monitor Closely. Enteric-coated budesonide dissolves at pH >5.5. Also, dissolution of extended-release budesonide tablets is pH dependent. Coadministration with drugs that increase gastric pH may cause these budesonide products to prematurely dissolve, and possibly affect release properties and absorption of the drug in the duodenum |
| budesonide + verapamil | 3 | verapamil will increase the level or effect of budesonide by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Use Caution/Monitor |
| | | budesonide will decrease the level or effect of verapamil by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Use Caution/Monitor |
| | | verapamil will increase the level or effect of budesonide by P-glycoprotein (MDR1) efflux transporter. Use Caution/Monitor |
| candesartan + spironolactone | 3 | candesartan and spironolactone both increase serum potassium. Modify Therapy/Monitor Closely |
| captopril + chlorthalidone | 3 | captopril, chlorthalidone. Either increases toxicity of the other by pharmacodynamic synergism. Use Caution/Monitor. Both drugs lower blood pressure. Increased risk of nephrotoxicity. Monitor blood pressure and renal function |
| captopril + insulin | 3 | captopril increases effects of insulin regular human by pharmacodynamic synergism. Use Caution/Monitor. Both drugs decrease blood glucose. Monitor blood glucose |
| carbamazepine + omeprazole | 3 | carbamazepine will decrease the level or effect of omeprazole by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Use Caution/Monitor |
| carvedilol + spironolactone | 3 | carvedilol and spironolactone both increase serum potassium. Modify Therapy/Monitor Closely |
| carvedilol + torsemide | 3 | carvedilol increases and torsemide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| clopidogrel + dabigatran | 3 | dabigatran, clopidogrel. Either increases effects of the other by pharmacodynamic synergism. Use Caution/Monitor. Both drugs have the potential to cause bleeding. Concomitant use may increase risk of bleeding |
| clopidogrel + felodipine | 3 | felodipine decreases effects of clopidogrel by decreasing metabolism. Use Caution/Monitor. Cytochrome P450 2C19 inhibitors decrease the conversion of clopidogrel to its active form |
| digoxin + formoterol | 3 | digoxin increases and formoterol decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |

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| digoxin + pantoprazole | 3 | pantoprazole increases toxicity of digoxin by Other (see comment). Use Caution/Monitor. Comment: Prolonged use of PPIs may cause hypomagnesemia and increase risk for digoxin toxicity |
| doxazosin + metoprolol | 3 | doxazosin and metoprolol both increase anti-hypertensive channel blocking. Modify Therapy/Monitor Closely |
| enalapril + enoxaparin | 3 | enoxaparin increases toxicity of enalapril by Other (see comment). Use Caution/Monitor. Comment: Low molecular weight heparins may suppress adrenal aldosterone secretion, which can potentially cause hyperkalemia |
| enalapril + furosemide | 3 | enalapril, furosemide. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of acute hypotension, renal insufficiency |
| enalapril + insulin | 3 | enalapril increases effects of insulin regular human by pharmacodynamic synergism. Use Caution/Monitor |
| formoterol + salmeterol | 3 | formoterol and salmeterol both decrease serum potassium. Use Caution/Monitor |
| | | formoterol and salmeterol both decrease sedation. Use Caution/Monitor |
| | | formoterol and salmeterol both increase sympathetic (adrenergic) effects, including increased blood pressure and heart rate. Use Caution/Monitor. |
| fosinopril + metformin | 3 | fosinopril increases toxicity of metformin by unspecified interaction mechanism. Use Caution/Monitor. Increases risk for hypoglycemia and lactic acidosis |
| hydrochlorothiazide + telmisartan | 3 | telmisartan increases and hydrochlorothiazide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| indomethacin + losartan | 3 | losartan, indomethacin. Either increases toxicity of the other by Other (see comment). Use Caution/Monitor. Comment: May result in renal function deterioration, particularly in elderly or volume depleted individuals |
| | | indomethacin decreases effects of losartan by pharmacodynamic antagonism. Modify Therapy/Monitor Closely. NSAIDs decrease synthesis of vasodilating renal prostaglandins, and thus affect fluid homeostasis and may diminish antihypertensive effect |
| | | losartan and indomethacin both increase serum potassium. Use Caution/Monitor |
| insulin + lisinopril | 3 | lisinopril increases effects of insulin regular human by pharmacodynamic synergism. Use Caution/Monitor |
| metoprolol + nifedipine | 3 | metoprolol and nifedipine both increase anti-hypertensive channel blocking. Modify Therapy/Monitor Closely |
| aceclofenac + aspirin | 2 | aceclofenac and aspirin both increase anticoagulation. Use Caution/Monitor |
| | | aceclofenac and aspirin both increase serum potassium. Use Caution/Monitor |
| acetazolamide + aspirin | 2 | acetazolamide, aspirin. Either increases levels of the other by Other (see comment). Use Caution/Monitor. Comment: Carbonic anhydrase inhibitors (CAIs) and salicylates inhibit each other's renal tubular secretion, resulting in increased plasma levels. CAIs also shift salicylates from plasma to the CNS, leading to potential neurotoxicity |
| | | acetazolamide, aspirin. Mechanism: passive renal tubular reabsorption due to increased pH. Use Caution/Monitor. Salicylate levels increased at moderate doses; risk of CNS toxicity. Salicylate levels decreased at large doses (d/t increased renal excretion of unchanged salicylic acid) |

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| aluminum hydroxide + bisoprolol | 2 | aluminum hydroxide decreases levels of bisoprolol by inhibition of GI absorption. Applies only to oral form of both agents. Use Caution/Monitor. Separate by 2 hours |
| amiodarone + atenolol | 2 | amiodarone, atenolol. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of cardiotoxicity with bradycardia |
| amiodarone + formoterol | 2 | amiodarone and formoterol both increase QTc interval. Use Caution/Monitor |
| amiodarone + nebivolol | 2 | amiodarone will increase the level or effect of nebivolol by affecting hepatic enzyme CYP2D6 metabolism. Use Caution/Monitor. Monitor cardiac function carefully and observe for signs of bradycardia or heart block when amiodarone and a beta adrenergic blocker are coadministered. Amiodarone should be used with caution in patients receiving a beta adrenergic blocker, particularly if there is suspicion of underlying dysfunction of the sinus node, such as bradycardia or sick sinus syndrome, or if there is partial AV block |
| | | amiodarone, nebivolol. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of cardiotoxicity with bradycardia |
| amlodipine + nebivolol | 2 | nebivolol, amlodipine. Either increases effects of the other by pharmacodynamic synergism. Use Caution/Monitor. Both drugs lower blood pressure |
| aspirin + celecoxib | 2 | aspirin and celecoxib both increase anticoagulation. Use Caution/Monitor |
| | | aspirin and celecoxib both increase serum potassium. Use Caution/Monitor |
| aspirin + fondaparinux | 2 | fondaparinux and aspirin both increase anticoagulation. Modify Therapy/Monitor Closely |
| aspirin + ibuprofen | 2 | aspirin and ibuprofen both increase anticoagulation. Use Caution/Monitor |
| | | aspirin and ibuprofen both increase serum potassium. Use Caution/Monitor |
| aspirin + lornoxicam | 2 | aspirin and lornoxicam both increase anticoagulation. Use Caution/Monitor |
| | | aspirin and lornoxicam both increase serum potassium. Use Caution/Monitor |
| aspirin + timolol | 2 | aspirin decreases effects of timolol by pharmacodynamic antagonism. Use Caution/Monitor. Long term (>1 wk) NSAID use. NSAIDs decrease prostaglandin synthesis |
| | | timolol and aspirin both increase serum potassium. Use Caution/Monitor |
| atenolol + torsemide | 2 | atenolol increases and torsemide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| azilsartan + meloxicam | 2 | meloxicam, azilsartan. Either increases toxicity of the other by Other (see comment). Use Caution/Monitor. Comment: May result in renal function deterioration, particularly in elderly or volume depleted individuals |
| | | meloxicam decreases effects of azilsartan by pharmacodynamic antagonism. Modify Therapy/Monitor Closely. NSAIDs decrease synthesis of vasodilating renal prostaglandins, and thus affect fluid homeostasis and may diminish antihypertensive effect |
| azithromycin + cetirizine | 2 | azithromycin will increase the level or effect of cetirizine by P-glycoprotein (MDR1) efflux transporter. Use Caution/Monitor |
| bisoprolol + calcium carbonate | 2 | calcium carbonate decreases effects of bisoprolol by unspecified interaction mechanism. Use Caution/Monitor |
| | | calcium carbonate decreases levels of bisoprolol by inhibition of GI absorption. Applies only to oral form of both agents. Use Caution/Monitor. Separate by 2 hours |
| bisoprolol + celecoxib | 2 | celecoxib decreases effects of bisoprolol by pharmacodynamic antagonism. Use Caution/Monitor. Long term (>1 wk) NSAID use. NSAIDs decrease prostaglandin synthesis |
| | | bisoprolol and celecoxib both increase serum potassium. Use Caution/Monitor |

