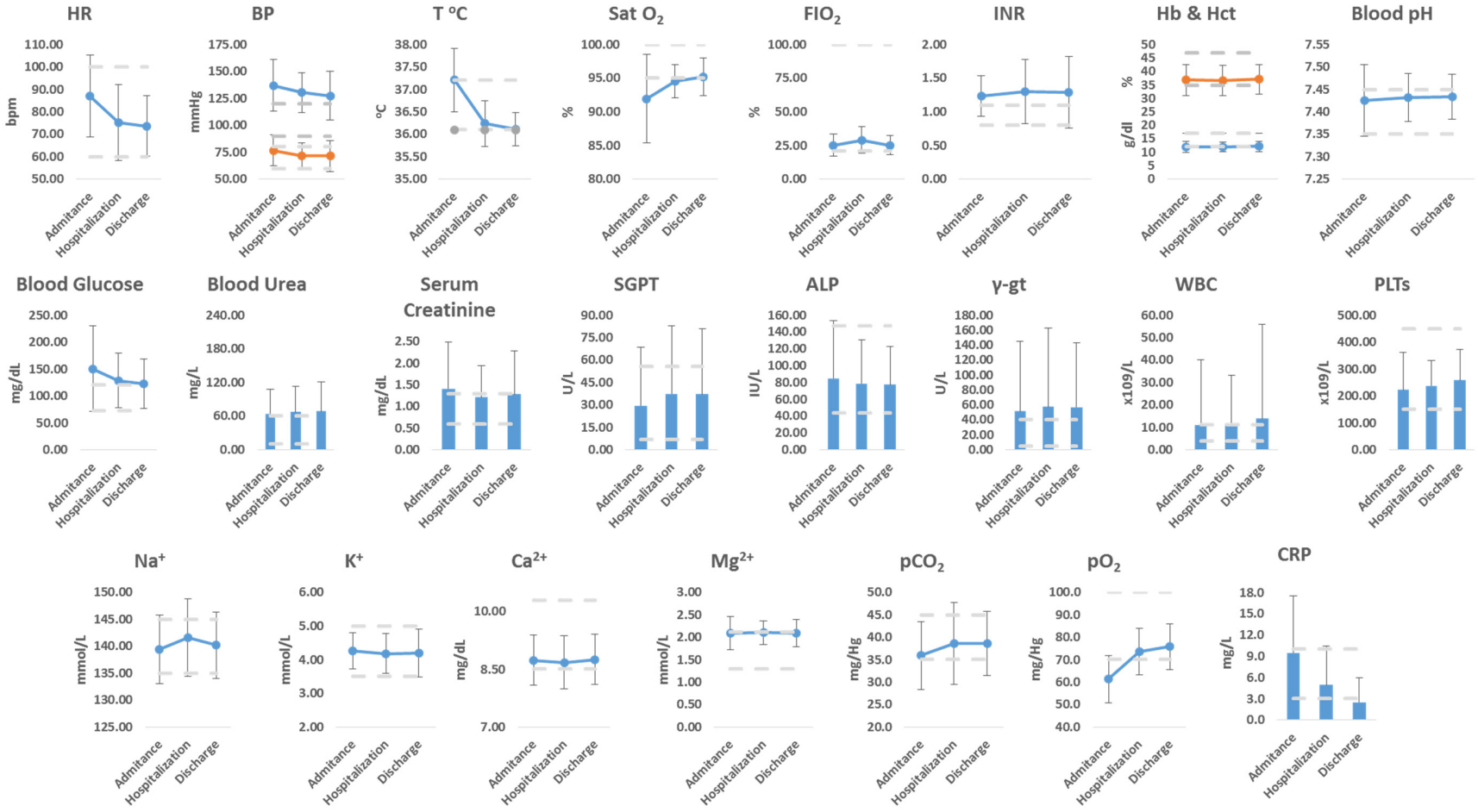
Supplementary Material: Drug-drug interactions among patients hospitalized with COVID-19 in Greece

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The supplementary file contains additional information as supplementary figures (SF) and/or tables (ST) regarding the scientific data that were presented in the manuscript

