

# Adalimumab Safety in Inflammatory Bowel Disease: A Clinical Cohort Study with Time-to-Event Analysis and FAERS Signal Assessment

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## Supplementary Materials

Table S1. All adverse events by MedDRA SOC, PT, and treatment phase, with incidence rates per 100 PYs.

| MedDRA SOC/ MedDRA PT                       | Induction | Maintenance | Other*   | Total     | Incidence/ 100 PYs |
|---------------------------------------------|-----------|-------------|----------|-----------|--------------------|
| <b>Blood and lymphatic system disorders</b> | <b>0</b>  | <b>9</b>    | <b>0</b> | <b>9</b>  | 1.52               |
| Leukopenia                                  | 0         | 1           | 0        | 1         | 0.17               |
| Lymph node pain                             | 0         | 1           | 0        | 1         | 0.17               |
| Lymphadenopathy                             | 0         | 2           | 0        | 2         | 0.34               |
| Splenomegaly                                | 0         | 1           | 0        | 1         | 0.17               |
| Thrombocytopenia                            | 0         | 3           | 0        | 3         | 0.51               |
| Thrombocytosis                              | 0         | 1           | 0        | 1         | 0.17               |
| <b>Cardiac disorders</b>                    | <b>1</b>  | <b>5</b>    | <b>0</b> | <b>6</b>  | 1.01               |
| Palpitations                                | 0         | 2           | 0        | 2         | 0.34               |
| Tachycardia                                 | 1         | 3           | 0        | 4         | 0.68               |
| <b>Ear and labyrinth disorders</b>          | <b>0</b>  | <b>1</b>    | <b>0</b> | <b>1</b>  | 0.17               |
| Ear pain                                    | 0         | 1           | 0        | 1         | 0.17               |
| <b>Eye disorders</b>                        | <b>1</b>  | <b>5</b>    | <b>0</b> | <b>6</b>  | 1.01               |
| Chalazion                                   | 0         | 1           | 0        | 1         | 0.17               |
| Conjunctivitis allergic                     | 0         | 1           | 0        | 1         | 0.17               |
| Eye irritation                              | 1         | 0           | 0        | 1         | 0.17               |
| Eye pruritus                                | 0         | 1           | 0        | 1         | 0.17               |
| Iridocyclitis                               | 0         | 1           | 0        | 1         | 0.17               |
| Vision blurred                              | 0         | 1           | 0        | 1         | 0.17               |
| <b>Gastrointestinal disorders</b>           | <b>0</b>  | <b>13</b>   | <b>0</b> | <b>13</b> | 2.20               |
| Abdominal pain upper                        | 0         | 1           | 0        | 1         | 0.17               |
| Dysphagia                                   | 0         | 1           | 0        | 1         | 0.17               |
| Gastroesophageal reflux disease             | 0         | 1           | 0        | 1         | 0.17               |
| Mouth swelling                              | 0         | 1           | 0        | 1         | 0.17               |

|                                                             |          |            |          |            |              |
|-------------------------------------------------------------|----------|------------|----------|------------|--------------|
| Nausea                                                      | 0        | 1          | 0        | 1          | 0.17         |
| Noninfective sialoadenitis                                  | 0        | 1          | 0        | 1          | 0.17         |
| Obstructive pancreatitis                                    | 0        | 2          | 0        | 2          | 0.34         |
| Pancreatitis acute                                          | 0        | 1          | 0        | 1          | 0.17         |
| Paraesthesia oral                                           | 0        | 1          | 0        | 1          | 0.17         |
| Tongue discomfort                                           | 0        | 1          | 0        | 1          | 0.17         |
| Vomiting                                                    | 0        | 2          | 0        | 2          | 0.34         |
| <b>General disorders and administration site conditions</b> | <b>3</b> | <b>52</b>  | <b>0</b> | <b>55</b>  | <b>9.30</b>  |
| Asthenia                                                    | 0        | 4          | 0        | 4          | 0.68         |
| Chest discomfort                                            | 0        | 1          | 0        | 1          | 0.17         |
| Chest pain                                                  | 0        | 1          | 0        | 1          | 0.17         |
| Chills                                                      | 1        | 1          | 0        | 2          | 0.34         |
| Drug intolerance                                            | 0        | 1          | 0        | 1          | 0.17         |
| Fatigue                                                     | 0        | 12         | 0        | 12         | 2.03         |
| Injection site erythema                                     | 0        | 2          | 0        | 2          | 0.34         |
| Injection site hypersensitivity                             | 0        | 1          | 0        | 1          | 0.17         |
| Injection site induration                                   | 0        | 1          | 0        | 1          | 0.17         |
| Injection site reaction                                     | 0        | 2          | 0        | 2          | 0.34         |
| Malaise                                                     | 1        | 9          | 0        | 10         | 1.69         |
| Non-cardiac chest pain                                      | 0        | 1          | 0        | 1          | 0.17         |
| Oedema peripheral                                           | 0        | 1          | 0        | 1          | 0.17         |
| Peripheral swelling                                         | 0        | 1          | 0        | 1          | 0.17         |
| Pyrexia                                                     | 1        | 14         | 0        | 15         | 2.54         |
| <b>Hepatobiliary disorders</b>                              | <b>3</b> | <b>18</b>  | <b>0</b> | <b>21</b>  | <b>3.55</b>  |
| Cholelithiasis                                              | 0        | 10         | 0        | 10         | 1.69         |
| Cholestasis                                                 | 1        | 0          | 0        | 1          | 0.17         |
| Hepatic cyst                                                | 0        | 1          | 0        | 1          | 0.17         |
| Hepatic cytolysis                                           | 2        | 6          | 0        | 8          | 1.35         |
| Hepatic steatosis                                           | 0        | 1          | 0        | 1          | 0.17         |
| <b>Immune system disorders</b>                              | <b>0</b> | <b>2</b>   | <b>0</b> | <b>2</b>   | <b>0.34</b>  |
| Hypersensitivity                                            | 0        | 2          | 0        | 2          | 0.34         |
| <b>Infections and infestations</b>                          | <b>9</b> | <b>182</b> | <b>0</b> | <b>191</b> | <b>32.30</b> |
| Abdominal abscess                                           | 0        | 1          | 0        | 1          | 0.17         |
| Abscess                                                     | 0        | 1          | 0        | 1          | 0.17         |
| Abscess limb                                                | 0        | 1          | 0        | 1          | 0.17         |
| Appendicitis                                                | 0        | 1          | 0        | 1          | 0.17         |
| Bacterial disease carrier                                   | 1        | 2          | 0        | 3          | 0.51         |
| Bacterial sepsis                                            | 0        | 1          | 0        | 1          | 0.17         |
| Bronchitis                                                  | 0        | 2          | 0        | 2          | 0.34         |
| Clostridium difficile infection                             | 0        | 3          | 0        | 3          | 0.51         |
| Conjunctivitis                                              | 0        | 1          | 0        | 1          | 0.17         |
| COVID-19                                                    | 1        | 59         | 0        | 60         | 10.15        |

|                                                       |          |           |          |            |       |
|-------------------------------------------------------|----------|-----------|----------|------------|-------|
| COVID-19 pneumonia                                    | 0        | 2         | 0        | 2          | 0.34  |
| Escherichia urinary tract infection                   | 1        | 3         | 0        | 4          | 0.68  |
| Gastroenteritis                                       | 0        | 2         | 0        | 2          | 0.34  |
| Gastroenteritis viral                                 | 0        | 5         | 0        | 5          | 0.85  |
| Helicobacter infection                                | 0        | 1         | 0        | 1          | 0.17  |
| Herpes simplex                                        | 2        | 4         | 0        | 6          | 1.01  |
| Herpes virus infection                                | 0        | 1         | 0        | 1          | 0.17  |
| Herpes zoster                                         | 1        | 7         | 0        | 8          | 1.35  |
| Herpes zoster reactivation                            | 0        | 1         | 0        | 1          | 0.17  |
| Influenza                                             | 0        | 2         | 0        | 2          | 0.34  |
| Nasal herpes                                          | 0        | 1         | 0        | 1          | 0.17  |
| Nasopharyngitis                                       | 2        | 27        | 0        | 29         | 4.90  |
| Oral herpes                                           | 0        | 5         | 0        | 5          | 0.85  |
| Oral infection                                        | 0        | 1         | 0        | 1          | 0.17  |
| Pelvic abscess                                        | 0        | 2         | 0        | 2          | 0.34  |
| Pharyngitis                                           | 0        | 6         | 0        | 6          | 1.01  |
| Pilonidal disease                                     | 0        | 1         | 0        | 1          | 0.17  |
| Pneumonia                                             | 0        | 3         | 0        | 3          | 0.51  |
| Respiratory tract infection                           | 1        | 14        | 0        | 15         | 2.54  |
| Rhinitis                                              | 0        | 2         | 0        | 2          | 0.34  |
| Sinusitis                                             | 0        | 4         | 0        | 4          | 0.68  |
| Staphylococcal skin infection                         | 0        | 1         | 0        | 1          | 0.17  |
| Stoma site infection                                  | 0        | 1         | 0        | 1          | 0.17  |
| Tonsillitis                                           | 0        | 2         | 0        | 2          | 0.34  |
| Tonsillitis bacterial                                 | 0        | 2         | 0        | 2          | 0.34  |
| Upper respiratory tract infection                     | 0        | 1         | 0        | 1          | 0.17  |
| Urinary tract infection                               | 0        | 6         | 0        | 6          | 1.01  |
| Urinary tract infection bacterial                     | 0        | 1         | 0        | 1          | 0.17  |
| Urinary tract infection enterococcal                  | 0        | 1         | 0        | 1          | 0.17  |
| Vaginal infection                                     | 0        | 1         | 0        | 1          | 0.17  |
| <b>Injury, poisoning and procedural complications</b> | <b>0</b> | <b>8</b>  | <b>0</b> | <b>8</b>   | 1.35  |
| Forearm fracture                                      | 0        | 1         | 0        | 1          | 0.17  |
| Ligament injury                                       | 0        | 1         | 0        | 1          | 0.17  |
| Ligament rupture                                      | 0        | 1         | 0        | 1          | 0.17  |
| Limb injury                                           | 0        | 1         | 0        | 1          | 0.17  |
| Meniscus injury                                       | 0        | 1         | 0        | 1          | 0.17  |
| Stoma site rash                                       | 0        | 1         | 0        | 1          | 0.17  |
| Upper limb fracture                                   | 0        | 2         | 0        | 2          | 0.34  |
| <b>Investigations</b>                                 | <b>6</b> | <b>95</b> | <b>0</b> | <b>101</b> | 17.08 |
| Alanine aminotransferase increased                    | 0        | 14        | 0        | 14         | 2.37  |
| Amylase increased                                     | 1        | 4         | 0        | 5          | 0.85  |
| Antineutrophil cytoplasmic antibody increased         | 0        | 1         | 0        | 1          | 0.17  |