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| bisoprolol + doxazosin | 2 | doxazosin and bisoprolol both increase anti-hypertensive channel blocking. Modify Therapy/Monitor Closely |
| bisoprolol + ketoprofen | 2 | ketoprofen decreases effects of bisoprolol by pharmacodynamic antagonism. Use Caution/Monitor. Long term (>1 wk) NSAID use. NSAIDs decrease prostaglandin synthesis |
| | | bisoprolol and ketoprofen both increase serum potassium. Use Caution/Monitor |
| bisoprolol + ketorolac | 2 | ketorolac decreases effects of bisoprolol by pharmacodynamic antagonism. Use Caution/Monitor. Long term (>1 wk) NSAID use. NSAIDs decrease prostaglandin synthesis |
| | | bisoprolol and ketorolac both increase serum potassium. Use Caution/Monitor |
| budesonide + omeprazole | 2 | omeprazole decreases effects of budesonide by increasing gastric pH. Applies only to oral form of both agents. Modify Therapy/Monitor Closely. Enteric-coated budesonide dissolves at pH >5.5. Also, dissolution of extended-release budesonide tablets is pH dependent. Coadministration with drugs that increase gastric pH may cause these budesonide products to prematurely dissolve, and possibly affect release properties and absorption of the drug in the duodenum |
| calcium carbonate + captopril | 2 | calcium carbonate decreases effects of captopril by unspecified interaction mechanism. Use Caution/Monitor. Calcium carbonate may decrease absorption of captopril |
| calcium carbonate + nifedipine | 2 | calcium carbonate decreases effects of nifedipine by pharmacodynamic antagonism. Use Caution/Monitor |
| calcium carbonate + vitamin D | 2 | calcium carbonate decreases effects of nifedipine by pharmacodynamic antagonism. Use Caution/Monitor |
| candesartan + metoprolol | 2 | metoprolol, candesartan. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of fetal compromise if given during pregnancy |
| | | candesartan and metoprolol both increase serum potassium. Use Caution/Monitor |
| captopril + doxazosin | 2 | captopril, doxazosin. Either increases effects of the other by Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Exaggerated first dose hypotensive response. Both drugs lower blood pressure. Monitor blood pressure |
| captopril + hydrochlorothiazide | 2 | captopril, hydrochlorothiazide. Either increases effects of the other by pharmacodynamic synergism. Use Caution/Monitor. Both drugs lower blood pressure. Increased risk of nephrotoxicity. Monitor blood pressure and renal function |
| captopril + ketoprofen | 2 | captopril, ketoprofen. Either increases toxicity of the other by Other (see comment). Use Caution/Monitor. Comment: May result in renal function deterioration, particularly in elderly or volume depleted individuals |
| captopril + potassium | 2 | captopril increases levels of potassium chloride by decreasing elimination. Use Caution/Monitor. Risk of hyperkalemia |
| | | potassium chloride increases toxicity of captopril by Mechanism: unspecified interaction mechanism. Modify Therapy/Monitor Closely. Both drugs increase potassium. Monitor potassium |
| carvedilol + losartan | 2 | carvedilol, losartan. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of fetal compromise if given during pregnancy |
| | | losartan and carvedilol both increase serum potassium. Use Caution/Monitor |
| carvedilol + telmisartan | 2 | carvedilol, telmisartan. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of fetal compromise if given during pregnancy |

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| | | telmisartan and carvedilol both increase serum potassium. Use Caution/Monitor |
| celecoxib + lisinopril | 2 | lisinopril, celecoxib. Either increases toxicity of the other by Other (see comment). Use Caution/Monitor. Comment: May result in renal function deterioration, particularly in elderly or volume depleted individuals |
| chlorthalidone + metoprolol | 2 | metoprolol increases and chlorthalidone decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| ciprofloxacin + dexamethasone | 2 | dexamethasone and ciprofloxacin both increase Other (see comment). Use Caution/Monitor. Coadministration of quinolone antibiotics and corticosteroids may increase risk of tendon rupture |
| clopidogrel + enoxaparin | 2 | enoxaparin, clopidogrel. Either increases effects of the other by pharmacodynamic synergism. Modify Therapy/Monitor Closely. Enhanced risk of hemorrhage; additive effects are intended when both drugs are prescribed as indicated for ACS |
| clopidogrel + heparin | 2 | heparin, clopidogrel. Either increases effects of the other by pharmacodynamic synergism. Modify Therapy/Monitor Closely. Enhanced risk of hemorrhage; additive effects are intended when both drugs are prescribed as indicated for ACS |
| dexamethasone + loratadine | 2 | dexamethasone will decrease the level or effect of loratadine by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Use Caution/Monitor |
| | | loratadine will increase the level or effect of dexamethasone by P-glycoprotein (MDR1) efflux transporter. Use Caution/Monitor |
| diclofenac + lornoxicam | 2 | diclofenac and lornoxicam both increase anticoagulation. Use Caution/Monitor |
| | | diclofenac and lornoxicam both increase serum potassium. Use Caution/Monitor |
| digoxin + esomeprazole | 2 | esomeprazole increases toxicity of digoxin by Other (see comment). Use Caution/Monitor. Comment: Prolonged use of PPIs may cause hypomagnesemia and increase risk for digoxin toxicity |
| digoxin + indapamide | 2 | indapamide increases effects of digoxin by pharmacodynamic synergism. Use Caution/Monitor. Hypokalemia increases digoxin effects |
| | | digoxin increases and indapamide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| digoxin + nebivolol | 2 | nebivolol increases effects of digoxin by pharmacodynamic synergism. Use Caution/Monitor. Enhanced bradycardia |
| | | nebivolol and digoxin both increase serum potassium. Use Caution/Monitor |
| digoxin + verapamil | 2 | verapamil will increase the level or effect of digoxin by P-glycoprotein (MDR1) efflux transporter. Use Caution/Monitor. Toxicity characterized by gastrointestinal and neuropsychiatric symptoms, and cardiac arrhythmias may result |
| | | digoxin will increase the level or effect of verapamil by basic (cationic) drug competition for renal tubular clearance. Use Caution/Monitor |
| doxazosin + nifedipine | 2 | doxazosin and nifedipine both increase anti-hypertensive channel blocking. Use Caution/Monitor |
| enalapril + potassium | 2 | enalapril increases levels of potassium chloride by decreasing elimination. Use Caution/Monitor. Risk of hyperkalemia |
| felodipine + metoprolol | 2 | metoprolol and felodipine both increase anti-hypertensive channel blocking. Modify Therapy/Monitor Closely |