SF1. Clinical values of COVID-19 hospitalized patients. Dashed lines show the normal range



(HR: Heart Rate, BP: blood pressure; T: Temperature; Sat O2: Saturated O2; FIO2: fraction of inspired oxygen; INR: international normalised ratio; Hb: Hemoglobin; Hct: Hematocrit; SGPT: serum glutamic-pyruvic transaminase; ALP: Alkaline phosphatase; γ-gt: gamma-glutamyl transferase; WBC: white blood cells; PLTs: platelets; PCO2: partial pressure of carbon dioxide; pO2: partial pressure of oxygen; CRP: C-reactive protein)

ST 1 Drug combinations that may lead in pharmacokinetic DDIs as they recorded in the current study. SUA: Serious-Use alternative, Monitor: use with caution-monitor, Moderate: moderate-minor, occurrence: number of cases

# DDIs	Drug A	Drug B	Occurrence	Significance	Pharmacological mechanism
1	Acenocoumarol	Esomeprazole	3	Moderate	Inhibition of CYP mediated metabolism
2	Acenocoumarol	Allopurinol	1	Moderate	Modulation of anticoagulation action and altered INR-monitor
3	Acenocoumarol	Remdesivir	3	Monitor	Modulation of anticoagulation action and altered INR-monitor
4	Allopurinol	Furosemide	11	Monitor	Increased serum urate & Ct of metabolite
5	Amiodarone	Atorvastatin	2	Moderate	P-glycoprotein (MDR1) efflux transporter inhibition-increased bioavailability
6	Amiodarone	Silodosin	1	Monitor	P-glycoprotein (MDR1) efflux transporter inhibition-increased bioavailability
7	Amiodarone	Rivaroxaban	1	Monitor	Inhibition of CYP mediated metabolism
8	Amiodarone	Metformin	2	Moderate	Renal tubular clearance
9	Amiodarone	Metoprolol	1	Monitor	Inhibition of CYP mediated metabolism
10	Amiodarone	Dabigatran	1	Monitor	P-glycoprotein (MDR1) efflux transporter inhibition-increased bioavailability
11	Amiodarone	Tamsulosin	1	Moderate	Inhibition of CYP mediated metabolism
12	Amlodipine	Tacrolimus	1	Monitor	Inhibition of CYP mediated metabolism & P-gp transport
13	Amlodipine	Atorvastatin	1	Moderate	Inhibition of CYP mediated metabolism & P-gp transport
14	Anakinra	Alprazolam	1	Moderate	Restore 3uppressed CYP expression from inflamation
15	Apixaban	Amiodarone	1	Monitor	Inhibition of CYP mediated metabolism & P-gp transport
16	Apixaban	Dexamethasone	1	Monitor	Induction of CYP mediated metabolism
17	Azithromycin	Simvastatin	1	Moderate	Inhibition of CYP mediated metabolism
18	Bosutinib	Esomeprazole	1	Monitor	Reduced bioavailability due to pH dependent solubility
19	Bupropion	Clopidogrel	1	Monitor	Inhibition of CYP mediated metabolism
20	Bupropion	Metformin	1	Moderate	Inhibition of OCT2 mediated transport
21	Bupropion	Tamsulosin	1	Moderate	Inhibition of CYP mediated metabolism
22	Carbamazepine	Risperidone	1	Moderate	Induction of CYP mediated metabolism
23	Carbamazepine	Olanzapine	1	Moderate	Induction of CYP mediated metabolism
24	Carbamazepine	Esomeprazole	1	Moderate	Induction of CYP mediated metabolism
25	Carbamazepine	Dexamethasone	1	Moderate	Induction of CYP mediated metabolism
26	Carvedilol	Dabigatran	2	Monitor	P-glycoprotein (MDR1) efflux transporter inhibition-increased bioavailability
27	Carvedilol	Paroxetine	1	Monitor	Inhibition of CYP mediated metabolism
28	Carvedilol	Calcium	1	Moderate	Ca2+ reduce the bioavailability of β-blockers
29	Clopidogrel	Esomeprazole	**9**	SUA	Inhibition of CYP mediated metabolism
30	Clopidogrel	Lansoprazole	1	Monitor	Inhibition of CYP mediated metabolism

