

NOT FOR PUBLICATION

COMMISSION ON HUMAN MEDICINES

COVID-19 VBR EWG

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| Title of paper: Second update on COVID-19 vaccine AstraZeneca safety Type of paper: Update |
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| Products: Covid19 vaccine AstraZeneca | Marketing Authorisation Holder (MAH): AstraZeneca |
| Active Constituent: COVID-19 Vaccine AstraZeneca solution for injection COVID-19 Vaccine (ChAdOx1 S [recombinant]) | |
| Therapeutic area: Prevention of coronavirus disease 2019 (COVID-19). | Legal status: POM |
| Previous assessments: n/a | Assessors: [REDACTED] [REDACTED] |
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Update on covid19 vaccine AstraZeneca vaccine safety

1. Background

COVID-19 Vaccine AstraZeneca was given a Regulation 174 authorisation on 30th December 2020. It is authorised for use in individuals aged 18 years and older for the prevention of coronavirus disease 2019 (COVID-19).

The Medicines and Healthcare products Regulatory Agency (MHRA) has developed an approach to allow Covid-19 vaccine pharmacovigilance that is continuous, proactive and as near real-time as is possible. This involves a four-stranded approach which consists of enhanced passive surveillance with 'observed vs expected' analysis, rapid cycle analysis and ecological analysis, targeted active surveillance using the Yellow Card Vaccine Monitor and formal epidemiological studies.

This is the second safety update for the COVID-19 Vaccine AstraZeneca.

2. Data for 4th – 19th February 2021

Usage data

Rollout of COVID-19 Vaccine AstraZeneca began on 4th January 2021. Up to the end of 21st February 2021, an estimated 8,374,208 doses of COVID-19 Vaccine AstraZeneca have been given in the UK¹. This includes just over 5000 second doses, however it is likely that many of these vaccinees received the Pfizer vaccine for their first dose.

Summary of ADR reports

Between vaccine rollout on 4th January 2021 up to 19th February 2021, the MHRA has received a total of 41,157 reports of suspected ADRs in association with COVID-19 Vaccine AstraZeneca. This represents a reporting rate of roughly 4.9 per 1000 doses given. This rate is higher than previous new vaccine campaigns (typically 1 per 1000 doses have been seen previously). This is likely due to very high publicity of this campaign and efforts to promote reporting of Yellow Cards. This rate is also higher than that seen for the Pfizer vaccine, this had previously been seen with analysis of reactogenicity reports, where more reports of reactogenicity reactions marked as serious were reported for the AstraZeneca vaccine than the Pfizer vaccine. This may indicate that the AstraZeneca vaccine is slightly more reactogenic than the Pfizer vaccine and could explain an overall higher reporting rate.

Table 1 shows the reaction terms (at MedDRA hierarchy Preferred Term (PT) level) most frequently reported in the Yellow Cards received. A full list of reported terms is presented in Annex 2.

¹ Please note: Please note- UK wide data are extrapolated from England data.

Table 1: The 20 PTs most frequently reported within with COVID-19 Vaccine AstraZeneca Yellow Card reports

| Reaction PT | Number of times reported |
|------------------------|---------------------------------|
| Headache | 17655 |
| Pyrexia | 13639 |
| Chills | 10480 |
| Fatigue | 9606 |
| Nausea | 7572 |
| Myalgia | 6090 |
| Arthralgia | 4597 |
| Dizziness | 3849 |
| Pain in extremity | 3144 |
| Pain | 3013 |
| Vomiting | 2749 |
| Malaise | 2575 |
| Tremor | 2534 |
| Influenza like illness | 2283 |
| Hyperhidrosis | 1867 |
| Diarrhoea | 1767 |
| Influenza | 1558 |
| Decreased appetite | 1521 |
| Feeling cold | 1289 |
| Illness | 1126 |

It is important to note that a Yellow Card report is not proof of a side effect occurring, but merely a suspicion by the reporter that the vaccine may have caused the medical condition. Whilst Yellow Card reports may include recognised side effects of the vaccine, they may also be due to coincidental, underlying medical conditions that would have occurred anyway in the absence of vaccination.

The most frequently reported terms have not changed significantly since the last report. These represent reactogenicity reactions and vasovagal type reactions. These terms, or associated umbrella terms are labelled in the product information.

A paper on reactogenicity reactions was presented to the EWG on 4th February 21. Here, it was shown that a number of reports of reactogenicity are being marked as serious by the reporter. Analysis showed that the seriousness criteria being flagged in these cases was usually “other medically significant” and this was in keeping with anecdotal reports of recipients feeling unwell and needing to take a day off work. The EWG recommended wording in the product

information and literature given to patients to inform them of the types of reactogenicity reactions recipients are experiencing in order to better prepare them for what's to be expected. Wording was proposed to the EWG and this has now been incorporated into the product information.

Fatal cases

The MHRA has received 227 fatal cases associated with this vaccine. The age of the patients, where reported, ranges from 20-101 years.

These events have occurred in 142 patients aged 80+, 49 patients in their 70s, 14 patients in their 60s, 9 patients in their 50s, [REDACTED] and [REDACTED]. Age was not reported in the remaining cases.

The fatalities regarding [REDACTED] patients concern:

- [REDACTED]
- [REDACTED] diagnosed with diabetic ketoacidosis (DKA) [REDACTED] which led to multiorgan failure and cardiac arrest and death [REDACTED]

The case regarding a [REDACTED] was of an intracranial haemorrhage following thrombocytopenia [REDACTED]. Events of thrombocytopenia are being closely monitored and are discussed in a separate paper at this meeting.

Fatal cases in patients in their 50s involved a range of fatal terms (metastatic cancer, death in a patient who had been palliative for months, post-mortem finding of severe triple vessel coronary artery atherosclerosis, cardiac arrest (noted possible multiple causes from PMH), sudden death (noted multiple co-morbidities and thought to be unrelated to vaccine), 1 case of immune thrombocytopenia, COVID-19 pneumonitis, aspiration, death). The majority of these cases do not raise concerns of an association with vaccination however the fatal case reporting immune thrombocytopenia will be further discussed in a separate paper.

Fatalities in patients in their 60s were often in patients with significant co-morbidities such as cardiac problems, TIA and COPD. In several cases the reporter states that they do not believe the death to have been related to vaccination but to underlying co-morbidities.

The same is true as we go further up the age groups, with significant co-morbidities increasingly more common. "Death" or "sudden death" are frequently reported as the fatal term and in some cases, these reports are too sparse of detail to assess and so will be followed up for further information.

Safety topics under review

Bell's palsy

MHRA has received 47 cases reporting facial paralysis associated with this vaccine and 10 cases reporting facial paresis. Four of these cases report both facial paralysis and facial paresis. Ages reported include 4 patients in their 30s, 5 patients in their 40s, 9 patients in their 50s, 8 patients in their 60s, 15 in their 70s and 5 patients aged 80+ (age not reported in 6 cases).

In 7 of the cases, a stroke or TIA is also reported and in one case encephalitis is reported. Facial paralysis would likely be secondary to these events in these cases. The reactions are occurring predominantly in female patients with cases reported in 35 females and 17 males (gender is not specified in one case).

3 cases report facial paralysis in the medical history and 3 report a history of stroke, which could be confounding factors. The time to onset was rapid in most cases with 28 reporting onset within 1 day, 4 cases reported a 2 day onset and 4 reported a 5 day onset. Only 8 cases reported onset times of 7 days or more. This is interesting as an effect associated with the vaccine, with an autoimmune mechanism would be expected to take roughly 7 days to develop. The facial paralysis or paresis as reported to have recovered at the time of reporting in 9 cases. Bell's Palsy is an Adverse Event of Special Interest and therefore observed vs expected analysis and rapid cycle analysis are being performed. These are not showing a statistically significant increase against the expected events for the AstraZeneca vaccine currently however an epidemiological study is planned for further analysis.

Transverse myelitis

2 cases of transverse myelitis were seen in the AstraZeneca vaccine arm of clinical trials (as well as 1 case in the control arm). Case summaries can be found in red in the table in Annex 1. This event is therefore monitored closely.