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| formoterol + furosemide | 2 | formoterol and furosemide both decrease serum potassium. Use Caution/Monitor |
| furosemide + lisinopril | 2 | lisinopril, furosemide. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of acute hypotension, renal insufficiency |
| furosemide + potassium | 2 | potassium chloride increases and furosemide decreases serum potassium. Effect of interaction is not clear, use caution. Modify Therapy/Monitor Closely |
| heparin + meloxicam | 2 | heparin and meloxicam both increase anticoagulation. Modify Therapy/Monitor Closely |
| heparin + rivaroxaban | 2 | rivaroxaban, heparin. Either increases effects of the other by anticoagulation. Use Caution/Monitor. Avoid concurrent use of rivaroxaban with other anticoagulants due to increased bleeding risk other than during therapeutic transition periods where patients should be observed closely. Monitor for signs/symptoms of blood loss |
| hydrochlorothiazide + losartan | 2 | losartan increases and hydrochlorothiazide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| hydrochlorothiazide + torsemide | 2 | torsemide and hydrochlorothiazide both decrease serum potassium. Use Caution/Monitor |
| indapamide + sotalol | 2 | sotalol increases and indapamide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| indapamide + valsartan | 2 | valsartan increases and indapamide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| insulin + torsemide | 2 | torsemide decreases effects of insulin degludec by Other (see comment). Use Caution/Monitor. Comment: Diuretics may cause hyperglycemia and glycosuria in patients with diabetes mellitus, possibly by diuretic-induced hpokalemia |
| insulin + valsartan | 2 | valsartan increases effects of insulin aspart by unspecified interaction mechanism. Use Caution/Monitor. Concomitant use of insulin and ARBs may require insulin dosage adjustment and increased glucose monitoring |
| ketorolac + lisinopril | 2 | lisinopril, ketorolac. Either increases toxicity of the other by Other (see comment). Use Caution/Monitor. Comment: May result in renal function deterioration, particularly in elderly or volume depleted individuals |
| ketorolac + meloxicam | 2 | ketorolac and meloxicam both increase anticoagulation. Use Caution/Monitor |
| | | ketorolac and meloxicam both increase serum potassium. Use Caution/Monitor |
| levothyroxine + metformin | 2 | levothyroxine decreases effects of metformin by pharmacodynamic antagonism. Use Caution/Monitor. Patient should be closely observed for loss of blood glucose control; when drugs are withdrawn from a patient receiving metformin, patient should be observed closely for hypoglycemia |
| levothyroxine + warfarin | 2 | levothyroxine increases effects of warfarin by unspecified interaction mechanism. Use Caution/Monitor |
| lisinopril + meloxicam | 2 | lisinopril, meloxicam. Either increases toxicity of the other by Other (see comment). Use Caution/Monitor. Comment: May result in renal function deterioration, particularly in elderly or volume depleted individuals |
| losartan + nebivolol | 2 | nebivolol, losartan. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of fetal compromise if given during pregnancy |
| | | losartan and nebivolol both increase serum potassium. Use Caution/Monitor |
| losartan + potassium | 2 | losartan and potassium chloride both increase serum potassium. Use Caution/Monitor |

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| metoprolol + ranolazine | 2 | ranolazine will increase the level or effect of metoprolol by affecting hepatic enzyme CYP2D6 metabolism. Use Caution/Monitor |
| metoprolol + telmisartan | 2 | metoprolol, telmisartan. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of fetal compromise if given during pregnancy |
| | | telmisartan and metoprolol both increase serum potassium. Use Caution/Monitor |
| nebivolol + spironolactone | 2 | nebivolol and spironolactone both increase serum potassium. Modify Therapy/Monitor Closely |
| nebivolol + torsemide | 2 | nebivolol increases and torsemide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| nifedipine + nitroglycerin | 2 | nifedipine, nitroglycerin sublingual. Either increases toxicity of the other by additive vasodilation. Modify Therapy/Monitor Closely. Marked orthostatic hypotension reported with concomitant use |
| phenylephrine + xylometazoline | 2 | phenylephrine and xylometazoline both decrease sedation. Use Caution/Monitor |
| | | phenylephrine and xylometazoline both increase sympathetic (adrenergic) effects, including increased blood pressure and heart rate. Use Caution/Monitor |
| ramipril + torsemide | 2 | ramipril, torsemide. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of acute hypotension, renal insufficiency |
| sacubitril/valsartan + sotalol | 2 | sotalol, sacubitril/valsartan. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of fetal compromise if given during pregnancy |
| | | sacubitril/valsartan and sotalol both increase serum potassium. Use Caution/Monitor |
| sotalol + spironolactone | 2 | sotalol and spironolactone both increase serum potassium. Modify Therapy/Monitor Closely |
| sotalol + telmisartan | 2 | sotalol, telmisartan. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of fetal compromise if given during pregnancy |
| | | telmisartan and sotalol both increase serum potassium. Use Caution/Monitor |
| telmisartan + torsemide | 2 | telmisartan increases and torsemide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| aceclofenac + hydrochlorothiazide | 1 | aceclofenac increases and hydrochlorothiazide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| aceclofenac + indapamide | 1 | aceclofenac increases and indapamide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| allopurinol + calcium carbonate | 1 | calcium carbonate decreases levels of allopurinol by inhibition of GI absorption. Applies only to oral form of both agents. Use Caution/Monitor. Separate by 2 hours |
| amiodarone + hydrochlorothiazide | 1 | amiodarone will increase the level or effect of hydrochlorothiazide by basic (cationic) drug competition for renal tubular clearance. Use Caution/Monitor |
| amitriptyline + atorvastatin | 1 | atorvastatin will increase the level or effect of amitriptyline by P-glycoprotein (MDR1) efflux transporter. Use Caution/Monitor |
| amitriptyline + carbamazepine | 1 | carbamazepine will decrease the level or effect of amitriptyline by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Use Caution/Monitor |
| amitriptyline + gabapentin | 1 | gabapentin, amitriptyline. Either increases effects of the other by pharmacodynamic synergism. Modify Therapy/Monitor Closely. Coadministration of CNS depressants can result in serious, life-threatening, and fatal respiratory depression. Use lowest dose possible and monitor for respiratory depression and sedation |

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| amlodipine + doxazosin | 1 | doxazosin and amlodipine both increase anti-hypertensive channel blocking. Use Caution/Monitor |
| amlodipine + magnesium supplement | 1 | magnesium supplement, amlodipine. Either increases toxicity of the other by pharmacodynamic synergism. Use Caution/Monitor. Calcium channel blockers may increase toxic effects of magnesium; magnesium may increase hypotensive effects of calcium channel blockers |
| amoxicillin + hydrochlorothiazide | 1 | amoxicillin, hydrochlorothiazide. Either increases levels of the other by decreasing renal clearance. Use Caution/Monitor |
| aspirin + cilostazol | 1 | aspirin, cilostazol. Either increases toxicity of the other by pharmacodynamic synergism. Use Caution/Monitor. The need for simultaneous use of low-dose aspirin and anticoagulant or antiplatelet agents are common for patients with cardiovascular disease; monitor closely |
| aspirin + escitalopram | 1 | escitalopram, aspirin. Either increases toxicity of the other by pharmacodynamic synergism. Use Caution/Monitor. Increased risk of upper GI bleeding. SSRIs inhib. serotonin uptake by platelets |
| aspirin + omega 3 fatty acids | 1 | omega 3 fatty acids, aspirin. Other (see comment). Use Caution/Monitor. Comment: Patients taking omega-3-fatty acids and an anticoagulant or other drug affecting coagulation should be monitored periodically due to potential increased risk of bleeding |
| aspirin + prasugrel | 1 | aspirin, prasugrel. Either increases toxicity of the other by pharmacodynamic synergism. Use Caution/Monitor. The need for simultaneous use of low-dose aspirin and anticoagulant or antiplatelet agents are common for patients with cardiovascular disease; monitor closely |
| atenolol + chlorthalidone | 1 | atenolol increases and chlorthalidone decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| atenolol + spironolactone | 1 | atenolol and spironolactone both increase serum potassium. Modify Therapy/Monitor Closely |
| atorvastatin + azithromycin | 1 | azithromycin will increase the level or effect of atorvastatin by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Use Caution/Monitor. If this combination is used, closely monitor for evidence of atorvastatin toxicity (eg, muscle aches or pains, renal dysfunction) |
| atorvastatin + tinidazole | 1 | atorvastatin will increase the level or effect of tinidazole by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Use Caution/Monitor |
| azithromycin + warfarin | 1 | azithromycin increases toxicity of warfarin by anticoagulation. Use Caution/Monitor. Postmarketing reports have suggested that concomitant administration of azithromycin may potentiate effects of oral warfarin but the interaction does not appear to alter prothrombin time |
| bisoprolol + timolol | 1 | bisoprolol and timolol both increase serum potassium. Use Caution/Monitor |
| bisoprolol + verapamil | 1 | bisoprolol and verapamil both increase anti-hypertensive channel blocking. Modify Therapy/Monitor Closely |
| budesonide + clarithromycin | 1 | clarithromycin will increase the level or effect of budesonide by P-glycoprotein (MDR1) efflux transporter. Use Caution/Monitor |
| calcium carbonate + levothyroxine | 1 | calcium carbonate decreases levels of levothyroxine by inhibition of GI absorption. Applies only to oral form of both agents. Use Caution/Monitor. Separate administration by 4 hours |
| calcium carbonate + ramipril | 1 | calcium carbonate decreases effects of ramipril by unspecified interaction mechanism. Use Caution/Monitor |
| calcium carbonate + rosuvastatin | 1 | calcium carbonate decreases levels of rosuvastatin by inhibition of GI absorption. Applies only to oral form of both agents. Use Caution/Monitor. Separate by 2 hours |