|                                           |          |           |          |           |             |
|-------------------------------------------|----------|-----------|----------|-----------|-------------|
| Antinuclear antibody increased            | 0        | 4         | 0        | 4         | 0.68        |
| Aspartate aminotransferase increased      | 0        | 8         | 0        | 8         | 1.35        |
| Bilirubin conjugated increased            | 0        | 1         | 0        | 1         | 0.17        |
| Blood alkaline phosphatase increased      | 0        | 3         | 0        | 3         | 0.51        |
| Blood bilirubin increased                 | 1        | 2         | 0        | 3         | 0.51        |
| Blood cholesterol increased               | 0        | 6         | 0        | 6         | 1.01        |
| Blood creatine phosphokinase MB increased | 0        | 1         | 0        | 1         | 0.17        |
| Blood creatinine increased                | 0        | 3         | 0        | 3         | 0.51        |
| Blood lactate dehydrogenase increased     | 0        | 2         | 0        | 2         | 0.34        |
| Blood pressure increased                  | 0        | 5         | 0        | 5         | 0.85        |
| Blood triglycerides increased             | 0        | 7         | 0        | 7         | 1.18        |
| Blood urea increased                      | 0        | 2         | 0        | 2         | 0.34        |
| Enterococcus test positive                | 0        | 1         | 0        | 1         | 0.17        |
| Escherichia test positive                 | 0        | 2         | 0        | 2         | 0.34        |
| Gamma-glutamyltransferase increased       | 1        | 10        | 0        | 11        | 1.86        |
| Glucose urine present                     | 1        | 0         | 0        | 1         | 0.17        |
| Haemophilus test positive                 | 0        | 2         | 0        | 2         | 0.34        |
| Hepatic enzyme increased                  | 0        | 1         | 0        | 1         | 0.17        |
| Lipase increased                          | 0        | 4         | 0        | 4         | 0.68        |
| Lipids increased                          | 0        | 2         | 0        | 2         | 0.34        |
| Moraxella test positive                   | 1        | 0         | 0        | 1         | 0.17        |
| Pancreatic enzymes increased              | 0        | 1         | 0        | 1         | 0.17        |
| Streptococcus test positive               | 0        | 2         | 0        | 2         | 0.34        |
| Transaminases increased                   | 0        | 3         | 0        | 3         | 0.51        |
| Urine ketone body present                 | 1        | 0         | 0        | 1         | 0.17        |
| Vitamin D decreased                       | 0        | 1         | 0        | 1         | 0.17        |
| Weight decreased                          | 0        | 2         | 0        | 2         | 0.34        |
| Weight increased                          | 0        | 1         | 0        | 1         | 0.17        |
| <b>Metabolism and nutrition disorders</b> | <b>3</b> | <b>24</b> | <b>0</b> | <b>27</b> | <b>4.57</b> |
| Decreased appetite                        | 1        | 1         | 0        | 2         | 0.34        |
| Dehydration                               | 0        | 1         | 0        | 1         | 0.17        |
| Dyslipidaemia                             | 1        | 0         | 0        | 1         | 0.17        |
| Hypercholesterolaemia                     | 0        | 3         | 0        | 3         | 0.51        |
| Hyperglycaemia                            | 1        | 1         | 0        | 2         | 0.34        |
| Hyperlipidaemia                           | 0        | 6         | 0        | 6         | 1.01        |
| Hypertriglyceridaemia                     | 0        | 1         | 0        | 1         | 0.17        |
| Hypoalbuminaemia                          | 0        | 2         | 0        | 2         | 0.34        |
| Hypochloraemia                            | 0        | 1         | 0        | 1         | 0.17        |
| Hypokalaemia                              | 0        | 2         | 0        | 2         | 0.34        |
| Hypomagnesaemia                           | 0        | 1         | 0        | 1         | 0.17        |
| Hyponatraemia                             | 0        | 1         | 0        | 1         | 0.17        |
| Hypophosphataemia                         | 0        | 1         | 0        | 1         | 0.17        |

|                                                                            |          |           |          |           |             |
|----------------------------------------------------------------------------|----------|-----------|----------|-----------|-------------|
| Hypoproteinaemia                                                           | 0        | 1         | 0        | 1         | 0.17        |
| Insulin resistance                                                         | 0        | 1         | 0        | 1         | 0.17        |
| Metabolic syndrome                                                         | 0        | 1         | 0        | 1         | 0.17        |
| <b>Musculoskeletal and connective tissue disorders</b>                     | <b>3</b> | <b>20</b> | <b>0</b> | <b>23</b> | <b>3.89</b> |
| Back pain                                                                  | 0        | 1         | 0        | 1         | 0.17        |
| Chest wall mass                                                            | 0        | 1         | 0        | 1         | 0.17        |
| Limb mass                                                                  | 0        | 1         | 0        | 1         | 0.17        |
| Lupus-like syndrome                                                        | 0        | 3         | 0        | 3         | 0.51        |
| Muscle spasms                                                              | 0        | 5         | 0        | 5         | 0.85        |
| Muscular weakness                                                          | 0        | 1         | 0        | 1         | 0.17        |
| Myalgia                                                                    | 1        | 4         | 0        | 5         | 0.85        |
| Neck mass                                                                  | 0        | 1         | 0        | 1         | 0.17        |
| Neck pain                                                                  | 1        | 0         | 0        | 1         | 0.17        |
| Osteonecrosis                                                              | 0        | 1         | 0        | 1         | 0.17        |
| Pain in extremity                                                          | 1        | 0         | 0        | 1         | 0.17        |
| Spinal pain                                                                | 0        | 1         | 0        | 1         | 0.17        |
| Systemic lupus erythematosus                                               | 0        | 1         | 0        | 1         | 0.17        |
| <b>Neoplasms benign, malignant and unspecified (incl cysts and polyps)</b> | <b>0</b> | <b>9</b>  | <b>2</b> | <b>11</b> | <b>1.86</b> |
| Adenocarcinoma pancreas                                                    | 0        | 0         | 1        | 1         | 0.17        |
| Adrenal adenoma                                                            | 0        | 2         | 0        | 2         | 0.34        |
| Brain neoplasm                                                             | 0        | 1         | 0        | 1         | 0.17        |
| Dysplastic naevus                                                          | 0        | 1         | 0        | 1         | 0.17        |
| Fibroma                                                                    | 0        | 1         | 0        | 1         | 0.17        |
| Haemangioma of liver                                                       | 0        | 1         | 0        | 1         | 0.17        |
| Hepatic cancer                                                             | 0        | 0         | 1        | 1         | 0.17        |
| Meningioma benign                                                          | 0        | 1         | 0        | 1         | 0.17        |
| Ovarian cancer                                                             | 0        | 1         | 0        | 1         | 0.17        |
| Skin papilloma                                                             | 0        | 1         | 0        | 1         | 0.17        |
| <b>Nervous system disorders</b>                                            | <b>1</b> | <b>27</b> | <b>0</b> | <b>28</b> | <b>4.74</b> |
| Ageusia                                                                    | 0        | 1         | 0        | 1         | 0.17        |
| Anosmia                                                                    | 0        | 1         | 0        | 1         | 0.17        |
| Balance disorder                                                           | 0        | 2         | 0        | 2         | 0.34        |
| Demyelination                                                              | 0        | 1         | 0        | 1         | 0.17        |
| Disturbance in attention                                                   | 0        | 1         | 0        | 1         | 0.17        |
| Dizziness                                                                  | 0        | 1         | 0        | 1         | 0.17        |
| Dyskinesia                                                                 | 0        | 1         | 0        | 1         | 0.17        |
| Epilepsy                                                                   | 0        | 1         | 0        | 1         | 0.17        |
| Headache                                                                   | 1        | 8         | 0        | 9         | 1.52        |
| Hyporeflexia                                                               | 0        | 1         | 0        | 1         | 0.17        |
| Ischaemic cerebral infarction                                              | 0        | 2         | 0        | 2         | 0.34        |
| Memory impairment                                                          | 0        | 2         | 0        | 2         | 0.34        |
| Migraine                                                                   | 0        | 1         | 0        | 1         | 0.17        |