Up to 19th February, MHRA has received 6 post-authorisation cases reporting transverse myelitis and 2 reporting myelitis. A summary of cases can be found in annex 1. The 8 reports were received in 3 females [REDACTED] and 5 males aged 68 to 81 years in 4 reports and the remaining report [REDACTED].

In 1 report, transverse myelitis was diagnosed with MRI scans. The onset time of transverse myelitis in this case [REDACTED] is in line with the onset of reported transverse myelitis in association with vaccines described previously as between several days and 3 months in most cases (Agmon-Leven et al.,2009²). Follow up has been sent in this case for information on any alternative aetiology, however a casual association between transverse myelitis and COVID-19 vaccine AstraZeneca may be possible in this case.

The remaining 7 reports contain only limited information for assessment of possible causality. Onset time was only reported in 4 cases, with 2 reports each reporting an onset of [REDACTED]. These times are not consistent with causality with COVID-19 vaccination with the proposed mechanism for vaccine associated transverse myelitis being autoimmune². It is not known whether the diagnosis of transverse myelitis or myelitis was confirmed in any of these cases with only one report [REDACTED]

[REDACTED]

² Agmon-Leven et al. Lupus 2009 Nov;18(13):1198-204. doi: 10.1177/0961203309345730.

[REDACTED]

[REDACTED].

In 2 of the 7 cases containing limited information, the patients' short recovery times [REDACTED] [REDACTED] are not in line with the usual recovery times for transverse myelitis (weeks to months) which may suggest that a diagnosis of transverse myelitis unlikely in these cases.

There is insufficient information in 3 of the cases to assess whether there is a possible association between 'transverse myelitis' and COVID-19 vaccine AstraZeneca in these cases.

A review was also performed of cases reporting terms in the "Paralysis and paresis (excl cranial nerve)" HLT group, in case this identified any additional cases which may be consistent with transverse myelitis but not reported as such. The vast majority of cases reporting terms in this HLT group had onset times within 1 day of vaccination and short times to recovery, which make them unlikely to be cases of transverse myelitis. In many cases it is unclear whether the patient is suffering paralysis or whether it is in fact muscle weakness that they are experiencing. Cases are often reported alongside severe fatigue and other reactogenicity reactions.

One case of note [REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

Overall, there is currently one post-authorisation case reporting transverse myelitis in which the diagnosis is well described and the onset time is plausible. This case requires further information to rule out alternative aetiologies. In 4 cases, the onset times are within 2 days and in 2 cases, recover very quickly, which makes a diagnosis of transverse myelitis unlikely. The remaining 3 cases do not report sufficient description of the events to make assessment of the case.

Transverse myelitis is an adverse event of special interest and as such, Observed vs Expected analysis of the Yellow Card reports and Rapid Cycle Analysis within the Clinical Practice Research Datalink (CPRD) are being performed.

The Observed vs Expected analyses are conducted on the totality of the cases reporting transverse myelitis (N=6). In both the <50 years age group and the 65+ years age group the log likelihood of the observed vs expected ratio crosses the signalling threshold with assumptions of 75% and 25% reporting levels respectively. The likelihood of significant under-reporting is unclear. Of note, the background rates for these analyses have been calculated including data on diagnoses at hospital discharge available in the Hospital Episode Statistics linked to CPRD and hence the approach to include all 6 case reports in the analysis is highly conservative given the details described above. Therefore, the observed vs expected analyses do not provide evidence of an increased risk of transverse myelitis.

The rapid cycle analyses in the CPRD show the observed number of recorded cases of transverse myelitis within 42 days of first vaccination to be consistent with the expected based on data up to 21st February 2021. No cases have been recorded within 42 days of a first AstraZeneca vaccination compared to an expected 3.5 based on nearly 35,000 patient years of follow up (adjusted for delays in recording of transverse myelitis in primary care records). Sensitivity analyses using a longer risk window of 90 days again show the observed recorded number of cases is consistent with the expected although there is very limited additional follow up time beyond 42 days.

Transverse myelitis is both particularly rare and likely to be under-recorded in primary care records which limit the rapid cycle analyses. Where it is recorded this is subject to delay, however the rapid cycle analyses are adjusted to account for this delay based on historical data. Rapid cycle analyses will continue for transverse myelitis alongside observed vs expected analyses with data from linked secondary care incorporated to improve case identification when they start to become available shortly.

Conclusion

The ADR data received since the last safety update are consistent with the last and broadly in line with the safety profile seen in clinical trials, with the vast majority of reports reporting reactogenicity reactions. Reports of Bell's Palsy and transverse myelitis are closely monitored. An epidemiological study is due to be performed to look further investigate reports of Bell's Palsy. Currently, most cases reporting transverse myelitis are not consistent with a vaccine associated reaction. Review of the cumulative data does not identify any new safety signals.

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|------------|------------|------------|------------|------------|------------|------------|------------|------------|
| | | [REDACTED] | | [REDACTED] | | | | |
| [REDACTED] | [REDACTED] | [REDACTED] | [REDACTED] | [REDACTED] | [REDACTED] | [REDACTED] | [REDACTED] | [REDACTED] |
| [REDACTED] | [REDACTED] | [REDACTED] | [REDACTED] | [REDACTED] | [REDACTED] | [REDACTED] | [REDACTED] | [REDACTED] |
| [REDACTED] | [REDACTED] | [REDACTED] | [REDACTED] | [REDACTED] | [REDACTED] | [REDACTED] | [REDACTED] | [REDACTED] |

* Comprehensive details of ADR progression & tests performed available for these cases

Tabulation of all PTs reported with the COVID-19 vaccine AstraZeneca, DLP 19/02/2021

| Reaction PT | No. times reported |
|------------------------|---------------------------|
| Headache | 17655 |
| Pyrexia | 13639 |
| Chills | 10480 |
| Fatigue | 9606 |
| Nausea | 7572 |
| Myalgia | 6090 |
| Arthralgia | 4597 |
| Dizziness | 3849 |
| Pain in extremity | 3144 |
| Pain | 3013 |
| Vomiting | 2749 |
| Malaise | 2575 |
| Tremor | 2534 |
| Influenza like illness | 2283 |
| Hyperhidrosis | 1867 |
| Diarrhoea | 1767 |
| Influenza | 1558 |
| Decreased appetite | 1521 |
| Feeling cold | 1289 |
| Illness | 1126 |
| Back pain | 1089 |
| Migraine | 1034 |
| Lethargy | 1014 |
| Rash | 970 |
| Pruritus | 950 |
| Paraesthesia | 919 |
| Asthenia | 893 |
| Injection site pain | 875 |
| Dyspnoea | 863 |
| Abdominal pain upper | 837 |
| Abdominal pain | 800 |
| Peripheral swelling | 799 |
| Palpitations | 773 |
| Oropharyngeal pain | 728 |
| Cough | 618 |
| Chest pain | 600 |
| Lymphadenopathy | 587 |
| Insomnia | 568 |
| Eye pain | 566 |
| Erythema | 560 |
| Hypoaesthesia | 500 |
| Neck pain | 486 |
| Dizziness postural | 444 |
| Tenderness | 418 |
| Feeling hot | 415 |
| Syncope | 387 |

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|------------------------------------|-----|
| Limb discomfort | 385 |
| Muscle spasms | 384 |
| Feeling abnormal | 382 |
| Swelling | 377 |
| Cold sweat | 366 |
| Heart rate increased | 365 |
| Musculoskeletal stiffness | 361 |
| Somnolence | 353 |
| Tachycardia | 349 |
| Night sweats | 349 |
| Hot flush | 349 |
| Confusional state | 337 |
| Urticaria | 329 |
| Vaccination site pain | 322 |
| Muscular weakness | 317 |
| Chest discomfort | 312 |
| Body temperature increased | 309 |
| Rhinorrhoea | 308 |
| Nasopharyngitis | 300 |
| Ear pain | 296 |
| Thirst | 291 |
| Dysgeusia | 291 |
| Rash erythematous | 282 |
| Body temperature | 278 |
| Abdominal discomfort | 265 |
| Tension headache | 261 |
| Injection related reaction | 238 |
| Injection site mass | 229 |
| Dry mouth | 223 |
| Feeling of body temperature change | 217 |
| Bone pain | 213 |
| Rash pruritic | 212 |
| Peripheral coldness | 211 |
| Adverse drug reaction | 204 |
| Hallucination | 200 |
| Pain of skin | 188 |
| Vertigo | 184 |
| Tinnitus | 183 |
| Muscle fatigue | 182 |
| Photophobia | 179 |
| Vision blurred | 171 |
| Heart rate | 166 |
| Renal pain | 165 |
| Seizure | 161 |
| Lip swelling | 156 |
| Epistaxis | 155 |
| Flushing | 155 |
| Sinus headache | 154 |
| Sweating fever | 152 |
| Hypersensitivity | 147 |