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| candesartan + digoxin | 1 | candesartan and digoxin both increase serum potassium. Use Caution/Monitor |
| candesartan + eplerenone | 1 | candesartan, eplerenone. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of hyperkalemia |
| candesartan + indapamide | 1 | candesartan increases and indapamide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| candesartan + insulin | 1 | candesartan increases effects of insulin regular human by unspecified interaction mechanism. Use Caution/Monitor. Concomitant use of insulin and ARBs may require insulin dosage adjustment and increased glucose monitoring |
| captopril + ibuprofen | 1 | captopril, ibuprofen. Either increases toxicity of the other by Other (see comment). Use Caution/Monitor. Comment: May result in renal function deterioration, particularly in elderly or volume depleted individuals |
| captopril + isosorbide dinitrate | 1 | isosorbide dinitrate, captopril. Either increases effects of the other by pharmacodynamic synergism. Use Caution/Monitor. Both drugs lower blood pressure. Monitor blood pressure |
| captopril + isosorbide mononitrate | 1 | isosorbide mononitrate, captopril. Either increases effects of the other by pharmacodynamic synergism. Use Caution/Monitor. Both drugs lower blood pressure. Monitor blood pressure |
| captopril + linagliptin | 1 | linagliptin increases toxicity of captopril by Mechanism: unspecified interaction mechanism. Use Caution/Monitor. Increased adverse/toxic effects, specifically, increased risk of angioedema |
| captopril + meloxicam | 1 | captopril, meloxicam. Either increases toxicity of the other by Other (see comment). Use Caution/Monitor. Comment: May result in renal function deterioration, particularly in elderly or volume depleted individuals |
| captopril + naproxen | 1 | captopril, naproxen. Either increases toxicity of the other by Other (see comment). Use Caution/Monitor. Comment: May result in renal function deterioration, particularly in elderly or volume depleted individuals |
| captopril + pentoxifylline | 1 | pentoxifylline, captopril. Either increases effects of the other by pharmacodynamic synergism. Use Caution/Monitor. Both drugs lower blood pressure. Monitor blood pressure |
| carbamazepine + enalapril | 1 | enalapril increases levels of carbamazepine by decreasing metabolism. Use Caution/Monitor |
| carbamazepine + eplerenone | 1 | carbamazepine will decrease the level or effect of eplerenone by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Use Caution/Monitor |
| carbamazepine + felodipine | 1 | felodipine increases levels of carbamazepine by decreasing metabolism. Use Caution/Monitor |
| carbamazepine + oxcarbazepine | 1 | oxcarbazepine will decrease the level or effect of carbamazepine by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Use Caution/Monitor |
| carbamazepine + pantoprazole | 1 | carbamazepine will decrease the level or effect of pantoprazole by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Use Caution/Monitor |
| carbamazepine + sacubitril/valsartan | 1 | carbamazepine will increase the level or effect of sacubitril/valsartan by Other (see comment). Use Caution/Monitor. The results from an in vitro study with human liver tissue indicate that valsartan is a substrate of the hepatic uptake transporter OATP1B1; coadministration with OATP1B1 inhibitors may increase valsartan systemic exposure |
| carvedilol + hydrochlorothiazide | 1 | carvedilol increases and hydrochlorothiazide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |

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| carvedilol + indapamide | 1 | carvedilol increases and indapamide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| carvedilol + nifedipine | 1 | carvedilol and nifedipine both increase anti-hypertensive channel blocking. Modify Therapy/Monitor Closely |
| ceftriaxone + warfarin | 1 | ceftriaxone increases effects of warfarin by unspecified interaction mechanism. Use Caution/Monitor |
| celecoxib + heparin | 1 | heparin and celecoxib both increase anticoagulation. Modify Therapy/Monitor Closely |
| celecoxib + indapamide | 1 | celecoxib increases and indapamide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| celecoxib + rivaroxaban | 1 | rivaroxaban, celecoxib. Other (see comment). Use Caution/Monitor. Comment: NSAIDs are known to increase bleeding. Bleeding risk may be increased when NSAIDs are used concomitantly with rivaroxaban. Monitor for signs/symptoms of blood loss |
| chlorthalidone + meloxicam | 1 | meloxicam increases and chlorthalidone decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| chlorthalidone + spironolactone | 1 | spironolactone increases and chlorthalidone decreases serum potassium. Effect of interaction is not clear, use caution. Modify Therapy/Monitor Closely |
| ciprofloxacin + ibuprofen | 1 | ibuprofen, ciprofloxacin. Other (see comment). Modify Therapy/Monitor Closely. Comment: Mechanism: unknown. Increased risk of CNS stimulation and seizures with high doses of fluoroquinolones |
| ciprofloxacin + tinidazole | 1 | ciprofloxacin will increase the level or effect of tinidazole by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Use Caution/Monitor |
| clarithromycin + dexamethasone | 1 | clarithromycin will increase the level or effect of dexamethasone by P-glycoprotein (MDR1) efflux transporter. Use Caution/Monitor |
| clarithromycin + warfarin | 1 | clarithromycin will increase the level or effect of warfarin by Other (see comment). Use Caution/Monitor. Warfarin's less potent R-enantiomer is metabolized in part by CYP3A4 (and also CYP1A2 and CYP2C19). Monitor INR more frequently if coadministered with inhibitors of these isoenzymes and adjust warfarin dose if needed |
| clopidogrel + omega 3 fatty acids | 1 | omega 3 fatty acids, clopidogrel. Other (see comment). Use Caution/Monitor. Comment: Patients taking omega-3-fatty acids and an anticoagulant or other drug affecting coagulation should be monitored periodically due to potential increased risk of bleeding |
| dabigatran + diclofenac | 1 | dabigatran and diclofenac both increase anticoagulation. Use Caution/Monitor. Caution is advised, both drugs have the potential to cause bleeding. Concomitant use may increase risk of bleeding |
| dabigatran + rivaroxaban | 1 | rivaroxaban, dabigatran. Either increases effects of the other by anticoagulation. Use Caution/Monitor. Avoid concurrent use of rivaroxaban with other anticoagulants due to increased bleeding risk other than during therapeutic transition periods where patients should be observed closely. Monitor for signs/symptoms of blood loss |
| dapagliflozin + dulaglutide | 1 | dulaglutide, dapagliflozin. Either increases effects of the other by pharmacodynamic synergism. Use Caution/Monitor. Antidiabetic agents are often used in combination; dosage adjustments may be required when initiating or discontinuing antidiabetic agents |