|                                                        |          |           |          |           |             |
|--------------------------------------------------------|----------|-----------|----------|-----------|-------------|
| Paraesthesia                                           | 0        | 3         | 0        | 3         | 0.51        |
| Speech disorder                                        | 0        | 1         | 0        | 1         | 0.17        |
| <b>Psychiatric disorders</b>                           | <b>0</b> | <b>5</b>  | <b>0</b> | <b>5</b>  | <b>0.85</b> |
| Bradyphrenia                                           | 0        | 1         | 0        | 1         | 0.17        |
| Depressed mood                                         | 0        | 1         | 0        | 1         | 0.17        |
| Depression                                             | 0        | 1         | 0        | 1         | 0.17        |
| Disorganised speech                                    | 0        | 1         | 0        | 1         | 0.17        |
| Insomnia                                               | 0        | 1         | 0        | 1         | 0.17        |
| <b>Renal and urinary disorders</b>                     | <b>0</b> | <b>15</b> | <b>0</b> | <b>15</b> | <b>2.54</b> |
| Acute kidney injury                                    | 0        | 1         | 0        | 1         | 0.17        |
| Dysuria                                                | 0        | 1         | 0        | 1         | 0.17        |
| Nephrolithiasis                                        | 0        | 4         | 0        | 4         | 0.68        |
| Pollakiuria                                            | 0        | 1         | 0        | 1         | 0.17        |
| Renal colic                                            | 0        | 2         | 0        | 2         | 0.34        |
| Renal cyst                                             | 0        | 4         | 0        | 4         | 0.68        |
| Renal pain                                             | 0        | 1         | 0        | 1         | 0.17        |
| Urinary incontinence                                   | 0        | 1         | 0        | 1         | 0.17        |
| <b>Reproductive system and breast disorders</b>        | <b>0</b> | <b>17</b> | <b>0</b> | <b>17</b> | <b>2.88</b> |
| Breast disorder                                        | 0        | 1         | 0        | 1         | 0.17        |
| Breast mass                                            | 0        | 1         | 0        | 1         | 0.17        |
| Cervical dysplasia                                     | 0        | 1         | 0        | 1         | 0.17        |
| Cervix disorder                                        | 0        | 1         | 0        | 1         | 0.17        |
| Heavy menstrual bleeding                               | 0        | 2         | 0        | 2         | 0.34        |
| Menometrorrhagia                                       | 0        | 1         | 0        | 1         | 0.17        |
| Menstruation irregular                                 | 0        | 1         | 0        | 1         | 0.17        |
| Ovarian cyst                                           | 0        | 5         | 0        | 5         | 0.85        |
| Ovarian cyst ruptured                                  | 0        | 1         | 0        | 1         | 0.17        |
| Uterine cervical metaplasia                            | 0        | 1         | 0        | 1         | 0.17        |
| Uterine polyp                                          | 0        | 2         | 0        | 2         | 0.34        |
| <b>Respiratory, thoracic and mediastinal disorders</b> | <b>3</b> | <b>31</b> | <b>0</b> | <b>34</b> | <b>5.75</b> |
| Cough                                                  | 0        | 7         | 0        | 7         | 1.18        |
| Dyspnoea                                               | 0        | 3         | 0        | 3         | 0.51        |
| Epistaxis                                              | 0        | 2         | 0        | 2         | 0.34        |
| Nasal congestion                                       | 1        | 0         | 0        | 1         | 0.17        |
| Nasal polyps                                           | 0        | 1         | 0        | 1         | 0.17        |
| Oropharyngeal pain                                     | 0        | 6         | 0        | 6         | 1.01        |
| Pneumothorax                                           | 0        | 1         | 0        | 1         | 0.17        |
| Productive cough                                       | 0        | 3         | 0        | 3         | 0.51        |
| Pulmonary embolism                                     | 0        | 1         | 0        | 1         | 0.17        |
| Respiration abnormal                                   | 0        | 1         | 0        | 1         | 0.17        |
| Rhinorrhoea                                            | 0        | 2         | 0        | 2         | 0.34        |
| Sneezing                                               | 1        | 2         | 0        | 3         | 0.51        |

|                                               |           |            |          |            |               |
|-----------------------------------------------|-----------|------------|----------|------------|---------------|
| Throat irritation                             | 1         | 0          | 0        | 1          | 0.17          |
| Throat tightness                              | 0         | 1          | 0        | 1          | 0.17          |
| Tonsillar hypertrophy                         | 0         | 1          | 0        | 1          | 0.17          |
| <b>Skin and subcutaneous tissue disorders</b> | <b>2</b>  | <b>48</b>  | <b>0</b> | <b>50</b>  | <b>8.46</b>   |
| Acne                                          | 0         | 2          | 0        | 2          | 0.34          |
| Alopecia                                      | 0         | 5          | 0        | 5          | 0.85          |
| Dermatitis                                    | 0         | 2          | 0        | 2          | 0.34          |
| Dermatitis psoriasiform                       | 0         | 1          | 0        | 1          | 0.17          |
| Eczema                                        | 0         | 1          | 0        | 1          | 0.17          |
| Erythema                                      | 0         | 6          | 0        | 6          | 1.01          |
| Hyperhidrosis                                 | 0         | 2          | 0        | 2          | 0.34          |
| Nail disorder                                 | 0         | 1          | 0        | 1          | 0.17          |
| Pain of skin                                  | 0         | 1          | 0        | 1          | 0.17          |
| Pigmentation disorder                         | 0         | 1          | 0        | 1          | 0.17          |
| Pruritus                                      | 1         | 6          | 0        | 7          | 1.18          |
| Rash                                          | 0         | 4          | 0        | 4          | 0.68          |
| Rash macular                                  | 0         | 1          | 0        | 1          | 0.17          |
| Rash maculo-papular                           | 0         | 1          | 0        | 1          | 0.17          |
| Rash papular                                  | 0         | 1          | 0        | 1          | 0.17          |
| Rash pruritic                                 | 1         | 2          | 0        | 3          | 0.51          |
| Rash vesicular                                | 0         | 1          | 0        | 1          | 0.17          |
| Skin discharge                                | 0         | 1          | 0        | 1          | 0.17          |
| Skin disorder                                 | 0         | 5          | 0        | 5          | 0.85          |
| Skin exfoliation                              | 0         | 1          | 0        | 1          | 0.17          |
| Skin hyperpigmentation                        | 0         | 1          | 0        | 1          | 0.17          |
| Skin induration                               | 0         | 1          | 0        | 1          | 0.17          |
| Urticaria                                     | 0         | 1          | 0        | 1          | 0.17          |
| <b>Vascular disorders</b>                     | <b>0</b>  | <b>7</b>   | <b>0</b> | <b>7</b>   | <b>1.18</b>   |
| Aortic occlusion                              | 0         | 1          | 0        | 1          | 0.17          |
| Haematoma                                     | 0         | 1          | 0        | 1          | 0.17          |
| Hypertension                                  | 0         | 3          | 0        | 3          | 0.51          |
| Iliac artery occlusion                        | 0         | 1          | 0        | 1          | 0.17          |
| Raynaud's phenomenon                          | 0         | 1          | 0        | 1          | 0.17          |
| <b>Total</b>                                  | <b>35</b> | <b>593</b> | <b>2</b> | <b>630</b> | <b>106.55</b> |

MedDRA: Medical Dictionary for Regulatory Activities; PT: preferred term; PYs: patient-years; SOC: system organ class.

\* The “Other” category includes events not occurring during the induction or maintenance phases; specifically, two malignancies detected after adalimumab discontinuation, in accordance with the study methodology.

Table S2. New EIMs by MedDRA SOC and PT, with incidence, disproportionality analysis of FAERS data, and listedness assessment.