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|---------------------------|-----|
| Balance disorder | 147 |
| Ageusia | 147 |
| Loss of consciousness | 145 |
| Neuralgia | 144 |
| Disorientation | 141 |
| Nervousness | 140 |
| Swelling face | 139 |
| Dyspepsia | 136 |
| Contusion | 131 |
| Paraesthesia oral | 128 |
| Death | 127 |
| Presyncope | 124 |
| COVID-19 | 123 |
| Anaphylactic reaction | 121 |
| Dehydration | 120 |
| Cluster headache | 115 |
| Poor quality sleep | 113 |
| Delirium | 110 |
| Sensitive skin | 110 |
| Injection site erythema | 106 |
| Vaccination site erythema | 106 |
| Pallor | 103 |
| Hypotension | 102 |
| Wheezing | 99 |
| Cellulitis | 98 |
| Anxiety | 98 |
| Skin burning sensation | 96 |
| Oral herpes | 94 |
| Hypertension | 93 |
| Sneezing | 91 |
| Swollen tongue | 90 |
| Restlessness | 90 |
| Skin warm | 88 |
| Vaccination site swelling | 87 |
| Inflammation | 86 |
| Hypoaesthesia oral | 85 |
| Nasal congestion | 81 |
| Taste disorder | 80 |
| Pain in jaw | 78 |
| Nightmare | 78 |
| Vaccination site mass | 76 |
| Herpes zoster | 75 |
| Eye swelling | 72 |
| Injection site warmth | 72 |
| Burning sensation | 72 |
| Sinus pain | 71 |
| Head discomfort | 67 |
| Parosmia | 67 |
| Sleep disorder | 67 |
| Flatulence | 66 |

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|------------------------------|----|
| Retching | 65 |
| Abnormal dreams | 65 |
| Rash macular | 64 |
| Mouth ulceration | 63 |
| Asthma | 63 |
| Gastrointestinal pain | 62 |
| Joint stiffness | 62 |
| Musculoskeletal chest pain | 62 |
| Disturbance in attention | 62 |
| Visual impairment | 60 |
| Axillary pain | 60 |
| Restless legs syndrome | 60 |
| Lymph node pain | 59 |
| Mental fatigue | 59 |
| Local reaction | 58 |
| Injection site pruritus | 58 |
| Pollakiuria | 58 |
| Dry throat | 58 |
| Joint swelling | 57 |
| Angioedema | 57 |
| Gait disturbance | 54 |
| Muscle twitching | 53 |
| Hyperaesthesia | 53 |
| Blood pressure increased | 51 |
| Oxygen saturation decreased | 50 |
| Rash papular | 49 |
| Toothache | 48 |
| Abdominal distension | 48 |
| Oral pain | 48 |
| Facial paralysis | 47 |
| Vaccination site warmth | 45 |
| Depressed mood | 45 |
| Irritability | 44 |
| Constipation | 43 |
| Hypopnoea | 43 |
| Injection site rash | 41 |
| Discomfort | 41 |
| Fall | 41 |
| Skin temperature | 41 |
| Gait inability | 40 |
| Injection site swelling | 40 |
| Facial pain | 40 |
| Body temperature fluctuation | 40 |
| Ocular hyperaemia | 39 |
| Dysarthria | 39 |
| Agitation | 39 |
| Blister | 39 |
| Skin reaction | 39 |
| Glossodynia | 38 |
| Anosmia | 38 |

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|------------------------------------|----|
| Asthenopia | 37 |
| Paralysis | 37 |
| Depression | 37 |
| Abdominal pain lower | 36 |
| Cerebrovascular accident | 36 |
| Dry skin | 36 |
| Atrial fibrillation | 35 |
| Infection | 35 |
| Throat irritation | 35 |
| COVID-19 immunisation | 35 |
| Gingival pain | 34 |
| Spinal pain | 34 |
| Freezing phenomenon | 34 |
| Dermatitis allergic | 34 |
| Epilepsy | 33 |
| Eye pruritus | 32 |
| Arthritis | 32 |
| Mobility decreased | 32 |
| Migraine with aura | 32 |
| Pharyngeal swelling | 32 |
| Eye irritation | 31 |
| Photopsia | 31 |
| Hypersomnia | 31 |
| Body temperature decreased | 30 |
| Breast pain | 30 |
| Vaginal haemorrhage | 30 |
| Photosensitivity reaction | 30 |
| Dry eye | 29 |
| Dysphagia | 29 |
| Blood glucose increased | 29 |
| Amnesia | 29 |
| Throat tightness | 29 |
| Micturition urgency | 28 |
| Pulmonary pain | 28 |
| Lacrimation increased | 27 |
| Gastrooesophageal reflux disease | 27 |
| Vomiting projectile | 27 |
| Mouth swelling | 27 |
| Sinusitis | 27 |
| Hyperglycaemia | 27 |
| Heart rate irregular | 26 |
| Muscle tightness | 26 |
| Panic attack | 26 |
| Skin irritation | 26 |
| Crying | 25 |
| Diplopia | 24 |
| Lower respiratory tract infection | 24 |
| Maternal exposure during pregnancy | 24 |
| Listless | 24 |
| Dermatitis | 24 |

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|----------------------------------|----|
| Immunisation | 24 |
| Feeding disorder | 23 |
| Memory impairment | 23 |
| Productive cough | 23 |
| Cardiac arrest | 22 |
| Deafness | 22 |
| Injection site reaction | 22 |
| Vaccination complication | 22 |
| Magnetic resonance imaging brain | 22 |
| Miliaria | 22 |
| Cyanosis | 22 |
| Hypoacusis | 21 |
| Q fever | 21 |
| Neuropathy peripheral | 21 |
| Arrhythmia | 20 |
| Hyperpyrexia | 20 |
| Body temperature abnormal | 20 |
| Musculoskeletal discomfort | 20 |
| Groin pain | 20 |
| Transient ischaemic attack | 20 |
| Urinary incontinence | 20 |
| Respiration abnormal | 20 |
| Dysphonia | 20 |
| Cardiac flutter | 19 |
| Blindness | 19 |
| Condition aggravated | 19 |
| Vaccination site joint pain | 19 |
| Vaccination site rash | 19 |
| Pneumonia | 19 |
| Urinary tract infection | 19 |
| Tearfulness | 19 |
| Circulatory collapse | 19 |
| Weight decreased | 18 |
| Coordination abnormal | 18 |
| Unresponsive to stimuli | 18 |
| Febrile convulsion | 18 |
| Yawning | 18 |
| Bedridden | 18 |
| Bradycardia | 17 |
| Hypothermia | 17 |
| Sepsis | 17 |
| Respiratory rate increased | 17 |
| Menorrhagia | 17 |
| Neutropenia | 16 |
| Hangover | 16 |
| Vaccination site pruritus | 16 |
| Localised infection | 16 |
| Post procedural complication | 16 |
| Fibromyalgia | 16 |
| Trismus | 16 |