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| dapagliflozin + glimepiride | 1 | glimepiride, dapagliflozin. Either increases effects of the other by pharmacodynamic synergism. Modify Therapy/Monitor Closely. Consider a lower dose of insulin or insulin secretagogue to avoid hypoglycemia when coadministered with dapagliflozin |
| dexamethasone + enoxaparin | 1 | dexamethasone, enoxaparin. Other (see comment). Use Caution/Monitor. Comment: Corticosteroids may decrease anticoagulant effects by increasing blood coagulability; conversely, they may impair vascular integrity, thus increasing bleeding risk. Monitor INR closely |
| dexamethasone + ketorolac | 1 | ketorolac, dexamethasone. Either increases toxicity of the other by pharmacodynamic synergism. Use Caution/Monitor. Increased risk of GI ulceration |
| dexamethasone + levofloxacin | 1 | dexamethasone and levofloxacin both increase Other (see comment). Use Caution/Monitor. Coadministration of quinolone antibiotics and corticosteroids may increase risk of tendon rupture |
| diclofenac + heparin | 1 | heparin and diclofenac both increase anticoagulation. Modify Therapy/Monitor Closely |
| diclofenac + hydrocortisone | 1 | diclofenac, hydrocortisone. Either increases toxicity of the other by pharmacodynamic synergism. Use Caution/Monitor. Increased risk of GI ulceration |
| diclofenac + levofloxacin | 1 | levofloxacin, diclofenac. Other (see comment). Modify Therapy/Monitor Closely. Comment: Risk of CNS stimulation/seizure. Mechanism: Displacement of GABA from receptors in brain |
| digoxin + felodipine | 1 | felodipine will increase the level or effect of digoxin by P-glycoprotein (MDR1) efflux transporter. Use Caution/Monitor |
| digoxin + meloxicam | 1 | meloxicam and digoxin both increase serum potassium. Use Caution/Monitor |
| digoxin + memantine | 1 | digoxin will increase the level or effect of memantine by basic (cationic) drug competition for renal tubular clearance. Use Caution/Monitor |
| digoxin + sacubitril/valsartan | 1 | sacubitril/valsartan and digoxin both increase serum potassium. Use Caution/Monitor |
| digoxin + valsartan | 1 | valsartan will increase the level or effect of digoxin by decreasing renal clearance. Use Caution/Monitor. Monitor digoxin levels closely when coadministered with drugs that may decrease glomerular filtration or tubular secretion |
| diltiazem + magnesium supplement | 1 | magnesium supplement, diltiazem. Either increases toxicity of the other by pharmacodynamic synergism. Use Caution/Monitor. Calcium channel blockers may increase toxic effects of magnesium; magnesium may increase hypotensive effects of calcium channel blockers |
| doxazosin + fosinopril | 1 | fosinopril, doxazosin. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Exaggerated first dose hypotensive response |
| doxazosin + lisinopril | 1 | lisinopril, doxazosin. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Exaggerated first dose hypotensive response |
| doxazosin + verapamil | 1 | doxazosin and verapamil both increase anti-hypertensive channel blocking. Use Caution/Monitor |
| dulaglutide + metformin | 1 | dulaglutide, metformin. Either increases effects of the other by pharmacodynamic synergism. Use Caution/Monitor. Antidiabetic agents are often used in combination; dosage adjustments may be required when initiating or discontinuing antidiabetic agents |
| empagliflozin + insulin | 1 | empagliflozin, insulin regular human. Either increases effects of the other by pharmacodynamic synergism. Modify Therapy/Monitor Closely. Consider a lower dose of |

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| | | insulin or insulin secretagogue to avoid hypoglycemia when coadministered with SGLT2 inhibitors |
| empagliflozin + spironolactone | 1 | empagliflozin, spironolactone. Either increases effects of the other by pharmacodynamic synergism. Use Caution/Monitor. Coadministration of empagliflozin with diuretics results in increased urine volume and frequency of voids, which might enhance the potential for volume depletion |
| enalapril + meloxicam | 1 | enalapril, meloxicam. Either increases toxicity of the other by Other (see comment). Use Caution/Monitor. Comment: May result in renal function deterioration, particularly in elderly or volume depleted individuals |
| enoxaparin + spironolactone | 1 | spironolactone, enoxaparin. Either increases toxicity of the other by serum potassium. Use Caution/Monitor. Both drugs may increase serum potassium levels |
| eplerenone + telmisartan | 1 | telmisartan, eplerenone. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of hyperkalemia |
| eplerenone + valsartan | 1 | valsartan, eplerenone. Mechanism: pharmacodynamic synergism. Use Caution/Monitor. Risk of hyperkalemia |
| eplerenone + verapamil | 1 | verapamil will increase the level or effect of eplerenone by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Use Caution/Monitor. Plasma concentrations and pharmacologic or toxic effects of eplerenone may be increased by verapamil |
| escitalopram + metformin | 1 | escitalopram increases effects of metformin by pharmacodynamic synergism. Use Caution/Monitor |
| escitalopram + omeprazole | 1 | omeprazole will increase the level or effect of escitalopram by affecting hepatic enzyme CYP2C19 metabolism. Use Caution/Monitor |
| felodipine + metformin | 1 | felodipine decreases effects of metformin by pharmacodynamic antagonism. Use Caution/Monitor. Patient should be closely observed for loss of blood glucose control; when drugs are withdrawn from a patient receiving metformin, patient should be observed closely for hypoglycemia |
| felodipine + rivaroxaban | 1 | felodipine increases levels of rivaroxaban by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Use Caution/Monitor. Patients with renal impairment receiving rivaroxaban with drugs that are combined P-gp and weak or moderate CYP3A4 inhibitors may have significant increases in exposure compared with patients with normal renal function and no inhibitor use, since both pathways of rivaroxaban elimination are affected. Since these increases may increase bleeding risk, use rivaroxaban in this situation only if the potential benefit justifies the potential risk |
| ferrous sulfate + pantoprazole | 1 | pantoprazole will decrease the level or effect of ferrous sulfate by increasing gastric pH. Applies only to oral form of both agents. Use Caution/Monitor |
| formoterol + indapamide | 1 | formoterol and indapamide both decrease serum potassium. Use Caution/Monitor |
| formoterol + olodaterol inhaled | 1 | formoterol and olodaterol inhaled both increase sympathetic (adrenergic) effects, including increased blood pressure and heart rate. Use Caution/Monitor. Caution with coadministration of adrenergic drugs by any route because of additive sympathetic effects |
| furosemide + metoprolol | 1 | metoprolol increases and furosemide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |

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| furosemide + valsartan | 1 | valsartan increases and furosemide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| garlic + nettle | 1 | garlic increases and nettle decreases anticoagulation. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| heparin + losartan | 1 | heparin increases toxicity of losartan by Other (see comment). Use Caution/Monitor. Comment: Low molecular weight heparins may suppress adrenal aldosterone secretion, which can potentially cause hyperkalemia |
| hydrochlorothiazide + spironolactone | 1 | spironolactone increases and hydrochlorothiazide decreases serum potassium. Effect of interaction is not clear, use caution. Modify Therapy/Monitor Closely |
| hydrochlorothiazide + valsartan | 1 | valsartan increases and hydrochlorothiazide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| ibuprofen + indapamide | 1 | ibuprofen increases and indapamide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| ibuprofen + lisinopril | 1 | lisinopril, ibuprofen. Either increases toxicity of the other by Other (see comment). Use Caution/Monitor. Comment: May result in renal function deterioration, particularly in elderly or volume depleted individuals |
| indapamide + ketorolac | 1 | ketorolac increases and indapamide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| indapamide + lornoxicam | 1 | lornoxicam increases and indapamide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| indapamide + naproxen | 1 | naproxen increases and indapamide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| indapamide + nebivolol | 1 | nebivolol increases and indapamide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| indapamide + potassium | 1 | potassium chloride increases and indapamide decreases serum potassium. Effect of interaction is not clear, use caution. Modify Therapy/Monitor Closely |
| indapamide + telmisartan | 1 | telmisartan increases and indapamide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| indapamide + timolol | 1 | timolol increases and indapamide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| insulin + levofloxacin | 1 | levofloxacin increases effects of insulin aspart by pharmacodynamic synergism. Use Caution/Monitor. Quinolone antibiotic administration may result in hyper- or hypoglycemia. Gatifloxacin is most likely to produce dysglycemia; moxifloxacin is least likely |
| insulin + lixisenatide (DSC) | 1 | lixisenatide (DSC), insulin degludec. Either increases effects of the other by pharmacodynamic synergism. Modify Therapy/Monitor Closely. Risk of hypoglycemia increased when coadministered with basal insulins. Basal insulin dose reduction may be required |
| insulin + perindopril | 1 | perindopril, insulin degludec. Either increases effects of the other by pharmacodynamic synergism. Use Caution/Monitor. Both drugs decrease blood glucose |
| ivabradine + sotalol | 1 | ivabradine, sotalol. Either increases effects of the other by pharmacodynamic synergism. Modify Therapy/Monitor Closely. Most patients receiving ivabradine will also be treated with a beta-blocker. The risk of bradycardia increases with coadministration of drugs that slow heart |