| Study data                                             |            |                       | FAERS data |                             |                            |            |                        |
|--------------------------------------------------------|------------|-----------------------|------------|-----------------------------|----------------------------|------------|------------------------|
| MedDRA SOC/ MedDRA PT                                  | n          | Incidence/<br>100 PYs | N          | ROR<br>(95% CI)             | PRR<br>(95% CI)            | Chi square | Listedness<br>per USPI |
| <b>Blood and lymphatic system disorders</b>            | <b>33</b>  | <b>5.58</b>           |            |                             |                            |            |                        |
| Anaemia                                                | 19         | 3.21                  | 1638       | 0.709<br>(0.675, 0.744)     | 0.71<br>(0.676, 0.745)     | 191.709    | Listed                 |
| Iron deficiency anaemia                                | 8          | 1.35                  | 146        | 1.532<br>(1.298, 1.807)*    | 1.531<br>(1.298, 1.806)    | 25.427     | Listed                 |
| Normocytic anaemia                                     | 6          | 1.01                  | 11         | 0.576<br>(0.318, 1.045)     | 0.576<br>(0.318, 1.045)    | 2.962      | Listed                 |
| <b>Eye disorders</b>                                   | <b>2</b>   | <b>0.34</b>           |            |                             |                            |            |                        |
| Iridocyclitis**                                        | 1          | 0.17                  | 128        | 2.873<br>(2.401, 3.437)*    | 2.872<br>(2.401, 3.436)*   | 144.169    | Unlisted               |
| Uveitis**                                              | 1          | 0.17                  | 1092       | 6.392<br>(5.996, 6.813)*    | 6.373<br>(5.98, 6.792)*    | 4,278.229  | Unlisted               |
| <b>Musculoskeletal and connective tissue disorders</b> | <b>64</b>  | <b>10.82</b>          |            |                             |                            |            |                        |
| Arthralgia**                                           | 51         | 8.63                  | 1313<br>7  | 2.57<br>(2.524, 2.616)*     | 2.506<br>(2.463, 2.55)*    | 11,395.938 | Unlisted               |
| Back pain                                              | 3          | 0.51                  | 3967       | 1.37<br>(1.327, 1.414)*     | 1.365<br>(1.323, 1.409)    | 377.737    | Unlisted               |
| Bone pain                                              | 1          | 0.17                  | 565        | 0.722<br>(0.665, 0.785)     | 0.723<br>(0.665, 0.785)    | 58.858     | Unlisted               |
| Joint stiffness**                                      | 2          | 0.34                  | 1106       | 3.626<br>(3.409, 3.856)*    | 3.617<br>(3.401, 3.846)*   | 1,923.315  | Unlisted               |
| Joint swelling**                                       | 1          | 0.17                  | 3570       | 2.413<br>(2.333, 2.497)*    | 2.398<br>(2.319, 2.480)*   | 2,759.806  | Unlisted               |
| Musculoskeletal stiffness**                            | 1          | 0.17                  | 2556       | 2.347<br>(2.255, 2.443)*    | 2.336<br>(2.245, 2.431)*   | 1,853.308  | Unlisted               |
| Myalgia                                                | 1          | 0.17                  | 1538       | 0.666<br>(0.633, 0.700)     | 0.667<br>(0.634, 0.702)    | 252.695    | Unlisted               |
| Osteoporosis                                           | 1          | 0.17                  | 578        | 0.999<br>(0.920, 1.085)     | 0.999<br>(0.920, 1.085)    | 0          | Unlisted               |
| Sacral pain                                            | 1          | 0.17                  | 0          | 0                           | 0                          |            | Unlisted               |
| Spinal pain**                                          | 2          | 0.34                  | 278        | 2.055<br>(1.822, 2.318)*    | 2.054<br>(1.821, 2.317)*   | 142.207    | Unlisted               |
| <b>Nervous system disorders</b>                        | <b>3</b>   | <b>0.51</b>           |            |                             |                            |            |                        |
| Hypoaesthesia                                          | 1          | 0.17                  | 2765       | 1.428<br>(1.375, 1.483)*    | 1.424<br>(1.372, 1.479)    | 339.412    | Unlisted               |
| Paraesthesia                                           | 1          | 0.17                  | 2334       | 1.114<br>(1.069, 1.161)*    | 1.114<br>(1.069, 1.160)    | 26.416     | Listed                 |
| Radiculopathy**                                        | 1          | 0.17                  | 95         | 2.874<br>(2.334, 3.539)*    | 2.874<br>(2.334, 3.538)*   | 106.657    | Unlisted               |
| <b>Skin and subcutaneous tissue disorders</b>          | <b>9</b>   | <b>1.52</b>           |            |                             |                            |            |                        |
| Eczema                                                 | 1          | 0.17                  | 565        | 0.797<br>(0.734, 0.867)     | 0.798<br>(0.734, 0.867)    | 28.321     | Unlisted               |
| Erythema nodosum**                                     | 2          | 0.34                  | 139        | 3.213<br>(2.703, 3.819)*    | 3.212<br>(2.703, 3.817)*   | 194.273    | Unlisted               |
| Psoriasis**                                            | 5          | 0.85                  | 8492       | 5.144<br>(5.028, 5.263)*    | 5.036<br>(4.925, 5.149)*   | 2,4593.684 | Listed                 |
| Pyoderma gangrenosum**                                 | 1          | 0.17                  | 517        | 13.940<br>(12.616, 15.404)* | 13.92<br>(12.599, 15.380)* | 4,617.014  | Unlisted               |
| <b>Total</b>                                           | <b>111</b> | <b>18.77</b>          |            |                             |                            |            |                        |

CI: confidence interval; EIMs: extraintestinal manifestations; FAERS: FDA Adverse Event Reporting System; MedDRA: Medical Dictionary for Regulatory Activities; PT: preferred term; PYs: patient-years; ROR: reporting odds ratio; PRR: proportional reporting ratio; SOC: system organ class; USPI: U.S. Prescribing Information.

\* Indicates that either ROR or PRR exceeds the predefined statistical threshold; \*\* Indicates MedDRA PTs meeting safety signal criteria, defined as both ROR and PRR exceeding the statistical thresholds.

Table S3. Disproportionality analysis for selected adverse events and their listedness according to the adalimumab USPI.

| MedDRA SOC/ MedDRA PT                                       | N    | ROR<br>(95% CI)          | PRR<br>(95% CI)          | Chi square | Listedness<br>per USPI |
|-------------------------------------------------------------|------|--------------------------|--------------------------|------------|------------------------|
| <b>Blood and lymphatic system disorders</b>                 |      |                          |                          |            |                        |
| Leukopenia                                                  | 173  | 0.274<br>(0.236, 0.318)  | 0.274<br>(0.236, 0.319)  | 329.487    | Listed                 |
| Lymph node pain**                                           | 53   | 2.448<br>(1.856, 3.230)* | 2.448<br>(1.856, 3.230)* | 41.451     | Unlisted               |
| Lymphadenopathy**                                           | 976  | 2.292<br>(2.149, 2.445)* | 2.289<br>(2.146, 2.441)* | 670.281    | Unlisted               |
| Splenomegaly                                                | 133  | 0.894<br>(0.753, 1.061)  | 0.894<br>(0.753, 1.061)  | 1.540      | Unlisted               |
| Thrombocytopenia                                            | 226  | 0.156<br>(0.137, 0.178)  | 0.157<br>(0.138, 0.179)  | 1,023.654  | Listed                 |
| Thrombocytosis                                              | 50   | 0.925<br>(0.699, 1.225)  | 0.925<br>(0.699, 1.225)  | 0.223      | Unlisted               |
| <b>Cardiac disorders</b>                                    |      |                          |                          |            |                        |
| Palpitations                                                | 699  | 0.436<br>(0.405, 0.470)  | 0.437<br>(0.406, 0.471)  | 502.535    | Listed                 |
| Tachycardia                                                 | 329  | 0.284<br>(0.255, 0.316)  | 0.285<br>(0.255, 0.317)  | 589.260    | Listed                 |
| <b>Ear and labyrinth disorders</b>                          |      |                          |                          |            |                        |
| Ear pain                                                    | 425  | 1.849<br>(1.678, 2.038)* | 1.848<br>(1.677, 2.037)  | 157.620    | Unlisted               |
| <b>Eye disorders</b>                                        |      |                          |                          |            |                        |
| Chalazion                                                   | 9    | 1.140<br>(0.588, 2.212)  | 1.140<br>(0.588, 2.212)  | 0.044      | Unlisted               |
| Conjunctivitis allergic                                     | 6    | 0.333<br>(0.149, 0.743)  | 0.333<br>(0.149, 0.743)  | 7.301      | Unlisted               |
| Eye irritation                                              | 225  | 0.285<br>(0.250, 0.325)  | 0.286<br>(0.251, 0.326)  | 398.813    | Unlisted               |
| Eye pruritus                                                | 184  | 0.378<br>(0.327, 0.437)  | 0.379<br>(0.327, 0.438)  | 185.659    | Unlisted               |
| Iridocyclitis**                                             | 128  | 2.873<br>(2.401, 3.437)* | 2.872<br>(2.401, 3.436)* | 144.169    | Unlisted               |
| Vision blurred                                              | 1218 | 0.642<br>(0.606, 0.679)  | 0.643<br>(0.608, 0.681)  | 238.367    | Unlisted               |
| <b>Gastrointestinal disorders</b>                           |      |                          |                          |            |                        |
| Abdominal pain upper                                        | 2373 | 0.908<br>(0.871, 0.945)  | 0.910<br>(0.874, 0.948)  | 21.610     | Listed                 |
| Dysphagia                                                   | 586  | 0.422<br>(0.389, 0.457)  | 0.423<br>(0.390, 0.458)  | 458.806    | Unlisted               |
| Gastroesophageal reflux disease                             | 647  | 0.627<br>(0.580, 0.678)  | 0.628<br>(0.581, 0.679)  | 140.540    | Unlisted               |
| Mouth swelling                                              | 37   | 0.450<br>(0.326, 0.622)  | 0.450<br>(0.326, 0.622)  | 24.036     | Listed                 |
| Nausea                                                      | 6562 | 0.603<br>(0.588, 0.618)  | 0.611<br>(0.597, 0.626)  | 1,653.764  | Listed                 |
| Noninfective sialoadenitis                                  | 3    | 1.116<br>(0.354, 3.514)  | 1.116<br>(0.354, 3.514)  | 0.014      | Unlisted               |
| Obstructive pancreatitis                                    | 18   | 1.934<br>(1.205, 3.102)* | 1.933<br>(1.205, 3.102)  | 6.860      | Unlisted               |
| Pancreatitis acute                                          | 95   | 0.304<br>(0.249, 0.372)  | 0.305<br>(0.249, 0.373)  | 149.189    | Listed                 |
| Paraesthesia oral                                           | 138  | 0.733<br>(0.619, 0.867)  | 0.733<br>(0.619, 0.867)  | 12.927     | Unlisted               |
| Tongue discomfort                                           | 28   | 0.452<br>(0.311, 0.655)  | 0.452<br>(0.311, 0.655)  | 17.887     | Unlisted               |
| Vomiting                                                    | 3806 | 0.606<br>(0.587, 0.626)  | 0.611<br>(0.591, 0.630)  | 949.082    | Listed                 |
| <b>General disorders and administration site conditions</b> |      |                          |                          |            |                        |
| Asthenia                                                    | 3557 | 0.748<br>(0.723, 0.773)  | 0.751<br>(0.726, 0.776)  | 293.597    | Unlisted               |
| Chest discomfort                                            | 775  | 0.595<br>(0.554, 0.639)  | 0.596<br>(0.555, 0.639)  | 210.018    | Listed                 |
| Chest pain                                                  | 1870 | 0.814<br>(0.777, 0.852)  | 0.815<br>(0.779, 0.853)  | 77.400     | Listed                 |