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|---------------------------------------|----|
| Monoplegia | 16 |
| Pelvic pain | 16 |
| Tachypnoea | 16 |
| Hypoxia | 16 |
| Aphonia | 16 |
| Skin sensitisation | 16 |
| Piloerection | 16 |
| Haemorrhage | 16 |
| Myocardial infarction | 15 |
| Periorbital swelling | 15 |
| Blood pressure decreased | 15 |
| Flank pain | 15 |
| Musculoskeletal pain | 15 |
| Urinary retention | 15 |
| Skin discolouration | 15 |
| Angina pectoris | 14 |
| Vertigo positional | 14 |
| Eructation | 14 |
| Oral discomfort | 14 |
| Injection site inflammation | 14 |
| Labyrinthitis | 14 |
| Gastroenteritis viral | 14 |
| Food aversion | 14 |
| Hypoglycaemia | 14 |
| Depressed level of consciousness | 14 |
| Dyskinesia | 14 |
| Vascular headache | 14 |
| Sciatica | 14 |
| Mental impairment | 14 |
| Sensory loss | 14 |
| Emotional disorder | 14 |
| Dysuria | 14 |
| Motion sickness | 13 |
| Procedural nausea | 13 |
| Food refusal | 13 |
| Dysstasia | 13 |
| Neurological symptom | 13 |
| Incontinence | 13 |
| Chronic obstructive pulmonary disease | 13 |
| Nasal discomfort | 13 |
| Skin exfoliation | 13 |
| Shock | 13 |
| Sinus tachycardia | 12 |
| Hyperacusis | 12 |
| Irritable bowel syndrome | 12 |
| Lip dry | 12 |
| Lip pain | 12 |
| Injection site bruising | 12 |
| Injection site joint pain | 12 |
| Vaccination site bruising | 12 |

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| Vaccination site induration | 12 |
| Drug hypersensitivity | 12 |
| SARS-CoV-2 test positive | 12 |
| Muscle rigidity | 12 |
| Rheumatoid arthritis | 12 |
| Aphasia | 12 |
| Dizziness exertional | 12 |
| Allodynia | 12 |
| Skin swelling | 12 |
| Ear discomfort | 11 |
| Administration site pain | 11 |
| Sudden death | 11 |
| Drug ineffective | 11 |
| Skin infection | 11 |
| Blood pressure measurement | 11 |
| Cognitive disorder | 11 |
| Sensory disturbance | 11 |
| Tension | 11 |
| Chromaturia | 11 |
| Polyuria | 11 |
| Tonsillar hypertrophy | 11 |
| Raynaud's phenomenon | 11 |
| Extrasystoles | 10 |
| Ear swelling | 10 |
| Adrenocortical insufficiency acute | 10 |
| Haematochezia | 10 |
| Vaccination site inflammation | 10 |
| Allergy to vaccine | 10 |
| Suspected COVID-19 | 10 |
| Rhinitis | 10 |
| Tonsillitis | 10 |
| Oxygen saturation | 10 |
| International normalised ratio increased | 10 |
| Urine output | 10 |
| Facial paresis | 10 |
| Generalised tonic-clonic seizure | 10 |
| Multiple sclerosis | 10 |
| Bradyphrenia | 10 |
| Acute kidney injury | 10 |
| Dysmenorrhoea | 10 |
| Hyperventilation | 10 |
| Haemoptysis | 10 |
| Eczema | 10 |
| Psoriasis | 10 |
| Petechiae | 10 |
| Injection | 10 |
| Crohn's disease | 9 |
| Abdominal rigidity | 9 |
| Stomatitis | 9 |
| Adverse reaction | 9 |

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| Hypophagia | 9 |
| Periarthritis | 9 |
| Hemiparesis | 9 |
| Middle insomnia | 9 |
| Nasal dryness | 9 |
| Lymphoedema | 9 |
| Deep vein thrombosis | 9 |
| Immune thrombocytopenia | 8 |
| Colitis ulcerative | 8 |
| Gastritis | 8 |
| Gingival swelling | 8 |
| Salivary hypersecretion | 8 |
| Feeling drunk | 8 |
| Loss of control of legs | 8 |
| Hepatic pain | 8 |
| Serum sickness | 8 |
| Kidney infection | 8 |
| Post viral fatigue syndrome | 8 |
| Maternal exposure during breast feeding | 8 |
| Limb injury | 8 |
| Heart rate decreased | 8 |
| Coronavirus test | 8 |
| SARS-CoV-2 test | 8 |
| Increased appetite | 8 |
| Fluid retention | 8 |
| Psychomotor hyperactivity | 8 |
| Myelitis transverse | 8 |
| Diplegia | 8 |
| Sleep deficit | 8 |
| Morning sickness | 8 |
| Hallucination, visual | 8 |
| Menstruation delayed | 8 |
| Pulmonary embolism | 8 |
| Drug eruption | 8 |
| Orthostatic hypotension | 8 |
| Lymphadenitis | 7 |
| Swelling of eyelid | 7 |
| Foreign body sensation in eyes | 7 |
| Gastrointestinal disorder | 7 |
| Rectal haemorrhage | 7 |
| Cheilitis | 7 |
| Lip blister | 7 |
| Lip pruritus | 7 |
| Temperature intolerance | 7 |
| Injected limb mobility decreased | 7 |
| No reaction on previous exposure to drug | 7 |
| Vaccination site reaction | 7 |
| Serum sickness-like reaction | 7 |
| Conjunctivitis | 7 |
| Cystitis | 7 |

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| Procedural dizziness | 7 |
| Infusion related reaction | 7 |
| Blood glucose | 7 |
| Heart rate abnormal | 7 |
| Respiratory rate decreased | 7 |
| Joint lock | 7 |
| Cerebral haemorrhage | 7 |
| Clumsiness | 7 |
| Extrapyramidal disorder | 7 |
| Migraine without aura | 7 |
| Muscle contractions involuntary | 7 |
| Formication | 7 |
| Monoparesis | 7 |
| Trigeminal neuralgia | 7 |
| Anger | 7 |
| Euphoric mood | 7 |
| Sleep terror | 7 |
| Enuresis | 7 |
| Suicidal ideation | 7 |
| Bladder pain | 7 |
| Testicular pain | 7 |
| Sinus congestion | 7 |
| Alopecia | 7 |
| Rash maculo-papular | 7 |
| Skin erosion | 7 |
| Immobile | 7 |
| Prophylaxis of nausea and vomiting | 7 |
| Giant cell arteritis | 7 |
| Thrombocytopenia | 6 |
| Sudden hearing loss | 6 |
| Ocular discomfort | 6 |
| Eye allergy | 6 |
| Hyperaesthesia teeth | 6 |
| Gingival bleeding | 6 |
| Oral mucosal blistering | 6 |
| Aphthous ulcer | 6 |
| Tongue coated | 6 |
| Tongue dry | 6 |
| Puncture site bruise | 6 |
| Application site pain | 6 |
| Feeling jittery | 6 |
| Sensation of foreign body | 6 |
| Injection site oedema | 6 |
| Injection site urticaria | 6 |
| Oedema peripheral | 6 |
| Non-cardiac chest pain | 6 |
| Herpes simplex | 6 |
| Vaccination site infection | 6 |
| Chillblains | 6 |
| Nerve injury | 6 |

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|---|---|
| Thermal burn | 6 |
| Blood glucose decreased | 6 |
| Osteoarthritis | 6 |
| Psoriatic arthropathy | 6 |
| Guillain-Barre syndrome | 6 |
| Ischaemic stroke | 6 |
| Movement disorder | 6 |
| Multiple sclerosis relapse | 6 |
| Partial seizures | 6 |
| Phantom limb syndrome | 6 |
| Oversensing | 6 |
| Apathy | 6 |
| Breast tenderness | 6 |
| Menstrual disorder | 6 |
| Bronchospasm | 6 |
| Oropharyngeal discomfort | 6 |
| Papule | 6 |
| Yellow skin | 6 |
| Livedo reticularis | 6 |
| Myocardial ischaemia | 5 |
| Supraventricular tachycardia | 5 |
| Eye movement disorder | 5 |
| Teething | 5 |
| Gingival blister | 5 |
| Discoloured vomit | 5 |
| Tongue blistering | 5 |
| Tongue discomfort | 5 |
| No adverse event | 5 |
| Chronic fatigue syndrome | 5 |
| Hunger | 5 |
| General physical health deterioration | 5 |
| Jaundice | 5 |
| Anaphylactic shock | 5 |
| Seasonal allergy | 5 |
| Bacille Calmette-Guerin scar reactivation | 5 |
| Infectious mononucleosis | 5 |
| Pharyngitis | 5 |
| Viral rash | 5 |
| Thermal burns of eye | 5 |
| Analgesic drug level | 5 |
| Blood urine present | 5 |
| Diabetes mellitus | 5 |
| Diabetes mellitus inadequate control | 5 |
| Gout | 5 |
| Polydipsia | 5 |
| Abnormal loss of weight | 5 |
| Polymyalgia rheumatica | 5 |
| Muscle swelling | 5 |
| Axillary mass | 5 |
| Akathisia | 5 |