31	Dexamethasone	Solifenacin	2	Moderate	Induction of CYP mediated metabolism
32	Dexamethasone	Propafenone	1	Moderate	Induction of CYP mediated metabolism
33	Dexamethasone	Tacrolimus	1	Monitor	Induction of CYP mediated metabolism and P-gp transport
34	Digoxin	Alprazolam	1	Monitor	Protein binding competition
35	Digoxin	Esomeprazole	**2**	Monitor	P-glycoprotein (MDR1) efflux transporter inhibition-increased bioavailability
36	Digoxin	Azithromycin	2	Monitor	P-glycoprotein (MDR1) efflux transporter inhibition-increased bioavailability
37	Digoxin	Spironolactone	1	Moderate	Decrease tubular secretion
38	Diltiazem	Rivaroxaban	2	Monitor	Inhibition of CYP mediated metabolism & P-gp transport
39	Diltiazem	Atorvastatin	1	Monitor	Inhibition of CYP mediated metabolism & P-gp transport
40	Diltiazem	Amlodipine	1	SUA	Inhibition of CYP mediated metabolism
41	Diltiazem	Eplerenone	1	SUA	Inhibition of CYP mediated metabolism & P-gp transport
42	Diltiazem	Proglitazone	1	Monitor	Inhibition of CYP mediated metabolism
43	Diltiazem	Tamsulosin	1	Monitor	Inhibition of CYP mediated metabolism
44	Enoxaparin	Azithromycin	**21**	Moderate	Reduced metabolism
45	Esomeprazole	Escitalopram	7	Monitor	Inhibition of CYP mediated metabolism
46	Esomeprazole	Tacrolimus	1	Monitor	Inhibition of CYP mediated metabolism
47	Ferrous gluconate	Esomeprazole	2	Moderate	Reduced bioavailability due to pH dependent solubility
48	Ferrous gluconate	Omeprazole	1	Moderate	Reduced bioavailability due to pH dependent solubility
49	Fluconazole	Esomeprazole	1	Moderate	Inhibition of CYP mediated metabolism
50	Fluconazole	Escitalopram	1	Monitor	Inhibition of CYP mediated metabolism
51	Fluconazole	Amlodipine	1	Monitor	Inhibition of CYP mediated metabolism
52	Fluconazole	Tacrolimus	1	SUA	Inhibition of CYP mediated metabolism
53	Isavuconazonium	Tacrolimus	1	Monitor	Inhibition of CYP mediated metabolism & P-gp transport
54	Isavuconazonium	Dexamethasone	1	Moderate	Induction of CYP mediated metabolism and P-gp transport
55	Levothyroxine	Esomeprazole	12	Moderate	Reduced bioavailability due to pH dependent solubility
56	Levothyroxine	Omeprazole	2	Moderate	Reduced bioavailability due to pH dependent solubility
57	Levothyroxine	Lansoprazole	2	Moderate	Reduced bioavailability due to pH dependent solubility
58	Levothyroxine	Calcium	2	Moderate	Inhibition of GI absorption reduced bioavailability
59	Levothyroxine	Rabeprazole	1	Moderate	Reduced bioavailability due to pH dependent solubility
60	Magnesium	Levofloxacin	1	Moderate	Modulation of GI absorption
61	Methotrexate	Gliclazide	1	Moderate	Protein binding competition
62	Methylprednisolone	Silodosin	1	Moderate	Induction of CYP mediated metabolism
63	Nifedipine	Atorvastatin	1	Monitor	Inhibition of CYP mediated metabolism & P-gp transport
64	Omeprazole	Ciprofloxacin	1	Moderate	Reduced bioavailability due to pH dependent solubility