|                                     |       |                          |                          |            |          |
|-------------------------------------|-------|--------------------------|--------------------------|------------|----------|
| Chills                              | 1508  | 1.043<br>(0.991, 1.098)  | 1.043<br>(0.991, 1.098)  | 2.570      | Listed   |
| Drug intolerance                    | 1024  | 0.718<br>(0.675, 0.764)  | 0.719<br>(0.676, 0.765)  | 110.816    | Listed   |
| Fatigue                             | 10652 | 1.010<br>(0.990, 1.029)  | 1.009<br>(0.990, 1.028)  | 0.891      | Unlisted |
| Injection site erythema**           | 6579  | 3.894<br>(3.796, 3.994)* | 3.835<br>(3.740, 3.932)* | 12,676.179 | Listed   |
| Injection site hypersensitivity**   | 127   | 2.972<br>(2.482, 3.559)* | 2.972<br>(2.482, 3.558)* | 153.036    | Listed   |
| Injection site induration**         | 369   | 2.032<br>(1.830, 2.256)* | 2.031<br>(1.829, 2.254)* | 182.978    | Unlisted |
| Injection site reaction**           | 3624  | 3.731<br>(3.606, 3.861)* | 3.701<br>(3.578, 3.828)* | 6,569.315  | Listed   |
| Malaise                             | 7305  | 1.188<br>(1.160, 1.216)* | 1.183<br>(1.157, 1.211)  | 205.673    | Unlisted |
| Non-cardiac chest pain              | 19    | 0.580<br>(0.369, 0.913)  | 0.580<br>(0.369, 0.913)  | 5.272      | Unlisted |
| Oedema peripheral                   | 1841  | 1.244<br>(1.188, 1.303)* | 1.243<br>(1.187, 1.302)  | 84.946     | Listed   |
| Peripheral swelling                 | 2648  | 1.383<br>(1.330, 1.438)* | 1.380<br>(1.328, 1.434)  | 269.345    | Listed   |
| Pyrexia                             | 5464  | 1.320<br>(1.285, 1.356)* | 1.315<br>(1.280, 1.350)  | 403.692    | Listed   |
| <b>Hepatobiliary disorders</b>      |       |                          |                          |            |          |
| Cholelithiasis                      | 483   | 1.192<br>(1.089, 1.305)* | 1.192<br>(1.089, 1.305)  | 14.360     | Listed   |
| Cholestasis                         | 50    | 0.216<br>(0.164, 0.285)  | 0.216<br>(0.164, 0.286)  | 140.571    | Unlisted |
| Hepatic cyst                        | 54    | 1.457<br>(1.111, 1.911)* | 1.457<br>(1.111, 1.911)  | 7.024      | Unlisted |
| Hepatic cytolysis                   | 62    | 0.273<br>(0.213, 0.350)  | 0.273<br>(0.213, 0.350)  | 118.55     | Listed   |
| Hepatic steatosis                   | 349   | 1.651<br>(1.483, 1.838)* | 1.650<br>(1.483, 1.837)  | 85.409     | Unlisted |
| <b>Immune system disorders</b>      |       |                          |                          |            |          |
| Hypersensitivity                    | 2143  | 0.854<br>(0.818, 0.892)  | 0.855<br>(0.819, 0.892)  | 51.856     | Listed   |
| <b>Infections and infestations</b>  |       |                          |                          |            |          |
| Abdominal abscess**                 | 185   | 4.090<br>(3.516, 4.758)* | 4.088<br>(3.514, 4.756)* | 388.826    | Unlisted |
| Abscess**                           | 948   | 5.456<br>(5.098, 5.840)* | 5.443<br>(5.086, 5.824)* | 3,024.853  | Unlisted |
| Abscess limb**                      | 125   | 2.649<br>(2.210, 3.175)* | 2.648<br>(2.210, 3.174)* | 118.744    | Unlisted |
| Appendicitis                        | 176   | 1.471<br>(1.265, 1.710)* | 1.471<br>(1.265, 1.709)  | 25.127     | Listed   |
| Bacterial disease carrier           | 9     | 0.962<br>(0.497, 1.862)  | 0.962<br>(0.497, 1.862)  | 0.002      | Listed   |
| Bacterial sepsis                    | 34    | 0.912<br>(0.649, 1.281)  | 0.912<br>(0.649, 1.281)  | 0.202      | Listed   |
| Bronchitis**                        | 1845  | 2.169<br>(2.070, 2.273)* | 2.162<br>(2.064, 2.266)* | 1,096.814  | Listed   |
| Clostridium difficile infection     | 446   | 1.855<br>(1.687, 2.040)* | 1.854<br>(1.686, 2.038)  | 167.128    | Unlisted |
| Conjunctivitis                      | 214   | 0.827<br>(0.723, 0.947)  | 0.827<br>(0.723, 0.947)  | 7.387      | Unlisted |
| COVID-19                            | 1707  | 1.743<br>(1.660, 1.829)* | 1.739<br>(1.657, 1.825)  | 514.838    | Unlisted |
| COVID-19 pneumonia                  | 53    | 0.661<br>(0.504, 0.868)  | 0.661<br>(0.504, 0.868)  | 8.699      | Unlisted |
| Escherichia urinary tract infection | 43    | 0.968<br>(0.716, 1.311)  | 0.969<br>(0.716, 1.310)  | 0.017      | Listed   |
| Gastroenteritis                     | 136   | 0.810<br>(0.683, 0.960)  | 0.810<br>(0.683, 0.960)  | 5.771      | Listed   |
| Gastroenteritis viral               | 350   | 1.540<br>(1.384, 1.714)* | 1.540<br>(1.384, 1.713)  | 63.322     | Listed   |
| Helicobacter infection              | 171   | 1.944<br>(1.668, 2.267)* | 1.944<br>(1.668, 2.266)  | 73.925     | Unlisted |
| Herpes simplex                      | 86    | 1.305<br>(1.052, 1.617)* | 1.305<br>(1.052, 1.617)  | 5.627      | Unlisted |

|                                                       |      |                           |                           |           |          |
|-------------------------------------------------------|------|---------------------------|---------------------------|-----------|----------|
| Herpes virus infection                                | 123  | 1.680<br>(1.403, 2.013)*  | 1.680<br>(1.403, 2.012)   | 31.873    | Unlisted |
| Herpes zoster**                                       | 1558 | 2.166<br>(2.059, 2.280)*  | 2.161<br>(2.054, 2.274)*  | 923.900   | Unlisted |
| Herpes zoster reactivation**                          | 8    | 2.242<br>(1.101, 4.569)*  | 2.242<br>(1.101, 4.569)*  | 4.084     | Unlisted |
| Influenza**                                           | 3066 | 2.156<br>(2.079, 2.236)*  | 2.145<br>(2.069, 2.224)*  | 1,787.494 | Listed   |
| Nasal herpes**                                        | 7    | 2.865<br>(1.331, 6.164)*  | 2.865<br>(1.331, 6.164)*  | 6.256     | Unlisted |
| Nasopharyngitis**                                     | 7227 | 3.165<br>(3.090, 3.243)*  | 3.117<br>(3.044, 3.192)*  | 9,727.557 | Listed   |
| Oral herpes                                           | 377  | 1.317<br>(1.188, 1.459)*  | 1.316<br>(1.188, 1.458)   | 27.477    | Unlisted |
| Oral infection                                        | 100  | 1.939<br>(1.586, 2.370)*  | 1.939<br>(1.586, 2.369)   | 42.486    | Unlisted |
| Pelvic abscess**                                      | 32   | 2.373<br>(1.661, 3.388)*  | 2.372<br>(1.661, 3.388)*  | 22.705    | Unlisted |
| Pharyngitis**                                         | 370  | 2.577<br>(2.320, 2.863)*  | 2.576<br>(2.319, 2.861)*  | 334.162   | Listed   |
| Pilonidal disease**                                   | 38   | 7.662<br>(5.418, 10.834)* | 7.661<br>(5.418, 10.832)* | 179.672   | Unlisted |
| Pneumonia                                             | 4761 | 1.124<br>(1.091, 1.157)*  | 1.122<br>(1.090, 1.154)   | 61.975    | Listed   |
| Respiratory tract infection                           | 507  | 1.598<br>(1.462, 1.746)*  | 1.597<br>(1.461, 1.745)   | 108.363   | Listed   |
| Rhinitis                                              | 154  | 1.767<br>(1.504, 2.077)*  | 1.767<br>(1.504, 2.076)   | 48.400    | Listed   |
| Sinusitis**                                           | 4103 | 3.465<br>(3.356, 3.578)*  | 3.434<br>(3.327, 3.545)*  | 6,554.415 | Listed   |
| Staphylococcal skin infection**                       | 49   | 3.388<br>(2.531, 4.534)*  | 3.387<br>(2.531, 4.533)*  | 73.906    | Unlisted |
| Stoma site infection                                  | 10   | 0.894<br>(0.478, 1.672)   | 0.894<br>(0.478, 1.672)   | 0.040     | Unlisted |
| Tonsillitis**                                         | 206  | 3.291<br>(2.855, 3.793)*  | 3.289<br>(2.854, 3.791)*  | 301.703   | Unlisted |
| Tonsillitis bacterial**                               | 6    | 2.889<br>(1.262, 6.611)*  | 2.889<br>(1.262, 6.611)*  | 5.232     | Unlisted |
| Upper respiratory tract infection**                   | 1416 | 2.639<br>(2.501, 2.785)*  | 2.632<br>(2.495, 2.777)*  | 1,347.117 | Listed   |
| Urinary tract infection                               | 3180 | 1.511<br>(1.458, 1.565)*  | 1.506<br>(1.454, 1.560)   | 523.777   | Listed   |
| Urinary tract infection bacterial                     | 16   | 0.548<br>(0.335, 0.898)   | 0.548<br>(0.335, 0.898)   | 5.424     | Listed   |
| Urinary tract infection enterococcal                  | 1    | 0.121<br>(0.017, 0.865)   | 0.121<br>(0.017, 0.865)   | 5.472     | Listed   |
| Vaginal infection                                     | 92   | 1.562<br>(1.268, 1.923)*  | 1.562<br>(1.268, 1.923)   | 17.353    | Unlisted |
| <b>Injury, poisoning and procedural complications</b> |      |                           |                           |           |          |
| Forearm fracture                                      | 12   | 1.479<br>(0.832, 2.631)   | 1.479<br>(0.832, 2.631)   | 1.355     | Listed   |
| Ligament injury**                                     | 43   | 3.520<br>(2.578, 4.806)*  | 3.520<br>(2.578, 4.806)*  | 69.062    | Unlisted |
| Ligament rupture**                                    | 279  | 5.626<br>(4.964, 6.376)*  | 5.622<br>(4.961, 6.371)*  | 928.091   | Unlisted |
| Limb injury**                                         | 729  | 2.173<br>(2.017, 2.341)*  | 2.170<br>(2.014, 2.338)*  | 436.088   | Unlisted |
| Meniscus injury**                                     | 576  | 8.119<br>(7.424, 8.879)*  | 8.106<br>(7.414, 8.864)*  | 2,989.676 | Unlisted |
| Stoma site rash**                                     | 3    | 4.911<br>(1.483, 16.266)* | 4.911<br>(1.483, 16.266)* | 5.149     | Unlisted |
| Upper limb fracture                                   | 394  | 1.387<br>(1.255, 1.534)*  | 1.387<br>(1.254, 1.533)   | 40.768    | Listed   |
| <b>Investigations</b>                                 |      |                           |                           |           |          |
| Alanine aminotransferase increased                    | 238  | 0.336<br>(0.296, 0.382)   | 0.337<br>(0.297, 0.383)   | 308.159   | Listed   |
| Amylase increased                                     | 15   | 0.217<br>(0.131, 0.361)   | 0.217<br>(0.131, 0.361)   | 41.257    | Unlisted |
| Antineutrophil cytoplasmic antibody increased         | 3    | 1.395<br>(0.441, 4.409)   | 1.395<br>(0.441, 4.409)   | 0.051     | Listed   |
| Antinuclear antibody increased**                      | 80   | 7.853<br>(6.182, 9.976)*  | 7.851<br>(6.181, 9.973)*  | 395.452   | Listed   |