| | |
|-----------------------------|---|
| Hypokinesia | 5 |
| Retinal migraine | 5 |
| Myoclonus | 5 |
| Tonic convulsion | 5 |
| Speech disorder | 5 |
| Head titubation | 5 |
| Dissociation | 5 |
| Initial insomnia | 5 |
| Mood altered | 5 |
| Autoscopy | 5 |
| Habit cough | 5 |
| Head banging | 5 |
| Haematuria | 5 |
| Urine odour abnormal | 5 |
| Menstruation irregular | 5 |
| Metrorrhagia | 5 |
| Respiratory arrest | 5 |
| Pneumonia aspiration | 5 |
| Hiccups | 5 |
| Pharyngeal paraesthesia | 5 |
| Choking | 5 |
| Rhinalgia | 5 |
| Purpura | 5 |
| Rash vesicular | 5 |
| Limb immobilisation | 5 |
| Haematoma | 5 |
| Vasculitis | 5 |
| Cardiac disorder | 4 |
| Cardiac failure | 4 |
| Tachyarrhythmia | 4 |
| Arrhythmia supraventricular | 4 |
| Atrial flutter | 4 |
| Cystic fibrosis | 4 |
| Adrenal insufficiency | 4 |
| Hypothyroidism | 4 |
| Vitreous floaters | 4 |
| Blepharospasm | 4 |
| Periorbital oedema | 4 |
| Abnormal sensation in eye | 4 |
| Pancreatitis | 4 |
| Faeces soft | 4 |
| Anal incontinence | 4 |
| Breath odour | 4 |
| Defaecation urgency | 4 |
| Noninfective gingivitis | 4 |
| Lip ulceration | 4 |
| Administration site bruise | 4 |
| Application site bruise | 4 |
| Application site erythema | 4 |
| Hyperthermia | 4 |

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|--|---|
| Temperature regulation disorder | 4 |
| Secretion discharge | 4 |
| Mass | 4 |
| Inflammatory pain | 4 |
| Extensive swelling of vaccinated limb | 4 |
| Vaccination site movement impairment | 4 |
| Vaccination site paraesthesia | 4 |
| Multiple allergies | 4 |
| Reaction to preservatives | 4 |
| Anaphylactoid reaction | 4 |
| Gastroenteritis | 4 |
| Bacterial infection | 4 |
| Vaccination site cellulitis | 4 |
| Gingivitis | 4 |
| Laryngitis | 4 |
| Post lumbar puncture syndrome | 4 |
| International normalised ratio decreased | 4 |
| Blood test | 4 |
| Urine output increased | 4 |
| Hyponatraemia | 4 |
| Muscle mass | 4 |
| Tendonitis | 4 |
| Ataxia | 4 |
| Dementia | 4 |
| Bradykinesia | 4 |
| Dystonia | 4 |
| Facial spasm | 4 |
| Cold-stimulus headache | 4 |
| Thunderclap headache | 4 |
| Nervous system disorder | 4 |
| Muscle spasticity | 4 |
| Burning feet syndrome | 4 |
| Hemiplegia | 4 |
| Parkinson's disease | 4 |
| Parkinsonism | 4 |
| Delusion | 4 |
| Mood swings | 4 |
| Panic reaction | 4 |
| Psychotic disorder | 4 |
| Tachyphrenia | 4 |
| Hypomenorrhoea | 4 |
| Vaginal discharge | 4 |
| Vulvovaginal pain | 4 |
| Dyspnoea exertional | 4 |
| Stridor | 4 |
| Pharyngeal hypoaesthesia | 4 |
| Respiratory symptom | 4 |
| Erythema multiforme | 4 |
| Eosinophilia | 3 |
| Pericarditis | 3 |

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|---------------------------------|---|
| Eyelid ptosis | 3 |
| Extraocular muscle paresis | 3 |
| Mydriasis | 3 |
| Metamorphopsia | 3 |
| Visual acuity reduced | 3 |
| Colitis | 3 |
| Diarrhoea haemorrhagic | 3 |
| Epigastric discomfort | 3 |
| Faeces discoloured | 3 |
| Reflux gastritis | 3 |
| Abdominal tenderness | 3 |
| Gastric dilatation | 3 |
| Acute abdomen | 3 |
| Frequent bowel movements | 3 |
| Small intestinal haemorrhage | 3 |
| Haematemesis | 3 |
| Palatal swelling | 3 |
| Tongue discolouration | 3 |
| Tongue oedema | 3 |
| Puncture site pain | 3 |
| Instillation site warmth | 3 |
| Sluggishness | 3 |
| Thirst decreased | 3 |
| Implant site warmth | 3 |
| Infusion site pain | 3 |
| Injection site hypoaesthesia | 3 |
| Face oedema | 3 |
| Localised oedema | 3 |
| Facial discomfort | 3 |
| Therapeutic response unexpected | 3 |
| Ulcer | 3 |
| Vaccination site discomfort | 3 |
| Withdrawal syndrome | 3 |
| Biliary colic | 3 |
| Sensitisation | 3 |
| Candida infection | 3 |
| Oral candidiasis | 3 |
| Vulvovaginal candidiasis | 3 |
| COVID-19 pneumonia | 3 |
| Genital herpes | 3 |
| Abscess | 3 |
| Injection site infection | 3 |
| Secondary transmission | 3 |
| Viral infection | 3 |
| Eye contusion | 3 |
| Heat oedema | 3 |
| Exposure to extreme temperature | 3 |
| Incision site pain | 3 |
| Product administration error | 3 |
| Burn of internal organs | 3 |

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|--|---|
| Blood pH increased | 3 |
| Blood glucose abnormal | 3 |
| Pulse abnormal | 3 |
| Grip strength decreased | 3 |
| Platelet count decreased | 3 |
| Blood urine | 3 |
| Urine output decreased | 3 |
| SARS-CoV-2 antibody test negative | 3 |
| Diabetic ketoacidosis | 3 |
| Food intolerance | 3 |
| Bursitis | 3 |
| Joint noise | 3 |
| Joint warmth | 3 |
| Myofascial pain syndrome | 3 |
| Growing pains | 3 |
| Sleep paralysis | 3 |
| Haemorrhage intracranial | 3 |
| Coma | 3 |
| Vascular dementia | 3 |
| Sedation | 3 |
| Drug withdrawal headache | 3 |
| Hypotonia | 3 |
| Narcolepsy | 3 |
| Hyposmia | 3 |
| Optic neuritis | 3 |
| Status epilepticus | 3 |
| Restless arm syndrome | 3 |
| Slow speech | 3 |
| Abortion spontaneous | 3 |
| Attention deficit hyperactivity disorder | 3 |
| Paranoia | 3 |
| Daydreaming | 3 |
| Major depression | 3 |
| Depersonalisation/derealisation disorder | 3 |
| Emotional distress | 3 |
| Factitious disorder | 3 |
| Fear | 3 |
| Hallucination, auditory | 3 |
| Decreased interest | 3 |
| Feeling of despair | 3 |
| Mania | 3 |
| Sleep talking | 3 |
| Illusion | 3 |
| Post-traumatic stress disorder | 3 |
| Thinking abnormal | 3 |
| Loss of bladder sensation | 3 |
| Chronic kidney disease | 3 |
| Renal failure | 3 |
| Genital ulceration | 3 |
| Uterine spasm | 3 |