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| | | rate (eg, digoxin, amiodarone, beta-blockers). Monitor heart rate in patients taking ivabradine with other negative chronotropes |
| ketoprofen + perindopril | 1 | perindopril, ketoprofen. Either increases toxicity of the other by Other (see comment). Use Caution/Monitor. Comment: May result in renal function deterioration, particularly in elderly or volume depleted individuals |
| ketoprofen + ramipril | 1 | ramipril, ketoprofen. Either increases toxicity of the other by Other (see comment). Use Caution/Monitor. Comment: May result in renal function deterioration, particularly in elderly or volume depleted individuals |
| ketoprofen + spironolactone | 1 | spironolactone and ketoprofen both increase serum potassium. Modify Therapy/Monitor Closely |
| ketoprofen + torsemide | 1 | ketoprofen increases and torsemide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| ketorolac + rivaroxaban | 1 | rivaroxaban, ketorolac. Other (see comment). Use Caution/Monitor. Comment: NSAIDs are known to increase bleeding. Bleeding risk may be increased when NSAIDs are used concomitantly with rivaroxaban. Monitor for signs/symptoms of blood loss |
| levofloxacin + magnesium sulfate | 1 | magnesium sulfate decreases levels of levofloxacin by inhibition of GI absorption. Applies only to oral form of both agents. Use Caution/Monitor. Separate by 2 hours |
| levofloxacin + metformin | 1 | levofloxacin increases effects of metformin by pharmacodynamic synergism. Use Caution/Monitor. Quinolone antibiotic administration may result in hyper- or hypoglycemia. Gatifloxacin is most likely to produce dysglycemia; moxifloxacin is least likely |
| lornoxicam + losartan | 2 | losartan and lornoxicam both increase serum potassium. Use Caution/Monitor |
| lornoxicam + spironolactone | 1 | spironolactone and lornoxicam both increase serum potassium. Modify Therapy/Monitor Closely |
| lornoxicam + torsemide | 1 | lornoxicam increases and torsemide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| losartan + tizanidine | 1 | tizanidine increases effects of losartan by pharmacodynamic synergism. Use Caution/Monitor. Risk of hypotension |
| magnesium hydroxide + vitamin D | 1 | vitamin D increases levels of magnesium hydroxide by Other (see comment). Use Caution/Monitor. Comment: Vitamin D can increase serum magnesium concentrations, particularly in the presence of renal impairment. The combined use of vitamin D and magnesium-containing products should be avoided, if possible, in patients with chronic renal failure |
| magnesium supplement + nifedipine | 1 | magnesium supplement, nifedipine. Either increases toxicity of the other by Other (see comment). Use Caution/Monitor. Comment: Calcium channel blockers may increase toxic effects of magnesium; magnesium may increase hypotensive effects of calcium channel blockers |
| magnesium hydroxide + torsemide | 1 | torsemide decreases levels of magnesium hydroxide by increasing renal clearance. Minor/Significance Unknown |
| meloxicam + torsemide | 1 | meloxicam increases and torsemide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |

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| meloxicam + warfarin | 1 | meloxicam, warfarin. Either increases effects of the other by pharmacodynamic synergism. Modify Therapy/Monitor Closely. Drugs with antiplatelet properties may increase anticoagulation effect of warfarin |
| metformin + nifedipine | 1 | nifedipine decreases effects of metformin by pharmacodynamic antagonism. Use Caution/Monitor. Patient should be closely observed for loss of blood glucose control; when drugs are withdrawn from a patient receiving metformin, patient should be observed closely for hypoglycemia |
| metformin + ramipril | 2 | ramipril increases toxicity of metformin by unspecified interaction mechanism. Use Caution/Monitor. Increases risk for hypoglycemia and lactic acidosis |
| methotrexate + omeprazole | 1 | omeprazole increases levels of methotrexate by decreasing renal clearance. Use Caution/Monitor. Temporary withdrawal of PPI may be considered in some patients |
| nifedipine + sotalol | 1 | sotalol and nifedipine both increase anti-hypertensive channel blocking. Modify Therapy/Monitor Closely |
| nitroglycerin + verapamil | 1 | verapamil, nitroglycerin sublingual. Either increases toxicity of the other by additive vasodilation. Modify Therapy/Monitor Closely. Marked orthostatic hypotension reported with concomitant use |
| olmesartan + torsemide | 1 | olmesartan increases and torsemide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor |
| omeprazole + tinidazole | 1 | omeprazole will increase the level or effect of tinidazole by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Use Caution/Monitor |
| rivaroxaban + saw palmetto | 1 | saw palmetto increases toxicity of rivaroxaban by unspecified interaction mechanism. Use Caution/Monitor. May increase risk of bleeding |
| rivaroxaban + verapamil | 1 | verapamil increases levels of rivaroxaban by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Use Caution/Monitor. Verapamil also inhibits P-gp activity, which can further increase rivaroxaban serum levels; since both pathways of rivaroxaban elimination are affected, patients with renal impairment receiving rivaroxaban with drugs that are combined P-gp and moderate CYP3A4 inhibitors may increase exposure compared to patients with normal renal function; monitor for bleeding |
| rosuvastatin + sodium bicarbonate | 1 | sodium bicarbonate decreases levels of rosuvastatin by inhibition of GI absorption. Applies only to oral form of both agents. Use Caution/Monitor. Separate by 2 hours |
| spironolactone + telmisartan | 1 | telmisartan and spironolactone both increase serum potassium. Modify Therapy/Monitor Closely |

Note: Impact of drug–drug interactions associated with the combinations “aspirin + captopril” and “aspirin + enalapril” may be considered insignificant due to the use of low-dose aspirin in the majority of cases. Administration of aspirin at doses less than 300 mg per day has little effect on the effectiveness of captopril and enalapril. Administration of aspirin in higher doses reduces the effectiveness of captopril and enalapril.

**Table S11.** Drug combinations resulting in potential minor drug–drug interactions in the list of prescribed medications in patients with cardiovascular diseases according to data derived from the electronic health records ($n$ = 1030) established in 2018–2023.

| Drug combinations | *n* | Potential minor drug-drug interactions (P-list) |
|---|---|---|
| magnesium hydroxide + torsemide | 65 | torsemide decreases levels of magnesium hydroxide by increasing renal clearance. Minor/Significance Unknown |
| magnesium hydroxide + spironolactone | 45 | spironolactone increases levels of magnesium hydroxide by decreasing renal clearance. Minor/Significance Unknown |
| clopidogrel + torsemide | 44 | clopidogrel increases levels of torsemide by decreasing metabolism. Minor/Significance Unknown |
| aspirin + eplerenone | 35 | aspirin decreases effects of eplerenone by pharmacodynamic antagonism. Minor/Significance Unknown. NSAIDs decrease prostaglandin synthesis |
| aspirin + indapamide | 32 | indapamide will increase the level or effect of aspirin by acidic (anionic) drug competition for renal tubular clearance. Minor/Significance Unknown |
| ascorbic acid + aspirin | 22 | ascorbic acid will increase the level or effect of aspirin by acidic (anionic) drug competition for renal tubular clearance. Minor/Significance Unknown |
| | | aspirin decreases levels of ascorbic acid by increasing renal clearance. Minor/Significance Unknown |
| | | ascorbic acid increases levels of aspirin by decreasing renal clearance. Minor/Significance Unknown |
| indapamide + magnesium hydroxide | 21 | indapamide decreases levels of magnesium hydroxide by increasing renal clearance. Minor/Significance Unknown |
| aspirin + hydrochlorothiazide | 13 | hydrochlorothiazide will increase the level or effect of aspirin by acidic (anionic) drug competition for renal tubular clearance. Minor/Significance Unknown |
| budesonide + torsemide | 11 | budesonide, torsemide. Mechanism: pharmacodynamic synergism. Minor/Significance Unknown. Risk of hypokalemia, especially with strong glucocorticoid activity |
| aspirin + furosemide | 10 | aspirin decreases effects of furosemide by pharmacodynamic antagonism. Minor/Significance Unknown. NSAIDs decrease prostaglandin synthesis |
| formoterol + torsemide | 10 | formoterol, torsemide. Mechanism: pharmacodynamic synergism. Minor/Significance Unknown. Hypokalemia |
| hydrochlorothiazide + magnesium hydroxide | 10 | hydrochlorothiazide decreases levels of magnesium hydroxide by increasing renal clearance. Minor/Significance Unknown |
| cyanocobalamin + omeprazole | 9 | omeprazole decreases levels of cyanocobalamin by inhibition of GI absorption. Applies only to oral form of both agents. Minor/Significance Unknown |
| diclofenac topical + meloxicam | 6 | diclofenac topical, meloxicam. Either increases effects of the other by pharmacodynamic synergism. Minor/Significance Unknown. Although low, there is systemic exposure to diclofenac topical; theoretically, concomitant administration with systemic NSAIDS or aspirin may result in increased NSAID adverse effects |
| furosemide + magnesium hydroxide | 5 | furosemide decreases levels of magnesium hydroxide by increasing renal clearance. Minor/Significance Unknown |
| aspirin + chlorthalidone | 4 | chlorthalidone will increase the level or effect of aspirin by acidic (anionic) drug competition for renal tubular clearance. Minor/Significance Unknown |