|                                           |      |                          |                         |         |          |
|-------------------------------------------|------|--------------------------|-------------------------|---------|----------|
| Aspartate aminotransferase increased      | 175  | 0.297<br>(0.256, 0.344)  | 0.297<br>(0.256, 0.345) | 288.592 | Listed   |
| Bilirubin conjugated increased            | 2    | 0.077<br>(0.019, 0.310)  | 0.077<br>(0.019, 0.310) | 21.034  | Unlisted |
| Blood alkaline phosphatase increased      | 51   | 0.191<br>(0.145, 0.252)  | 0.191<br>(0.145, 0.252) | 172.894 | Listed   |
| Blood bilirubin increased                 | 68   | 0.210<br>(0.165, 0.266)  | 0.210<br>(0.166, 0.267) | 200.266 | Unlisted |
| Blood cholesterol increased               | 499  | 0.882<br>(0.807, 0.963)  | 0.882<br>(0.807, 0.964) | 7.635   | Listed   |
| Blood creatine phosphokinase MB increased | 1    | 0.084<br>(0.012, 0.600)  | 0.084<br>(0.012, 0.600) | 9.001   | Unlisted |
| Blood creatinine increased                | 214  | 0.261<br>(0.228, 0.298)  | 0.261<br>(0.228, 0.299) | 445.104 | Unlisted |
| Blood lactate dehydrogenase increased     | 30   | 0.189<br>(0.132, 0.271)  | 0.189<br>(0.132, 0.271) | 102.885 | Unlisted |
| Blood pressure increased                  | 823  | 0.416<br>(0.388, 0.445)  | 0.417<br>(0.389, 0.447) | 666.986 | Listed   |
| Blood triglycerides increased             | 129  | 0.568<br>(0.477, 0.675)  | 0.568<br>(0.477, 0.675) | 41.470  | Listed   |
| Blood urea increased                      | 38   | 0.221<br>(0.161, 0.304)  | 0.221<br>(0.161, 0.305) | 102.723 | Unlisted |
| Enterococcus test positive                | 2    | 0.262<br>(0.065, 1.054)  | 0.262<br>(0.065, 1.054) | 3.405   | Unlisted |
| Escherichia test positive                 | 6    | 0.429<br>(0.192, 0.960)  | 0.429<br>(0.192, 0.960) | 3.945   | Unlisted |
| Gamma-glutamyltransferase increased       | 57   | 0.247<br>(0.190, 0.320)  | 0.247<br>(0.190, 0.320) | 129.635 | Unlisted |
| Glucose urine present                     | 6    | 0.406<br>(0.182, 0.907)  | 0.406<br>(0.182, 0.907) | 4.582   | Unlisted |
| Haemophilus test positive                 | 0    | 0                        | 0                       | 0.839   | Unlisted |
| Hepatic enzyme increased                  | 1184 | 1.373<br>(1.296, 1.456)* | 1.372<br>(1.295, 1.454) | 115.554 | Listed   |
| Lipase increased                          | 42   | 0.431<br>(0.318, 0.584)  | 0.431<br>(0.318, 0.584) | 30.714  | Unlisted |
| Lipids increased                          | 17   | 0.590<br>(0.366, 0.952)  | 0.590<br>(0.366, 0.952) | 4.367   | Listed   |
| Moraxella test positive                   | 0    | 0                        | 0                       | 0.012   | Unlisted |
| Pancreatic enzymes increased              | 10   | 0.500<br>(0.268, 0.933)  | 0.500<br>(0.268, 0.933) | 4.438   | Unlisted |
| Streptococcus test positive               | 19   | 1.467<br>(0.928, 2.319)  | 1.467<br>(0.928, 2.319) | 2.286   | Unlisted |
| Transaminases increased                   | 119  | 0.401<br>(0.335, 0.480)  | 0.401<br>(0.335, 0.480) | 104.875 | Listed   |
| Urine ketone body present                 | 2    | 0.100<br>(0.025, 0.400)  | 0.100<br>(0.025, 0.400) | 15.267  | Unlisted |
| Vitamin D decreased                       | 121  | 1.665<br>(1.388, 1.997)* | 1.665<br>(1.388, 1.996) | 30.201  | Unlisted |
| Weight decreased                          | 3102 | 0.906<br>(0.874, 0.938)  | 0.906<br>(0.875, 0.939) | 29.544  | Unlisted |
| Weight increased                          | 2025 | 0.677<br>(0.648, 0.708)  | 0.679<br>(0.650, 0.710) | 304.355 | Unlisted |
| <b>Metabolism and nutrition disorders</b> |      |                          |                         |         |          |
| Decreased appetite                        | 1616 | 0.525<br>(0.500, 0.551)  | 0.527<br>(0.502, 0.554) | 681.71  | Unlisted |
| Dehydration                               | 1218 | 0.785<br>(0.742, 0.831)  | 0.786<br>(0.743, 0.832) | 69.524  | Listed   |
| Dyslipidaemia                             | 29   | 0.445<br>(0.309, 0.642)  | 0.445<br>(0.309, 0.642) | 19.283  | Listed   |
| Hypercholesterolaemia                     | 78   | 0.959<br>(0.766, 1.200)  | 0.959<br>(0.766, 1.200) | 0.098   | Listed   |
| Hyperglycaemia                            | 73   | 0.157<br>(0.125, 0.198)  | 0.158<br>(0.125, 0.198) | 326.793 | Unlisted |
| Hyperlipidaemia                           | 33   | 0.256<br>(0.182, 0.361)  | 0.257<br>(0.182, 0.361) | 69.944  | Listed   |
| Hypertriglyceridaemia                     | 28   | 0.380<br>(0.262, 0.551)  | 0.380<br>(0.262, 0.551) | 27.495  | Listed   |
| Hypoalbuminaemia                          | 39   | 0.472<br>(0.344, 0.647)  | 0.472<br>(0.344, 0.647) | 22.218  | Unlisted |
| Hypochloraemia                            | 1    | 0.078<br>(0.011, 0.552)  | 0.078<br>(0.011, 0.552) | 10.012  | Unlisted |