65	Omeprazole	Olanzapine	1	Moderate	Induction of CYP mediated metabolism
66	Omeprazole	Diazepam	1	Moderate	Inhibition of CYP mediated metabolism
67	Omeprazole	Clopidogrel	1	SUA	Inhibition of CYP mediated metabolism
68	Omeprazole	Duloxetine	1	Monitor	Reduced bioavailability due to pH dependent solubility
69	Proglitazone	Rosuvastatin	1	Moderate	Inhibition of OATP1B1 mediated transport-risk of myopathy
70	Ranolazine	Rosuvastatin	1	Moderate	Inhibition of OATP1B1 mediated transport-risk of myopathy
71	Sertraline	Haloperidol	1	Monitor	Inhibition of CYP mediated metabolism
72	Tamsulosin	Fluoxetine	1	Monitor	Inhibition of CYP mediated metabolism

ST 2 Drug combinations that may lead in pharmacodynamic DDIs as they recorded in the current study. SUA: Serious-Use alternative, Monitor: use with caution-monitor, Moderate: moderate-minor, occurrence: number of cases

DDIs #	Drug A	Drug B	Occurrence	Significance	Description
1	Abatacept	Adalimumab	1	SUA	PD-synergism increased risk for serious infection
2	Acenocoumarol	Rosuvastatin	2	Moderate	Modulation of anticoagulation action and altered INR-monitor
3	Acenocoumarol	Methylprednisolone	3	Monitor	Modulation of anticoagulation action and altered INR-monitor
4	Acenocoumarol	Piperacilin	1	Moderate	Modulation of anticoagulation action and altered INR-monitor
5	Acenocoumarol	Ceftriaxone	2	SUA	Modulation of anticoagulation action and altered INR-monitor
6	Acenocoumarol	Dexamethasone	1	Moderate	Modulation of anticoagulation action and altered INR-monitor
7	Alprazolam	Moxonidine	1	Moderate	PD synergism, sedation
8	Amiodarone	Citalopram	1	Monitor	QT prolongation
9	Amiodarone	Formoterol	1	Monitor	QT prolongation
10	Amiodarone	Ciprofloxacin	1	Monitor	QT prolongation
11	Amiodarone	Quetiapine	1	Monitor	QT prolongation
12	Amiodarone	Escitalopram	1	Monitor	QT prolongation
13	Amiodarone	Levofloxacin	1	Monitor	QT prolongation
14	Amisulpride	Haloperidol	1	Monitor	QT prolongation
15	Amisulpride	Quetiapine	1	Monitor	QT prolongation
16	amitriptyline	Risperidone	1	Monitor	QT prolongation
17	Amlodipine	Calcium	1	Moderate	PD-antagonism of Ca2+ with Ca2+ channel blockers
18	Apixaban	Escitalopram	1	Moderate	SSRIs may alter serotonin release from platelets and induce bleeding
19	Aspirin	Olmesartan	2	Moderate	Kidney function, NSAIDs & ARBs may produce deterioration in renal function (elderly)