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| aspirin + cyanocobalamin | 4 | aspirin decreases levels of cyanocobalamin by inhibition of GI absorption. Applies only to oral form of both agents. Minor/Significance Unknown |
| carvedilol + omeprazole | 4 | omeprazole will increase the level or effect of carvedilol by affecting hepatic enzyme CYP2C9/10 metabolism. Minor/Significance Unknown |
| chlorthalidone + magnesium hydroxide | 4 | chlorthalidone decreases levels of magnesium hydroxide by increasing renal clearance. Minor/Significance Unknown |
| hydrochlorothiazide + metformin | 4 | hydrochlorothiazide will increase the level or effect of metformin by basic (cationic) drug competition for renal tubular clearance. Minor/Significance Unknown |
| | | hydrochlorothiazide decreases effects of metformin by pharmacodynamic antagonism. Minor/Significance Unknown. Thiazide dosage >50 mg/day may increase blood glucose |
| indapamide + metformin | 4 | indapamide decreases effects of metformin by pharmacodynamic antagonism. Minor/Significance Unknown. Thiazide dosage >50 mg/day may increase blood glucose |
| bisoprolol + tizanidine | 3 | tizanidine increases effects of bisoprolol by pharmacodynamic synergism. Minor/Significance Unknown. Risk of hypotension |
| captopril + tizanidine | 3 | tizanidine increases effects of captopril by pharmacodynamic synergism. Minor/Significance Unknown. Risk of hypotension |
| carbamazepine + omeprazole | 3 | omeprazole increases levels of carbamazepine by decreasing metabolism. Minor/Significance Unknown. Monitor plasma levels when used concomitantly |
| cyanocobalamin + pantoprazole | 3 | pantoprazole decreases levels of cyanocobalamin by inhibition of GI absorption. Applies only to oral form of both agents. Minor/Significance Unknown |
| aluminum hydroxide + aspirin | 2 | aluminum hydroxide, aspirin. Mechanism: passive renal tubular reabsorption due to increased pH. Minor/Significance Unknown. Salicylate levels increased at moderate doses; salicylate levels decreased at large doses (d/t increased renal excretion of unchanged salicylic acid) |
| amiodarone + celecoxib | 2 | amiodarone will increase the level or effect of celecoxib by affecting hepatic enzyme CYP2C9/10 metabolism. Minor/Significance Unknown |
| amiodarone + pyridoxine | 2 | pyridoxine increases toxicity of amiodarone by unspecified interaction mechanism. Minor/Significance Unknown. Increased risk of photosensitivity |
| amlodipine + tizanidine | 2 | tizanidine increases effects of amlodipine by pharmacodynamic synergism. Minor/Significance Unknown. Risk of hypotension |
| aspirin + ascorbic acid | 2 | ascorbic acid will increase the level or effect of aspirin by acidic (anionic) drug competition for renal tubular clearance. Minor/Significance Unknown |
| | | aspirin decreases levels of ascorbic acid by increasing renal clearance. Minor/Significance Unknown |
| | | ascorbic acid increases levels of aspirin by decreasing renal clearance. Minor/Significance Unknown |
| aspirin + calcium carbonate | 2 | calcium carbonate, aspirin. Mechanism: passive renal tubular reabsorption due to increased pH. Minor/Significance Unknown. Salicylate levels increased at moderate doses; salicylate levels decreased at large doses (d/t increased renal excretion of unchanged salicylic acid) |
| aspirin + folic acid | 2 | aspirin decreases levels of folic acid by inhibition of GI absorption. Applies only to oral form of both agents. Minor/Significance Unknown |
| aspirin + ketoprofen | 2 | aspirin will increase the level or effect of ketoprofen by acidic (anionic) drug competition for renal tubular clearance. Minor/Significance Unknown |

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| aspirin + verapamil | 2 | verapamil increases effects of aspirin by unknown mechanism. Minor/Significance Unknown. Enhanced antiplatelet activity |
| budesonide + eplerenone | 2 | budesonide will decrease the level or effect of eplerenone by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Minor/Significance Unknown |
| budesonide + insulin | 2 | budesonide decreases effects of insulin regular human by pharmacodynamic antagonism. Minor/Significance Unknown |
| budesonide + metformin | 2 | budesonide decreases effects of metformin by pharmacodynamic antagonism. Minor/Significance Unknown |
| captopril + tamsulosin | 2 | tamsulosin, captopril. Either increases effects of the other by pharmacodynamic synergism. Minor/Significance Unknown. May increase risk of hypotension |
| carbamazepine + cyanocobalamin | 2 | carbamazepine decreases levels of cyanocobalamin by inhibition of GI absorption. Applies only to oral form of both agents. Minor/Significance Unknown |
| celecoxib + meloxicam | 2 | celecoxib will increase the level or effect of meloxicam by acidic (anionic) drug competition for renal tubular clearance. Minor/Significance Unknown |
| chlorthalidone + metformin | 2 | chlorthalidone decreases effects of metformin by pharmacodynamic antagonism. Minor/Significance Unknown. Thiazide dosage >50 mg/day may increase blood glucose |
| cyanocobalamin + gabapentin | 2 | gabapentin decreases levels of cyanocobalamin by inhibition of GI absorption. Applies only to oral form of both agents. Minor/Significance Unknown |
| digoxin + magnesium hydroxide | 2 | digoxin decreases levels of magnesium hydroxide by increasing renal clearance. Minor/Significance Unknown |
| folic acid + indapamide | 2 | indapamide decreases levels of folic acid by increasing renal clearance. Minor/Significance Unknown |
| folic acid + methotrexate | 2 | folic acid decreases effects of methotrexate by pharmacodynamic antagonism. Minor/Significance Unknown. Vitamin preparations containing folic acid or its derivatives may decrease responses to systemically administered methotrexate |
| formoterol + furosemide | 2 | formoterol, furosemide. Mechanism: pharmacodynamic synergism. Minor/Significance Unknown. Hypokalemia |
| ketoprofen + meloxicam | 2 | ketoprofen will increase the level or effect of meloxicam by acidic (anionic) drug competition for renal tubular clearance. Minor/Significance Unknown |
| levothyroxine + omeprazole | 2 | omeprazole decreases levels of levothyroxine by increasing gastric pH. Applies only to oral form of both agents. Minor/Significance Unknown. Conflicting evidence regarding this interaction exists |
| aceclofenac + aspirin | 1 | aceclofenac will increase the level or effect of aspirin by acidic (anionic) drug competition for renal tubular clearance. Minor/Significance Unknown |
| aceclofenac + hydrochlorothiazide | 1 | hydrochlorothiazide will increase the level or effect of aceclofenac by acidic (anionic) drug competition for renal tubular clearance. Minor/Significance Unknown |
| aceclofenac + indapamide | 1 | indapamide will increase the level or effect of aceclofenac by acidic (anionic) drug competition for renal tubular clearance. Minor/Significance Unknown |
| aceclofenac + lisinopril | 1 | aceclofenac decreases effects of lisinopril by pharmacodynamic antagonism. Minor/Significance Unknown. NSAIDs decrease prostaglandin synthesis |
| acetazolamide + aspirin | 1 | aspirin will decrease the level or effect of acetazolamide by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Minor/Significance Unknown |