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|--------------------------------------|---|
| Irregular breathing | 3 |
| Sleep apnoea syndrome | 3 |
| Pulmonary oedema | 3 |
| Aspiration | 3 |
| Catarrh | 3 |
| Choking sensation | 3 |
| Upper-airway cough syndrome | 3 |
| Skin disorder | 3 |
| Skin odour abnormal | 3 |
| Dermatitis atopic | 3 |
| Rosacea | 3 |
| Vasculitic rash | 3 |
| Sight disability | 3 |
| Hormone replacement therapy | 3 |
| Hospitalisation | 3 |
| Anaemia | 2 |
| Haemolytic anaemia | 2 |
| Coagulopathy | 2 |
| Leukopenia | 2 |
| Lymphopenia | 2 |
| Pancytopenia | 2 |
| Sickle cell anaemia with crisis | 2 |
| Atrioventricular block | 2 |
| Acute cardiac event | 2 |
| Cardiovascular insufficiency | 2 |
| Acute myocardial infarction | 2 |
| Pericardial effusion | 2 |
| Ventricular tachycardia | 2 |
| Cerebral palsy | 2 |
| Paroxysmal extreme pain disorder | 2 |
| Deafness transitory | 2 |
| Vertigo labyrinthine | 2 |
| Diabetes insipidus | 2 |
| Conjunctival haemorrhage | 2 |
| Uveitis | 2 |
| Erythema of eyelid | 2 |
| Eye haemorrhage | 2 |
| Eye inflammation | 2 |
| Eyelid sensory disorder | 2 |
| Hypoaesthesia eye | 2 |
| Miosis | 2 |
| Pupils unequal | 2 |
| Episcleritis | 2 |
| Blindness transient | 2 |
| Anal hypoaesthesia | 2 |
| Dental paraesthesia | 2 |
| Abnormal faeces | 2 |
| Gastric ulcer | 2 |
| Functional gastrointestinal disorder | 2 |
| Gastric disorder | 2 |

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|---|---|
| Haemorrhoids | 2 |
| Gastrointestinal haemorrhage | 2 |
| Chapped lips | 2 |
| Oral blood blister | 2 |
| Lip exfoliation | 2 |
| Oral mucosal eruption | 2 |
| Oral pruritus | 2 |
| Salivary gland pain | 2 |
| Parotid gland enlargement | 2 |
| Glossitis | 2 |
| Tongue disorder | 2 |
| Trichoglossia | 2 |
| Scalloped tongue | 2 |
| Application site pruritus | 2 |
| Foaming at mouth | 2 |
| Induration | 2 |
| Moaning | 2 |
| Multiple organ dysfunction syndrome | 2 |
| Injection site discomfort | 2 |
| Injection site indentation | 2 |
| Injection site joint erythema | 2 |
| Injection site papule | 2 |
| Injection site paraesthesia | 2 |
| Injection site vesicles | 2 |
| Drug interaction | 2 |
| Oedema | 2 |
| Adverse event | 2 |
| Treatment failure | 2 |
| Vaccination site granuloma | 2 |
| Vaccination site joint movement impairment | 2 |
| Allergic oedema | 2 |
| Type III immune complex mediated reaction | 2 |
| Immune system disorder | 2 |
| Appendicitis | 2 |
| Mastitis | 2 |
| Myelitis | 2 |
| Severe acute respiratory syndrome | 2 |
| Gingival abscess | 2 |
| Ear infection | 2 |
| Eyelid infection | 2 |
| Severe fever with thrombocytopenia syndrome | 2 |
| Urosepsis | 2 |
| Rash pustular | 2 |
| Subcutaneous abscess | 2 |
| Furuncle | 2 |
| Lymphangitis | 2 |
| Viral pharyngitis | 2 |
| Exposure via breast milk | 2 |
| Foetal exposure during pregnancy | 2 |
| Exposure to SARS-CoV-2 | 2 |

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|--|---|
| Eye injury | 2 |
| Procedural vomiting | 2 |
| Heat exhaustion | 2 |
| Medication error | 2 |
| Epicondylitis | 2 |
| Arthropod bite | 2 |
| Arthropod sting | 2 |
| Toxicity to various agents | 2 |
| Expired product administered | 2 |
| Blood glucose fluctuation | 2 |
| Computerised tomogram head | 2 |
| Liver function test abnormal | 2 |
| Transaminases increased | 2 |
| Blood ketone body | 2 |
| Head lag | 2 |
| Respiratory rate | 2 |
| Haematocrit | 2 |
| Haemoglobin | 2 |
| Forced expiratory volume increased | 2 |
| Anticoagulation drug level below therapeutic | 2 |
| pH urine | 2 |
| SARS-CoV-2 test negative | 2 |
| White blood cell count decreased | 2 |
| Appetite disorder | 2 |
| Food craving | 2 |
| Hyperphagia | 2 |
| Fluid intake reduced | 2 |
| Abnormal weight gain | 2 |
| Myositis | 2 |
| Nuchal rigidity | 2 |
| Rhabdomyolysis | 2 |
| Still's disease | 2 |
| Arthritis reactive | 2 |
| Synovitis | 2 |
| Tendon pain | 2 |
| Trigger finger | 2 |
| Chronic lymphocytic leukaemia | 2 |
| Autonomic nervous system imbalance | 2 |
| Cerebral infarction | 2 |
| Haemorrhagic stroke | 2 |
| Cerebral venous sinus thrombosis | 2 |
| Nystagmus | 2 |
| Altered state of consciousness | 2 |
| Consciousness fluctuating | 2 |
| Noninfective encephalitis | 2 |
| Exertional headache | 2 |
| Medication overuse headache | 2 |
| Primary headache associated with sexual activity | 2 |
| Brain oedema | 2 |
| Intellectual disability | 2 |

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|--|---|
| Transient global amnesia | 2 |
| Hemiplegic migraine | 2 |
| Nerve compression | 2 |
| Psychomotor skills impaired | 2 |
| Tunnel vision | 2 |
| Visual field defect | 2 |
| Persistent postural-perceptual dizziness | 2 |
| Dysaesthesia | 2 |
| Hemianaesthesia | 2 |
| Paraparesis | 2 |
| Dreamy state | 2 |
| Post herpetic neuralgia | 2 |
| Incoherent | 2 |
| Resting tremor | 2 |
| Pregnancy | 2 |
| Pregnancy with implant contraceptive | 2 |
| Product taste abnormal | 2 |
| Paramnesia | 2 |
| Stress | 2 |
| Aggression | 2 |
| Frustration tolerance decreased | 2 |
| Fear of death | 2 |
| Hallucinations, mixed | 2 |
| Mental disorder | 2 |
| Anhedonia | 2 |
| Negative thoughts | 2 |
| Confusional arousal | 2 |
| Derealisation | 2 |
| Hypervigilance | 2 |
| Loss of libido | 2 |
| Logorrhoea | 2 |
| Bruxism | 2 |
| Urinary hesitation | 2 |
| Urine flow decreased | 2 |
| Bladder disorder | 2 |
| Hypertonic bladder | 2 |
| Oliguria | 2 |
| Urine abnormality | 2 |
| Nocturia | 2 |
| Breast mass | 2 |
| Premenstrual pain | 2 |
| Scrotal swelling | 2 |
| Vaginal lesion | 2 |
| Vulvovaginal swelling | 2 |
| Mouth breathing | 2 |
| Respiratory distress | 2 |
| Bronchiectasis | 2 |
| Pleuritic pain | 2 |
| Nasal inflammation | 2 |
| Nasal pruritus | 2 |

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|--|---|
| Pulmonary congestion | 2 |
| Suffocation feeling | 2 |
| Lung disorder | 2 |
| Paranasal sinus discomfort | 2 |
| Acne | 2 |
| Dermatitis bullous | 2 |
| Scab | 2 |
| Scar pain | 2 |
| Palmar erythema | 2 |
| Trichodynia | 2 |
| Butterfly rash | 2 |
| Skin mass | 2 |
| Skin ulcer | 2 |
| Idiopathic urticaria | 2 |
| Urticaria chronic | 2 |
| Impaired work ability | 2 |
| Bed rest | 2 |
| Localised alternating hot and cold therapy | 2 |
| Neurogenic shock | 2 |
| Shock symptom | 2 |
| Vascular pain | 2 |
| Vasodilatation | 2 |
| Ischaemic limb pain | 2 |
| Poor peripheral circulation | 2 |
| Capillary leak syndrome | 2 |
| Autoimmune haemolytic anaemia | 1 |
| Increased tendency to bruise | 1 |
| Bone marrow oedema | 1 |
| Methaemoglobinaemia | 1 |
| Haemolysis | 1 |
| Lymphocytosis | 1 |
| Lymphatic disorder | 1 |
| Purpura non-thrombocytopenic | 1 |
| Spleen disorder | 1 |
| Splenomegaly | 1 |
| White blood cell disorder | 1 |
| Aortic valve stenosis | 1 |
| Long QT syndrome | 1 |
| Cardiac discomfort | 1 |
| Congestive cardiomyopathy | 1 |
| Cardiac failure acute | 1 |
| Cardiopulmonary failure | 1 |
| Angina unstable | 1 |
| Microvascular coronary artery disease | 1 |
| Left ventricular failure | 1 |
| Mitral valve incompetence | 1 |
| Right ventricular failure | 1 |
| Sinus arrhythmia | 1 |
| Ventricular arrhythmia | 1 |
| Ventricular extrasystoles | 1 |