20	Aspirin	Telmisartan	3	Moderate	Kidney function, NSAIDs & ARBs may produce deterioration in renal function (elderly)
21	Aspirin	Duloxetine	1	Monitor	SSRIs may alter serotonin release from platelets and induce bleeding
22	Aspirin	Valsartan	4	Moderate	Kidney function, NSAIDs & ARBs may produce deterioration in renal function (elderly)
23	Aspirin	Carvedilol	5	Moderate	PD antagonism
24	Aspirin	Citalopram	2	Moderate	SSRIs may alter serotonin release from platelets and induce bleeding
25	Aspirin	Escitalopram	2	Moderate	SSRIs may alter serotonin release from platelets and induce bleeding
26	Aspirin	Irbesartan	1	Moderate	Kidney function, NSAIDs & ARBs may produce deterioration in renal function (elderly)
27	Aspirin	Ramipril	3	Moderate	Reduce renal function & antihypertensive effect of ACE inhibitors
28	Aspirin	Candesartan	1	Moderate	Kidney function, NSAIDs & ARBs may produce deterioration in renal function (elderly)
29	Aspirin	Vortioxetine	1	Moderate	SSRIs may alter serotonin release from platelets and induce bleeding
30	Aspirin	Metoprolol	1	Moderate	PD antagonism
31	Aspirin	Bisoprolol	1	Moderate	PD antagonism
32	Aspirin	Perindopril	1	Moderate	Reduce renal function & antihypertensive effect of ACE inhibitors
33	Atenolol	Alprazolam	1	Moderate	Additive hypotensive effects
34	Atenolol	Zolpidem	1	Moderate	Additive hypotensive effects
35	Atenolol	Insulin	1	Moderate	Hypoglycemia
36	Azithromycin	Mirtazapine	2	Monitor	QT prolongation
37	Biperiden	Levomepromazine	1	Moderate	CNS/Respiratory depression
38	Bisoprolol	Silodosin	1	Moderate	PD synergism
39	Bisoprolol	Formoterol	1	Moderate	PD antagonism
40	Carbamazepine	Levomepromazine	1	Moderate	PD synergism, sedation
41	Carbamazepine	Biperiden	1	Moderate	CNS/Respiratory depression
42	Carvedilol	Salbutamol	1	Moderate	PD antagonism
43	Ciprofloxacin	Fluoxetine	1	Monitor	QT prolongation
44	Citalopram	Furosemide	2	Moderate	Risk for hypnatriemia
45	Citalopram	Clopidogrel	1	Moderate	SSRIs may alter serotonin release from platelets and induce bleeding
46	Dexamethasone	Aspirin	10	Moderate	GI Side effects
47	Dexamethasone	Levofloxacin	11	Moderate	Quinolones & corticosteroids increase risk of tendon rupture
48	Dexamethasone	Ciprofloxacin	**5**	Moderate	Quinolones & corticosteroids increase risk of tendon rupture
49	Donepezile	Paroxetine	1	Monitor	QT prolongation
50	Donepezile	Haloperidol	1	Moderate	Additive anticholinergic effects,

51	Donepezile	Olanzapine	1	Moderate	Additive anticholinergic effects,
52	Drospirenone	Spironolactone	1	Moderate	Risk for hyperkalemia
53	Drospirenone	Candesartan	1	Moderate	Risk for hyperkalemia
54	Drospirenone	Carvedilol	1	Moderate	Risk for hyperkalemia
55	Empagliflozin	Furosemide	1	Moderate	SGLT-2 inhibitors may potentiate the diuretic/ hypotensive effects of loop diuretics/ loop diuretics can cause hyperglycemia and may reduce the therapeutic effects of SGLT-2 inhibitors
56	Empagliflozin	Spironolactone	1	Moderate	SGLT-2 inhibitors may potentiate the diuretic/ hypotensive effects of loop diuretics/ loop diuretics can cause hyperglycemia and may reduce the therapeutic effects of SGLT-2 inhibitors
57	Enoxaparin	Methylprednisolone	**32**	Moderate	Corticosteroids may decrease anticoagulant activity/impair vascular integrity
58	Enoxaparin	Ceftaroline	6	Moderate	cephalosporins may decrease prothrombin activity
59	Enoxaparin	Budesonide	**28**	Moderate	Corticosteroids may decrease anticoagulant activity/impair vascular integrity
60	Enoxaparin	Dexamethasone	59	Moderate	Corticosteroids may decrease anticoagulant activity/impair vascular integrity
61	Enoxaparin	Ceftriaxone	**16**	Moderate	cephalosporins may decrease prothrombin activity
62	Enoxaparin	Piperacilin	**12**	Moderate	PD-synergism anticoagulation
63	Enoxaparin	Perindopril	**1**	Moderate	LMW-Heps may suppress adrenal aldosterone secretion. Hyperkalemia (also from ACE inhb)
64	Enoxaparin	Irbesartan	7	Moderate	LMW-Heps may suppress adrenal aldosterone secretion. Hyperkalemia (also from ACE inhb)
65	Enoxaparin	Ramipril	**5**	Moderate	LMW-Heps may suppress adrenal aldosterone secretion. Hyperkalemia (also from ACE inhb)
66	Enoxaparin	Dabigatran	2	SUA	PD synergism enhanced bleeding risk
67	Enoxaparin	Citalopram	4	Moderate	PD synergism enhanced bleeding risk
68	Enoxaparin	Telmisartan	**2**	Moderate	LMW-Heps may suppress adrenal aldosterone secretion. Hyperkalemia (also from ACE inhb)
69	Enoxaparin	Prednisolone	1	Moderate	Corticosteroids may decrease anticoagulant activity/impair vascular integrity
70	Enoxaparin	Valsartan	1	Moderate	LMW-Heps may suppress adrenal aldosterone secretion. Hyperkalemia (also from ACE inhb)
71	Eplerenone	Potassium Chloride	1	Monitor	Risk for hyperkalemia
72	Escitalopram	Levofloxacin	1	Monitor	QT prolongation
73	Escitalopram	Leuprolide	3	SUA	QT prolongation
74	Escitalopram	Clopidogrel	2	Moderate	SSRIs may alter serotonin release from platelets and induce bleeding
75	Escitalopram	Mirtazapine	1	Monitor	Risk for serotonine syndrome
76	Furosemide	Sertraline	1	Moderate	PD-synergism hyponatriemia