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| acetazolamide + atorvastatin | 1 | acetazolamide will increase the level or effect of atorvastatin by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Minor/Significance Unknown |
| acetylcysteine + nitroglycerin | 1 | acetylcysteine increases effects of nitroglycerin sublingual by Other (see comment). Minor/Significance Unknown. Comment: Acetylcysteine may enhance vasodilatory effects of nitroglycerin |
| amitriptyline + carbamazepine | 1 | carbamazepine decreases levels of amitriptyline by increasing metabolism. Minor/Significance Unknown |
| amoxicillin + clarithromycin | 1 | clarithromycin decreases effects of amoxicillin by pharmacodynamic antagonism. Minor/Significance Unknown |
| apixaban + dexamethasone | 1 | dexamethasone will decrease the level or effect of apixaban by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Contraindicated. Reduces anticoagulant effect by decreasing apixaban systemic exposure |
| aspirin + cefixime | 1 | cefixime will increase the level or effect of aspirin by acidic (anionic) drug competition for renal tubular clearance. Minor/Significance Unknown |
| aspirin + celecoxib | 1 | aspirin will increase the level or effect of celecoxib by acidic (anionic) drug competition for renal tubular clearance. Minor/Significance Unknown |
| aspirin + diclofenac topical | 1 | diclofenac topical, aspirin. Either increases effects of the other by pharmacodynamic synergism. Minor/Significance Unknown. Although low, there is systemic exposure to diclofenac topical; theoretically, concomitant administration with systemic NSAIDS or aspirin may result in increased NSAID adverse effects |
| aspirin + ibuprofen | 1 | aspirin will increase the level or effect of ibuprofen by acidic (anionic) drug competition for renal tubular clearance. Minor/Significance Unknown |
| aspirin + ketorolac | 1 | aspirin will increase the level or effect of ketorolac by acidic (anionic) drug competition for renal tubular clearance. Minor/Significance Unknown |
| aspirin + lornoxicam | 1 | aspirin will increase the level or effect of lornoxicam by acidic (anionic) drug competition for renal tubular clearance. Minor/Significance Unknown |
| aspirin + meloxicam | 1 | aspirin will increase the level or effect of meloxicam by acidic (anionic) drug competition for renal tubular clearance. Minor/Significance Unknown |
| atorvastatin + orlistat | 1 | orlistat increases effects of atorvastatin by pharmacodynamic synergism. Minor/Significance Unknown |
| bisoprolol + escitalopram | 1 | escitalopram increases levels of bisoprolol by decreasing metabolism. Minor/Significance Unknown |
| budesonide + clarithromycin | 1 | budesonide will decrease the level or effect of clarithromycin by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Minor/Significance Unknown |
| budesonide + furosemide | 1 | budesonide, furosemide. Mechanism: pharmacodynamic synergism. Minor/Significance Unknown. Risk of hypokalemia, especially with strong glucocorticoid activity |
| calcium carbonate + manganese | 1 | calcium carbonate, manganese. Either decreases levels of the other by inhibition of GI absorption. Applies only to oral form of both agents. Minor/Significance Unknown. Separate by 2 hours |
| captopril + lornoxicam | 1 | lornoxicam decreases effects of captopril by pharmacodynamic antagonism. Minor/Significance Unknown. NSAIDs decrease prostaglandin synthesis |

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| carbamazepine + flurbiprofen | 1 | carbamazepine will decrease the level or effect of flurbiprofen by affecting hepatic enzyme CYP2C9/10 metabolism. Minor/Significance Unknown. |
| carbamazepine + folic acid | 1 | carbamazepine decreases levels of folic acid by unspecified interaction mechanism. Minor/Significance Unknown |
| carbamazepine + meloxicam | 1 | carbamazepine will decrease the level or effect of meloxicam by affecting hepatic enzyme CYP2C9/10 metabolism. Minor/Significance Unknown |
| carbamazepine + oxcarbazepine | 1 | carbamazepine decreases levels of oxcarbazepine by increasing metabolism. Minor/Significance Unknown |
| celecoxib + indapamide | 1 | indapamide will increase the level or effect of celecoxib by acidic (anionic) drug competition for renal tubular clearance. Minor/Significance Unknown |
| chlorthalidone + meloxicam | 1 | chlorthalidone will increase the level or effect of meloxicam by acidic (anionic) drug competition for renal tubular clearance. Minor/Significance Unknown |
| chlorthalidone + tizanidine | 1 | tizanidine increases effects of chlorthalidone by pharmacodynamic synergism. Minor/Significance Unknown. Risk of hypotension |
| cyanocobalamin + esomeprazole | 1 | esomeprazole |
| cyanocobalamin + metformin | 1 | metformin decreases levels of cyanocobalamin by unspecified interaction mechanism. Minor/Significance Unknown. It may take several years of metformin therapy to develop vitamin B12 deficiency |
| cyanocobalamin + rabeprazole | 1 | rabeprazole decreases levels of cyanocobalamin by inhibition of GI absorption. Applies only to oral form of both agents. Minor/Significance Unknown |
| dexamethasone + ciprofloxacin | 1 | dexamethasone and ciprofloxacin both increase Other (see comment). Use Caution/Monitor. Coadministration of quinolone antibiotics and corticosteroids may increase risk of tendon rupture |
| dexamethasone + pantoprazole | 1 | dexamethasone will decrease the level or effect of pantoprazole by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Minor/Significance Unknown |
| diclofenac + lornoxicam | 1 | diclofenac will increase the level or effect of lornoxicam by acidic (anionic) drug competition for renal tubular clearance. Minor/Significance Unknown |
| diclofenac topical + ketoprofen | 1 | diclofenac topical, ketoprofen. Either increases effects of the other by pharmacodynamic synergism. Minor/Significance Unknown. Although low, there is systemic exposure to diclofenac topical; theoretically, concomitant administration with systemic NSAIDS or aspirin may result in increased NSAID adverse effects |
| felodipine + loratadine | 1 | felodipine will increase the level or effect of loratadine by P-glycoprotein (MDR1) efflux transporter. Minor/Significance Unknown |
| folic acid + furosemide | 1 | furosemide decreases levels of folic acid by increasing renal clearance. Minor/Significance Unknown |
| folic acid + metformin | 1 | metformin decreases levels of folic acid by unspecified interaction mechanism. Minor/Significance Unknown |
| folic acid + torsemide | 1 | torsemide decreases levels of folic acid by increasing renal clearance. Minor/Significance Unknown |
| formoterol + indapamide | 1 | formoterol, indapamide. Mechanism: pharmacodynamic synergism. Minor/Significance Unknown. Hypokalemia |

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| furosemide + magnesium sulfate | 1 | furosemide decreases levels of magnesium sulfate by increasing renal clearance. Minor/Significance Unknown |
| furosemide + spironolactone | 1 | spironolactone increases and furosemide decreases serum potassium. Effect of interaction is not clear, use caution. Modify Therapy/Monitor Closely |
| ibuprofen + indapamide | 1 | indapamide will increase the level or effect of ibuprofen by acidic (anionic) drug competition for renal tubular clearance. Minor/Significance Unknown |
| indapamide + insulin glargine | 1 | indapamide decreases effects of insulin glargine by pharmacodynamic antagonism. Minor/Significance Unknown. Thiazide dosage >50 mg/day may increase blood glucose |
| indapamide + lornoxicam | 1 | indapamide will increase the level or effect of lornoxicam by acidic (anionic) drug competition for renal tubular clearance. Minor/Significance Unknown |
| indapamide + naproxen | 1 | indapamide will increase the level or effect of naproxen by acidic (anionic) drug competition for renal tubular clearance. Minor/Significance Unknown |
| indapamide + tizanidine | 1 | tizanidine increases effects of indapamide by pharmacodynamic synergism. Minor/Significance Unknown. Risk of hypotension |
| lisinopril + lornoxicam | 1 | lornoxicam decreases effects of lisinopril by pharmacodynamic antagonism. Minor/Significance Unknown. NSAIDs decrease prostaglandin synthesis |
| lisinopril + tizanidine | 1 | tizanidine increases effects of lisinopril by pharmacodynamic synergism. Minor/Significance Unknown. Risk of hypotension |
| metformin + perindopril | 1 | perindopril increases toxicity of metformin by unspecified interaction mechanism. Use Caution/Monitor. Increases risk for hypoglycemia and lactic acidosis |
| spironolactone + tizanidine | 1 | tizanidine increases effects of spironolactone by pharmacodynamic synergism. Minor/Significance Unknown. Risk of hypotension |
| thiamine + torsemide | 1 | torsemide decreases levels of thiamine by increasing renal clearance. Minor/Significance Unknown |
| tizanidine + torsemide | 1 | tizanidine increases effects of torsemide by pharmacodynamic synergism. Minor/Significance Unknown. Risk of hypotension |