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|--|---|
| Arnold-Chiari malformation | 1 |
| Heterotaxia | 1 |
| Ear haemorrhage | 1 |
| Excessive cerumen production | 1 |
| External ear pain | 1 |
| Red ear syndrome | 1 |
| Auditory disorder | 1 |
| Deafness bilateral | 1 |
| Deafness unilateral | 1 |
| Meniere's disease | 1 |
| Thyroid pain | 1 |
| Cataract | 1 |
| Dyschromatopsia | 1 |
| Eye colour change | 1 |
| Eyelid bleeding | 1 |
| Blepharitis | 1 |
| Eyelid oedema | 1 |
| Eye disorder | 1 |
| Eye oedema | 1 |
| Eye symptom | 1 |
| Periorbital pain | 1 |
| Eye discharge | 1 |
| Retinal aneurysm | 1 |
| Retinal vascular thrombosis | 1 |
| Neovascular age-related macular degeneration | 1 |
| Vitreoretinal traction syndrome | 1 |
| Chromatopsia | 1 |
| Xanthopsia | 1 |
| Halo vision | 1 |
| Visual snow syndrome | 1 |
| Night blindness | 1 |
| Sudden visual loss | 1 |
| Abdominal mass | 1 |
| Gastrointestinal sounds abnormal | 1 |
| Obstructive pancreatitis | 1 |
| Pancreatitis acute | 1 |
| Proctalgia | 1 |
| Anal pruritus | 1 |
| Anorectal discomfort | 1 |
| Colitis ischaemic | 1 |
| Colitis microscopic | 1 |
| Tooth discolouration | 1 |
| Faecaloma | 1 |
| Gastric haemorrhage | 1 |
| Oesophageal pain | 1 |
| Neurogenic bowel | 1 |
| Change of bowel habit | 1 |
| Oesophageal achalasia | 1 |
| Gastrointestinal tract irritation | 1 |
| Abdominal symptom | 1 |

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|-------------------------------|---|
| Oesophageal spasm | 1 |
| Intestinal obstruction | 1 |
| Gingival discomfort | 1 |
| Gingival oedema | 1 |
| Gingival pruritus | 1 |
| Inguinal hernia | 1 |
| Anal haemorrhage | 1 |
| Coeliac disease | 1 |
| Melaena | 1 |
| Aptyalism | 1 |
| Saliva altered | 1 |
| Enlarged uvula | 1 |
| Lip disorder | 1 |
| Oral disorder | 1 |
| Mouth haemorrhage | 1 |
| Anaesthesia oral | 1 |
| Burning mouth syndrome | 1 |
| Lip erythema | 1 |
| Odynophagia | 1 |
| Oral mucosal exfoliation | 1 |
| Lip oedema | 1 |
| Oedema mouth | 1 |
| Proctitis | 1 |
| Noninfective sialoadenitis | 1 |
| Plicated tongue | 1 |
| Tongue ulceration | 1 |
| Tongue eruption | 1 |
| Tongue movement disturbance | 1 |
| Tongue pruritus | 1 |
| Tongue spasm | 1 |
| Administration site urticaria | 1 |
| Puncture site reaction | 1 |
| Application site joint pain | 1 |
| Phantom shocks | 1 |
| Cardiac death | 1 |
| Masked fever | 1 |
| Feeling of relaxation | 1 |
| Fibrosis | 1 |
| Decreased gait velocity | 1 |
| Energy increased | 1 |
| Exercise tolerance decreased | 1 |
| General symptom | 1 |
| Nonspecific reaction | 1 |
| Screaming | 1 |
| Infusion site bruising | 1 |
| Injection site coldness | 1 |
| Injection site haemorrhage | 1 |
| Cyst | 1 |
| Nodule | 1 |
| Mucosal inflammation | 1 |

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|---|---|
| Mucosal pain | 1 |
| Diet failure | 1 |
| Drug intolerance | 1 |
| Therapeutic product effect decreased | 1 |
| Vaccine positive rechallenge | 1 |
| Shoulder injury related to vaccine administration | 1 |
| Vaccination site discolouration | 1 |
| Vaccination site extravasation | 1 |
| Vaccination site haemorrhage | 1 |
| Vaccination site hypersensitivity | 1 |
| Vaccination site irritation | 1 |
| Vaccination site joint erythema | 1 |
| Vaccination site joint swelling | 1 |
| Vaccination site nodule | 1 |
| Vaccination site urticaria | 1 |
| Vaccination site vesicles | 1 |
| Drug withdrawal syndrome | 1 |
| Cholelithiasis | 1 |
| Ocular icterus | 1 |
| Hepatic cirrhosis | 1 |
| Allergy to sting | 1 |
| Infusion related hypersensitivity reaction | 1 |
| Reaction to excipient | 1 |
| Anaphylactoid shock | 1 |
| Autoimmune disorder | 1 |
| Immunodeficiency | 1 |
| Gastrointestinal infection | 1 |
| Administration site cellulitis | 1 |
| Arthritis bacterial | 1 |
| Urinary tract infection bacterial | 1 |
| Intervertebral discitis | 1 |
| Pertussis | 1 |
| Skin candida | 1 |
| Encephalitis | 1 |
| Clostridium difficile colitis | 1 |
| Asymptomatic COVID-19 | 1 |
| Abscess oral | 1 |
| Oral pustule | 1 |
| Tooth abscess | 1 |
| Eye infection | 1 |
| Hordeolum | 1 |
| Fungal infection | 1 |
| Genital herpes simplex | 1 |
| Herpes virus infection | 1 |
| Ophthalmic herpes zoster | 1 |
| Varicella | 1 |
| Abscess limb | 1 |
| Respiratory tract infection | 1 |
| H2N2 influenza | 1 |
| Orchitis | 1 |

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|--|---|
| Mumps | 1 |
| Pneumocystis jirovecii pneumonia | 1 |
| AIDS related complex | 1 |
| Septic rash | 1 |
| Folliculitis | 1 |
| Pustule | 1 |
| Staphylococcal scalded skin syndrome | 1 |
| Cellulitis streptococcal | 1 |
| Erysipelas | 1 |
| Body tinea | 1 |
| Tinea cruris | 1 |
| Tuberculosis | 1 |
| Acute sinusitis | 1 |
| Infected lymphocele | 1 |
| Arthritis viral | 1 |
| Vestibular neuronitis | 1 |
| Viral diarrhoea | 1 |
| Viral sepsis | 1 |
| Oral contusion | 1 |
| Splenic rupture | 1 |
| Barotrauma | 1 |
| Subdural haematoma | 1 |
| Subdural haemorrhage | 1 |
| Chest crushing | 1 |
| Maternal exposure timing unspecified | 1 |
| Paternal exposure during pregnancy | 1 |
| Clavicle fracture | 1 |
| Device use issue | 1 |
| Vaccination error | 1 |
| Wrong technique in product usage process | 1 |
| Ligament sprain | 1 |
| Muscle strain | 1 |
| Tendon rupture | 1 |
| Exposure to noise | 1 |
| Electric shock | 1 |
| Inflammation of wound | 1 |
| Road traffic accident | 1 |
| Wound complication | 1 |
| Suture related complication | 1 |
| Occupational exposure to product | 1 |
| Intentional overdose | 1 |
| Overdose | 1 |
| Ulnar nerve injury | 1 |
| Systemic toxicity | 1 |
| Accidental overdose | 1 |
| Extra dose administered | 1 |
| Inappropriate schedule of product administration | 1 |
| Incorrect route of product administration | 1 |
| Product administered to patient of inappropriate age | 1 |
| Product label confusion | 1 |