77	Furosemide	Metformin	1	Moderate	Hypoglycemia
78	Gliclazide	Furosemide	2	Moderate	PD antagonism
79	Gliclazide	Aspirin	2	Moderate	Hypoglycemia
80	Gliclazide	Lisinopril	1	Moderate	Hypoglycemia
81	Haloperidol	Quetiapine	3	Monitor	QT prolongation
82	Indacaterol	Propafenone	1	Monitor	QT prolongation
83	Indacaterol	Quetiapine	1	Monitor	QT prolongation
84	Indacaterol	Furosemide	1	Moderate	Risk of hypokalemia
85	Indacaterol	Bisoprolol	2	Moderate	Antagonism -brochospasm
86	Insulin	Risperidone	1	Moderate	Antipsychotics can produce hyperglycemia and alter blood glucose control
87	Insulin	Levofloxacin	2	Monitor	Quinolone antibiotic administration may result in hyper- or hypoglycemia
88	Ipratropium	Haloperidol	**1**	Moderate	Additive anticholinergic effects,
89	Ipratropium	Quetiapine	7	Monitor	Hypoglycemia
90	Leuprolide	Escitalopram	1	Monitor	QT prolongation
91	Levodopa	Haloperidol	1	SUA	PD-antagonism decreased effect of levodopa
92	Levodopa	Quetiapine	1	Monitor	PD-antagonism decreased effect of levodopa
93	Levodopa	Telmisartan	1	Moderate	PD-synergism hypotension
94	Levofloxacin	Fluoxetine	1	Monitor	QT prolongation
95	Linezolid	Salbutamol	1	Monitor	MAOIs can potentiate the cardiovascular ADE of β-2-adrenergic agonists
96	Linezolid	Escitalopram	1	SUA	Risk for serotonine syndrome
97	Linezolid	Aripiprazole	1	Monitor	Risk for serotonine syndrome
98	Methylprednisolone	Aspirin	6	Moderate	GI Side effects
99	Methylprednisolone	Metformin	1	Moderate	PD antagonism
100	Methylprednisolone	Levofloxacin	5	Moderate	Quinolones & corticosteroids increase risk of tendon rupture
101	Methylprednisolone	Moxifloxacin	**1**	Moderate	Quinolones & corticosteroids increase risk of tendon rupture
102	Methylprednisolone	Ciprofloxacin	2	Moderate	Quinolones & corticosteroids increase risk of tendon rupture
103	Olanzapine	Levomepromazine	1	Moderate	PD-synergism & excessive parasympatholytic effects
104	Olanzapine	Codeine	1	Monitor	PD synergism, sedation
105	Olanzapine	Aclidinium	1	Moderate	Hypoglycemia
106	Olanzapine	Ipratropium	1	Moderate	Hypoglycemia