|                                                                            |      |                          |                          |           |          |
|----------------------------------------------------------------------------|------|--------------------------|--------------------------|-----------|----------|
| Hypokalaemia                                                               | 134  | 0.241<br>(0.204, 0.286)  | 0.242<br>(0.204, 0.286)  | 316.589   | Unlisted |
| Hypomagnesaemia                                                            | 23   | 0.122<br>(0.081, 0.184)  | 0.122<br>(0.081, 0.184)  | 143.499   | Unlisted |
| Hyponatraemia                                                              | 87   | 0.124<br>(0.100, 0.152)  | 0.124<br>(0.100, 0.153)  | 538.405   | Unlisted |
| Hypophosphataemia                                                          | 11   | 0.124<br>(0.069, 0.225)  | 0.124<br>(0.069, 0.225)  | 66.816    | Unlisted |
| Hypoproteinaemia                                                           | 8    | 0.408<br>(0.203, 0.818)  | 0.408<br>(0.203, 0.818)  | 6.228     | Unlisted |
| Insulin resistance                                                         | 6    | 0.203<br>(0.091, 0.452)  | 0.203<br>(0.091, 0.452)  | 17.912    | Unlisted |
| Metabolic syndrome                                                         | 14   | 0.531<br>(0.313, 0.900)  | 0.531<br>(0.313, 0.900)  | 5.261     | Unlisted |
| <b>Musculoskeletal and connective tissue disorders</b>                     |      |                          |                          |           |          |
| Back pain                                                                  | 3967 | 1.370<br>(1.327, 1.414)* | 1.365<br>(1.323, 1.409)  | 377.737   | Listed   |
| Chest wall mass                                                            | 5    | 1.373<br>(0.563, 3.348)  | 1.373<br>(0.563, 3.348)  | 0.191     | Unlisted |
| Limb mass**                                                                | 131  | 3.641<br>(3.045, 4.353)* | 3.640<br>(3.044, 4.352)* | 227.852   | Unlisted |
| Lupus-like syndrome**                                                      | 722  | 7.480<br>(6.909, 8.098)* | 7.465<br>(6.897, 8.081)* | 3,414.581 | Listed   |
| Muscle spasms                                                              | 1863 | 0.767<br>(0.732, 0.803)  | 0.768<br>(0.734, 0.804)  | 128.767   | Listed   |
| Muscular weakness                                                          | 1159 | 0.789<br>(0.744, 0.836)  | 0.790<br>(0.745, 0.837)  | 63.87     | Unlisted |
| Myalgia                                                                    | 1538 | 0.666<br>(0.633, 0.700)  | 0.667<br>(0.634, 0.702)  | 252.695   | Unlisted |
| Neck mass**                                                                | 112  | 3.303<br>(2.725, 4.005)* | 3.302<br>(2.724, 4.003)* | 164.193   | Unlisted |
| Neck pain                                                                  | 1068 | 1.576<br>(1.483, 1.676)* | 1.574<br>(1.481, 1.674)  | 215.466   | Unlisted |
| Osteonecrosis                                                              | 162  | 0.305<br>(0.261, 0.355)  | 0.305<br>(0.261, 0.356)  | 254.514   | Listed   |
| Pain in extremity                                                          | 6361 | 1.742<br>(1.698, 1.786)* | 1.727<br>(1.685, 1.770)  | 1,889.092 | Listed   |
| Spinal pain**                                                              | 278  | 2.055<br>(1.822, 2.318)* | 2.054<br>(1.821, 2.317)* | 142.207   | Unlisted |
| Systemic lupus erythematosus**                                             | 2357 | 6.218<br>(5.953, 6.494)* | 6.180<br>(5.919, 6.452)* | 8,897.756 | Unlisted |
| <b>Neoplasms benign, malignant and unspecified (incl cysts and polyps)</b> |      |                          |                          |           |          |
| Adenocarcinoma pancreas                                                    | 9    | 0.600<br>(0.311, 1.158)  | 0.606<br>(0.314, 1.170)  | 1.981     | Unlisted |
| Adrenal adenoma                                                            | 9    | 1.306<br>(0.673, 2.536)  | 1.306<br>(0.673, 2.536)  | 0.359     | Listed   |
| Brain neoplasm**                                                           | 301  | 2.130<br>(1.897, 2.392)* | 2.129<br>(1.896, 2.390)* | 170.277   | Unlisted |
| Dysplastic naevus**                                                        | 17   | 4.117<br>(2.500, 6.779)* | 4.117<br>(2.500, 6.778)* | 33.604    | Unlisted |
| Fibroma**                                                                  | 22   | 3.021<br>(1.960, 4.659)* | 3.021<br>(1.959, 4.659)* | 25.811    | Unlisted |
| Haemangioma of liver                                                       | 19   | 1.662<br>(1.050, 2.629)* | 1.661<br>(1.050, 2.628)  | 4.18      | Unlisted |
| Hepatic cancer                                                             | 120  | 0.222<br>(0.186, 0.266)  | 0.222<br>(0.186, 0.266)  | 324.537   | Unlisted |
| Meningioma benign                                                          | 10   | 1.112<br>(0.593, 2.084)  | 1.112<br>(0.593, 2.084)  | 0.027     | Unlisted |
| Ovarian cancer                                                             | 104  | 0.690<br>(0.568, 0.838)  | 0.690<br>(0.569, 0.838)  | 13.923    | Unlisted |
| Skin papilloma**                                                           | 181  | 3.748<br>(3.219, 4.365)* | 3.747<br>(3.218, 4.363)* | 331.387   | Unlisted |
| <b>Nervous system disorders</b>                                            |      |                          |                          |           |          |
| Ageusia                                                                    | 124  | 0.424<br>(0.355, 0.506)  | 0.424<br>(0.355, 0.506)  | 95.603    | Unlisted |
| Anosmia                                                                    | 87   | 0.659<br>(0.533, 0.814)  | 0.659<br>(0.533, 0.814)  | 14.815    | Unlisted |
| Balance disorder                                                           | 494  | 0.435<br>(0.398, 0.475)  | 0.435<br>(0.398, 0.476)  | 358.593   | Unlisted |
| Disturbance in attention                                                   | 171  | 0.234<br>(0.201, 0.271)  | 0.234<br>(0.201, 0.272)  | 426.608   | Unlisted |

|                                                 |      |                          |                          |           |          |
|-------------------------------------------------|------|--------------------------|--------------------------|-----------|----------|
| Dizziness                                       | 4133 | 0.606<br>(0.588, 0.625)  | 0.611<br>(0.593, 0.630)  | 1,029.476 | Unlisted |
| Dyskinesia                                      | 101  | 0.179<br>(0.147, 0.217)  | 0.179<br>(0.147, 0.217)  | 379.004   | Unlisted |
| Epilepsy                                        | 321  | 0.758<br>(0.678, 0.846)  | 0.758<br>(0.679, 0.846)  | 24.159    | Unlisted |
| Headache                                        | 8258 | 0.975<br>(0.953, 0.996)  | 0.975<br>(0.954, 0.997)  | 5.165     | Listed   |
| Hyporeflexia                                    | 9    | 0.377<br>(0.196, 0.727)  | 0.377<br>(0.196, 0.727)  | 8.54      | Unlisted |
| Ischaemic cerebral infarction                   | 10   | 0.723<br>(0.387, 1.351)  | 0.723<br>(0.387, 1.351)  | 0.782     | Listed   |
| Memory impairment                               | 1128 | 0.563<br>(0.531, 0.598)  | 0.565<br>(0.533, 0.599)  | 374.592   | Unlisted |
| Migraine                                        | 1472 | 1.156<br>(1.097, 1.217)* | 1.155<br>(1.097, 1.216)  | 29.806    | Unlisted |
| Paraesthesia                                    | 2334 | 1.114<br>(1.069, 1.161)* | 1.114<br>(1.069, 1.160)  | 26.416    | Listed   |
| Speech disorder                                 | 347  | 0.481<br>(0.433, 0.535)  | 0.482<br>(0.433, 0.535)  | 191.179   | Unlisted |
| <b>Nervous system disorders</b>                 |      |                          |                          |           |          |
| Demyelination**                                 | 318  | 6.676<br>(5.930, 7.517)* | 6.670<br>(5.925, 7.51)*  | 1,313.283 | Listed   |
| <b>Psychiatric disorders</b>                    |      |                          |                          |           |          |
| Bradyphrenia                                    | 17   | 0.172<br>(0.107, 0.277)  | 0.172<br>(0.107, 0.277)  | 66.563    | Unlisted |
| Depressed mood                                  | 496  | 0.661<br>(0.605, 0.722)  | 0.661<br>(0.605, 0.723)  | 84.565    | Unlisted |
| Depression                                      | 2088 | 0.654<br>(0.626, 0.683)  | 0.656<br>(0.629, 0.685)  | 372.849   | Unlisted |
| Disorganised speech                             | 4    | 0.137<br>(0.051, 0.366)  | 0.137<br>(0.051, 0.366)  | 20.781    | Unlisted |
| Insomnia                                        | 1836 | 0.505<br>(0.482, 0.529)  | 0.508<br>(0.485, 0.531)  | 875.641   | Unlisted |
| <b>Renal and urinary disorders</b>              |      |                          |                          |           |          |
| Acute kidney injury                             | 494  | 0.185<br>(0.170, 0.202)  | 0.187<br>(0.171, 0.204)  | 1,757.839 | Unlisted |
| Dysuria                                         | 402  | 0.877<br>(0.794, 0.968)  | 0.877<br>(0.794, 0.968)  | 6.702     | Unlisted |
| Nephrolithiasis                                 | 1118 | 1.906<br>(1.795, 2.024)* | 1.903<br>(1.792, 2.02)   | 457.551   | Listed   |
| Pollakiuria                                     | 313  | 0.572<br>(0.512, 0.640)  | 0.572<br>(0.512, 0.640)  | 98.325    | Unlisted |
| Renal colic**                                   | 76   | 2.954<br>(2.341, 3.729)* | 2.954<br>(2.340, 3.728)* | 89.753    | Unlisted |
| Renal cyst                                      | 135  | 1.561<br>(1.314, 1.854)* | 1.561<br>(1.314, 1.853)  | 25.651    | Unlisted |
| Renal pain                                      | 109  | 0.777<br>(0.643, 0.94)   | 0.778<br>(0.643, 0.940)  | 6.588     | Unlisted |
| Urinary incontinence                            | 200  | 0.535<br>(0.465, 0.615)  | 0.535<br>(0.466, 0.615)  | 79.288    | Unlisted |
| <b>Reproductive system and breast disorders</b> |      |                          |                          |           |          |
| Breast disorder                                 | 42   | 1.442<br>(1.060, 1.962)* | 1.442<br>(1.060, 1.962)  | 5.068     | Unlisted |
| Breast mass**                                   | 269  | 3.277<br>(2.894, 3.711)* | 3.275<br>(2.893, 3.708)* | 391.661   | Unlisted |
| Cervical dysplasia**                            | 94   | 3.355<br>(2.718, 4.140)* | 3.354<br>(2.718, 4.139)* | 141.325   | Unlisted |
| Cervix disorder                                 | 14   | 1.401<br>(0.822, 2.386)  | 1.401<br>(0.822, 2.386)  | 1.181     | Unlisted |
| Heavy menstrual bleeding                        | 205  | 0.566<br>(0.493, 0.649)  | 0.566<br>(0.493, 0.649)  | 66.998    | Unlisted |
| Menometrorrhagia                                | 7    | 0.271<br>(0.129, 0.570)  | 0.271<br>(0.129, 0.570)  | 12.904    | Unlisted |
| Menstruation irregular                          | 136  | 0.329<br>(0.278, 0.389)  | 0.329<br>(0.278, 0.390)  | 184.112   | Listed   |
| Ovarian cyst**                                  | 331  | 2.823<br>(2.525, 3.156)* | 2.821<br>(2.524, 3.153)* | 362.372   | Unlisted |
| Ovarian cyst ruptured**                         | 47   | 2.875<br>(2.139, 3.865)* | 2.875<br>(2.139, 3.865)* | 51.929    | Unlisted |