107	Olanzapine	Mirtazapine	1	Monitor	QT prolongation
108	Olanzapine	Chloropromazine	1	Monitor	QT prolongation
109	Paroxetine	Clopidogrel	1	Monitor	SSRIs may alter serotonin release from platelets and induce bleeding
110	Perindopril	Alogliptin	1	Moderate	Hypoglycemia
111	perphenazine	Risperidone	1	Monitor	QT prolongation
112	Prednisolone	Furosemide	2	Moderate	PD synergism risk for hypokalemia
113	Pregabalin	Sertraline	1	Monitor	Respiratory depression
114	Quetiapine	Propafenone	1	Monitor	QT prolongation
115	Quetiapine	Ciprofloxacin	3	Monitor	QT prolongation
116	Quetiapine	Codeine	1	Monitor	PD synergism, sedation
117	Quetiapine	Sertraline	2	Monitor	QT prolongation
118	Quetiapine	Risperidone	2	Monitor	QT prolongation
119	Quetiapine	Diazepam	1	Monitor	PD synergism, sedation
120	Quetiapine	Levofloxacin	2	Monitor	QT prolongation
121	Quetiapine	Fluoxetine	1	Monitor	QT prolongation
122	Ramipril	Potassium Chloride	1	Monitor	Risk for hyperkalemia
123	Ramipril	Metformin	3	Moderate	Hypoglycemia
124	Risperidone	Paroxetine	1	Monitor	QT prolongation
125	Rivaroxaban	Escitalopram	1	Moderate	SSRIs may alter serotonin release from platelets and induce bleeding
126	Salbutamol	Haloperidol	**1**	Monitor	QT prolongation
127	Salbutamol	Furosemide	3	Moderate	PD synergism risk for hypokalemia
128	Salbutamol	Propafenone	1	Monitor	QT prolongation
129	Salbutamol	Escitalopram	2	Monitor	QT prolongation
130	Salbutamol	Bisoprolol	3	Moderate	PD antagonism
131	Salbutamol	Levofloxacin	6	Monitor	QT prolongation
132	Salbutamol	Azithromycin	**1**	Monitor	QT prolongation
133	Salbutamol	Moxifloxacin	**1**	Monitor	QT prolongation
134	Salbutamol	Metoprolol	2	Moderate	PD antagonism
135	Salbutamol	Formoterol	1	Moderate	PD-synergism cardiovascular side effects
136	Salbutamol	Norfloxacin	1	Monitor	QT prolongation
137	Salbutamol	Fluoxetine	2	Monitor	QT prolongation
138	Salbutamol	Quetiapine	3	Monitor	QT prolongation
139	Salbutamol	Ciprofloxacin	1	Monitor	QT prolongation
140	Salmeterol	Bisoprolol	2	Moderate	PD antagonism

141	Salmeterol	Furosemide	1	Moderate	Risk of hypokalemia
142	Saxagliptin	Chloropromazine	1	Moderate	Antipsychotics can produce hyperglycemia and alter blood glucose control
143	Saxagliptin	Olanzapine	1	Moderate	Antipsychotics can produce hyperglycemia and alter blood glucose control
144	Sertraline	Clopidogrel	2	Moderate	SSRIs may alter serotonin release from platelets and induce bleeding
145	Sertraline	Olanzapine	1	Monitor	QT prolongation
146	Spironlactone	Candesartan	2	Moderate	Risk for hyperkalemia
147	Spironlactone	Potassium Chloride	2	Monitor	PD -synergism hyperkaliemia
148	Trazodone	Paroxetine	1	Monitor	QT prolongation
149	Vancomycin	Tacrolimus	1	Monitor	Risk for nephrotoxicity and/or ototoxicity.
150	Venlafaxine	Risperidone	1	Monitor	QT prolongation
151	Venlafaxine	Paroxetine	1	Monitor	Risk for serotonine syndrome
152	Venlafaxine	Mirtazapine	1	Monitor	QT prolongation
153	Venlafaxine	Azithromycin	1	Monitor	QT prolongation
154	Zolpidem	Alprazolam	1	Monitor	PD synergism, sedation