|                                                        |      |                           |                           |           |          |
|--------------------------------------------------------|------|---------------------------|---------------------------|-----------|----------|
| Uterine cervical metaplasia                            | 2    | 2.728<br>(0.652, 1.417)   | 2.728<br>(0.652, 1.417)*  | 0.728     | Unlisted |
| Uterine polyp**                                        | 79   | 4.067<br>(3.228, 5.126)*  | 4.067<br>(3.227, 5.125)*  | 163.35    | Unlisted |
| <b>Respiratory, thoracic and mediastinal disorders</b> |      |                           |                           |           |          |
| Cough                                                  | 4534 | 1.266<br>(1.229, 1.305)*  | 1.263<br>(1.226, 1.300)   | 242.639   | Listed   |
| Dyspnoea                                               | 3972 | 0.533<br>(0.517, 0.550)   | 0.539<br>(0.522, 0.556)   | 1,582.797 | Listed   |
| Epistaxis                                              | 523  | 0.534<br>(0.490, 0.582)   | 0.535<br>(0.491, 0.583)   | 209.199   | Unlisted |
| Nasal congestion                                       | 1087 | 1.427<br>(1.343, 1.516)*  | 1.426<br>(1.342, 1.515)   | 133.473   | Unlisted |
| Nasal polyps                                           | 59   | 0.906<br>(0.700, 1.173)   | 0.906<br>(0.700, 1.173)   | 0.468     | Unlisted |
| Oropharyngeal pain**                                   | 2387 | 2.023<br>(1.941, 2.108)*  | 2.015<br>(1.934, 2.099)*  | 1,166.611 | Unlisted |
| Pneumothorax                                           | 292  | 1.393<br>(1.239, 1.565)*  | 1.392<br>(1.239, 1.564)   | 30.847    | Unlisted |
| Productive cough                                       | 594  | 1.101<br>(1.014, 1.194)*  | 1.101<br>(1.014, 1.194)   | 5.220     | Unlisted |
| Pulmonary embolism                                     | 610  | 0.469<br>(0.433, 0.508)   | 0.470<br>(0.434, 0.509)   | 360.709   | Listed   |
| Respiration abnormal                                   | 32   | 0.329<br>(0.233, 0.466)   | 0.329<br>(0.233, 0.466)   | 42.678    | Unlisted |
| Rhinorrhoea                                            | 1208 | 1.426<br>(1.346, 1.510)*  | 1.424<br>(1.345, 1.508)   | 147.522   | Unlisted |
| Sneezing                                               | 335  | 1.116<br>(1.001, 1.244)*  | 1.116<br>(1.001, 1.244)   | 3.814     | Unlisted |
| Throat irritation                                      | 445  | 0.758<br>(0.690, 0.832)   | 0.758<br>(0.690, 0.832)   | 33.585    | Unlisted |
| Throat tightness                                       | 174  | 0.489<br>(0.421, 0.568)   | 0.489<br>(0.422, 0.568)   | 91.137    | Unlisted |
| Tonsillar hypertrophy**                                | 80   | 3.760<br>(2.990, 4.727)*  | 3.759<br>(2.990, 4.726)*  | 145.800   | Unlisted |
| <b>Skin and subcutaneous tissue disorders</b>          |      |                           |                           |           |          |
| Acne                                                   | 730  | 1.523<br>(1.414, 1.640)*  | 1.521<br>(1.413, 1.638)   | 125.37    | Unlisted |
| Alopecia                                               | 2764 | 1.030<br>(0.992, 1.069)   | 1.030<br>(0.992, 1.070)   | 2.411     | Listed   |
| Dermatitis                                             | 231  | 0.904<br>(0.793, 1.030)   | 0.904<br>(0.793, 1.030)   | 2.208     | Unlisted |
| Dermatitis psoriasiform**                              | 135  | 5.527<br>(4.617, 6.615)*  | 5.525 (4.616 ,<br>6.612)* | 436.747   | Unlisted |
| Eczema                                                 | 565  | 0.797<br>(0.734, 0.867)   | 0.798<br>(0.734, 0.867)   | 28.321    | Unlisted |
| Erythema                                               | 2273 | 1.028<br>(0.986, 1.071)   | 1.027<br>(0.986, 1.071)   | 1.599     | Unlisted |
| Hyperhidrosis                                          | 1163 | 0.688<br>(0.649, 0.729)   | 0.689<br>(0.650, 0.730)   | 161.186   | Unlisted |
| Nail disorder                                          | 128  | 1.291<br>(1.083, 1.539)*  | 1.291<br>(1.083, 1.539)   | 7.849     | Unlisted |
| Pain of skin                                           | 358  | 1.906<br>(1.715, 2.120)*  | 1.905<br>(1.714, 2.118)   | 146.386   | Unlisted |
| Pigmentation disorder                                  | 51   | 0.594<br>(0.451, 0.783)   | 0.594<br>(0.451, 0.784)   | 13.520    | Unlisted |
| Pruritus                                               | 4600 | 0.862<br>(0.837, 0.888)   | 0.864<br>(0.839, 0.890)   | 97.697    | Unlisted |
| Rash                                                   | 6915 | 1.122<br>(1.095, 1.149)*  | 1.119<br>(1.093, 1.146)   | 87.173    | Listed   |
| Rash macular**                                         | 816  | 2.063<br>(1.922, 2.213)*  | 2.060<br>(1.920, 2.210)*  | 423.246   | Unlisted |
| Rash maculo-papular                                    | 99   | 0.352<br>(0.289, 0.429)   | 0.352<br>(0.289, 0.430)   | 116.211   | Unlisted |
| Rash papular**                                         | 841  | 4.251<br>(3.959, 4.564)*  | 4.242<br>(3.952, 4.554)*  | 1,886.516 | Unlisted |
| Rash pruritic                                          | 1130 | 1.661<br>(1.565, 1.763)*  | 1.659<br>(1.563, 1.760)   | 284.128   | Unlisted |
| Rash vesicular                                         | 99   | 1.710<br>(1.399, 2.091)*  | 1.710<br>(1.399, 2.091)   | 27.34     | Unlisted |
| Skin discharge**                                       | 40   | 9.745<br>(6.903, 13.758)* | 9.744<br>(6.902, 13.756)* | 246.328   | Unlisted |

|                           |      |                          |                          |         |          |
|---------------------------|------|--------------------------|--------------------------|---------|----------|
| Skin disorder**           | 1117 | 2.452<br>(2.309, 2.605)* | 2.447<br>(2.304, 2.599)* | 902.137 | Unlisted |
| Skin exfoliation          | 957  | 1.121<br>(1.051, 1.195)* | 1.121<br>(1.051, 1.195)  | 11.966  | Unlisted |
| Skin hyperpigmentation    | 26   | 0.333<br>(0.226, 0.489)  | 0.333<br>(0.226, 0.489)  | 33.847  | Unlisted |
| Skin induration**         | 73   | 3.431<br>(2.702, 4.356)* | 3.430<br>(2.701, 4.355)* | 113.676 | Unlisted |
| Urticaria                 | 2136 | 0.948<br>(0.908, 0.990)  | 0.949<br>(0.909, 0.990)  | 5.781   | Listed   |
| <b>Vascular disorders</b> |      |                          |                          |         |          |
| Aortic occlusion**        | 14   | 2.879<br>(1.675, 4.950)* | 2.879<br>(1.675, 4.950)* | 14.294  | Unlisted |
| Haematoma                 | 183  | 0.565<br>(0.489, 0.654)  | 0.566<br>(0.489, 0.654)  | 59.872  | Unlisted |
| Hypertension              | 2052 | 0.763<br>(0.730, 0.797)  | 0.764<br>(0.732, 0.798)  | 147.237 | Listed   |
| Iliac artery occlusion**  | 10   | 2.966<br>(1.561, 5.635)* | 2.966<br>(1.561, 5.635)* | 10.343  | Unlisted |
| Raynaud's phenomenon      | 69   | 1.023<br>(0.806, 1.299)  | 1.023<br>(0.806, 1.299)  | 0.016   | Unlisted |

CI: confidence interval; MedDRA: Medical Dictionary for Regulatory Activities; N: number of cases; PRR: proportional reporting ratio; PT: preferred term; ROR: reporting odds ratio; SOC: system organ class; USPI: U.S. Prescribing Information.

\* Indicates that either ROR or PRR exceeds the predefined statistical threshold; \*\* Indicates MedDRA PTs meeting safety signal criteria, defined as both ROR and PRR exceeding the statistical thresholds.