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|---|---|
| Product dispensing error | 1 |
| Sunburn | 1 |
| Postmastectomy lymphoedema syndrome | 1 |
| Head injury | 1 |
| Limb crushing injury | 1 |
| Skin injury | 1 |
| Skin wound | 1 |
| Gastrointestinal stoma complication | 1 |
| Burn oral cavity | 1 |
| Burns second degree | 1 |
| Intentional underdose | 1 |
| Vaccination failure | 1 |
| Cortisol increased | 1 |
| Cold agglutinins positive | 1 |
| Glycosylated haemoglobin increased | 1 |
| Cardiac murmur | 1 |
| Heart sounds | 1 |
| Inflammatory marker decreased | 1 |
| Inflammatory marker increased | 1 |
| Coagulation time prolonged | 1 |
| Hormone level abnormal | 1 |
| Faecal calprotectin increased | 1 |
| Semen volume decreased | 1 |
| Computerised tomogram abdomen | 1 |
| Gastrointestinal stoma output increased | 1 |
| Swallow study | 1 |
| Blood gastrin normal | 1 |
| Blood insulin | 1 |
| Maximum heart rate | 1 |
| Maximum heart rate decreased | 1 |
| Orthostatic heart rate response increased | 1 |
| Sinus rhythm | 1 |
| Computerised tomogram | 1 |
| Immunology test | 1 |
| Immunology test normal | 1 |
| Allergy alert test | 1 |
| Alanine aminotransferase increased | 1 |
| Aspartate aminotransferase increased | 1 |
| Ubiquinone | 1 |
| Blood phosphorus increased | 1 |
| Blood sodium decreased | 1 |
| Lumbar puncture | 1 |
| Intraocular pressure test | 1 |
| Breath sounds abnormal | 1 |
| Grip strength | 1 |
| Weight increased | 1 |
| C-reactive protein abnormal | 1 |
| Mean cell volume abnormal | 1 |
| Blood creatinine decreased | 1 |
| Forced expiratory volume | 1 |

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|--|---|
| Forced expiratory volume normal | 1 |
| Peak expiratory flow rate | 1 |
| Peak expiratory flow rate decreased | 1 |
| Computerised tomogram thorax | 1 |
| Blood creatine phosphokinase increased | 1 |
| Analgesic drug level therapeutic | 1 |
| Anticoagulation drug level above therapeutic | 1 |
| Tri-iodothyronine | 1 |
| Lactate dehydrogenase urine increased | 1 |
| Cells in urine | 1 |
| Protein urine present | 1 |
| pH urine increased | 1 |
| Blood pressure abnormal | 1 |
| Blood pressure systolic increased | 1 |
| SARS-CoV-2 antibody test positive | 1 |
| SARS-CoV-2 test false negative | 1 |
| White blood cell count increased | 1 |
| Diet refusal | 1 |
| Salt craving | 1 |
| Cachexia | 1 |
| Starvation | 1 |
| Hyperlipidaemia | 1 |
| Hyperinsulinaemic hypoglycaemia | 1 |
| Ketosis | 1 |
| Metabolic acidosis | 1 |
| Hyperkalaemia | 1 |
| Arthropathy | 1 |
| Polyarthritis | 1 |
| Sacroiliitis | 1 |
| Jaw disorder | 1 |
| Medial tibial stress syndrome | 1 |
| Costochondritis | 1 |
| Morphoea | 1 |
| Hand deformity | 1 |
| Limb deformity | 1 |
| Joint laxity | 1 |
| Patellofemoral pain syndrome | 1 |
| Rotator cuff syndrome | 1 |
| Temporomandibular joint syndrome | 1 |
| Lupus-like syndrome | 1 |
| Systemic lupus erythematosus | 1 |
| Osteopenia | 1 |
| Muscle discomfort | 1 |
| Muscle disorder | 1 |
| Muscle oedema | 1 |
| Torticollis | 1 |
| Limb mass | 1 |
| Somatic dysfunction | 1 |
| Weight bearing difficulty | 1 |
| Connective tissue inflammation | 1 |

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| Rheumatic disorder | 1 |
| Myopathy | 1 |
| Nodal osteoarthritis | 1 |
| Neck mass | 1 |
| Soft tissue mass | 1 |
| Ankylosing spondylitis | 1 |
| Breast cancer | 1 |
| Lymphoproliferative disorder in remission | 1 |
| Neoplasm malignant | 1 |
| Oesophageal squamous cell carcinoma | 1 |
| Cancer fatigue | 1 |
| Plasma cell myeloma | 1 |
| Clear cell renal cell carcinoma | 1 |
| Uterine leiomyoma | 1 |
| Hyporeflexia | 1 |
| Petit mal epilepsy | 1 |
| Dementia Alzheimer's type | 1 |
| Brain stem infarction | 1 |
| Brain stem stroke | 1 |
| Embolic stroke | 1 |
| Subarachnoid haemorrhage | 1 |
| Central nervous system inflammation | 1 |
| Cerebral small vessel ischaemic disease | 1 |
| Cerebrovascular disorder | 1 |
| Superior sagittal sinus thrombosis | 1 |
| Cervicobrachial syndrome | 1 |
| Cerebellar ataxia | 1 |
| Neurologic neglect syndrome | 1 |
| Senile dementia | 1 |
| Motor dysfunction | 1 |
| Dystonic tremor | 1 |
| Encephalopathy | 1 |
| 3rd nerve paralysis | 1 |
| Cervicogenic headache | 1 |
| External compression headache | 1 |
| New daily persistent headache | 1 |
| Occipital neuralgia | 1 |
| Post-traumatic headache | 1 |
| Tongue paralysis | 1 |
| Intracranial pressure increased | 1 |
| Status migrainosus | 1 |
| Typical aura without headache | 1 |
| Diabetic mononeuropathy | 1 |
| Peroneal nerve palsy | 1 |
| Ulnar nerve palsy | 1 |
| Band sensation | 1 |
| Cerebral disorder | 1 |
| Drooling | 1 |
| Exaggerated startle response | 1 |
| Infant irritability | 1 |

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| Meningism | 1 |
| Patient elopement | 1 |
| Neuromuscular pain | 1 |
| Myasthenia gravis | 1 |
| Anaesthesia | 1 |
| Lhermitte's sign | 1 |
| Paraplegia | 1 |
| Reduced facial expression | 1 |
| Alcoholic seizure | 1 |
| Atonic seizures | 1 |
| Clonic convulsion | 1 |
| Seizure anoxic | 1 |
| Seizure cluster | 1 |
| Seizure like phenomena | 1 |
| Aura | 1 |
| Central pain syndrome | 1 |
| Complex regional pain syndrome | 1 |
| Hypogeusia | 1 |
| Myelopathy | 1 |
| Action tremor | 1 |
| Essential tremor | 1 |
| Intention tremor | 1 |
| Facial neuralgia | 1 |
| Premature labour | 1 |
| Premature rupture of membranes | 1 |
| Patient-device incompatibility | 1 |
| Stent malfunction | 1 |
| Undersensing | 1 |
| Adjustment disorder with depressed mood | 1 |
| Constricted affect | 1 |
| Flat affect | 1 |
| Inappropriate affect | 1 |
| Indifference | 1 |
| Social avoidant behaviour | 1 |
| Soliloquy | 1 |
| Violence-related symptom | 1 |
| Mutism | 1 |
| Dissociative disorder | 1 |
| Terminal insomnia | 1 |
| Eating disorder | 1 |
| Agoraphobia | 1 |
| Fear of disease | 1 |
| Fear of falling | 1 |
| Phonophobia | 1 |
| Mental status changes | 1 |
| Sense of a foreshortened future | 1 |
| Hypnagogic hallucination | 1 |
| Obsessive thoughts | 1 |
| Exploding head syndrome | 1 |
| Rapid eye movements sleep abnormal | 1 |

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| Sleep-related eating disorder | 1 |
| Somnambulism | 1 |
| Time perception altered | 1 |
| Psychological trauma | 1 |
| Conversion disorder | 1 |
| Somatic symptom disorder | 1 |
| Lack of spontaneous speech | 1 |
| Acute stress disorder | 1 |
| Burnout syndrome | 1 |
| Hyperarousal | 1 |
| Alcohol abuse | 1 |
| Drug dependence | 1 |
| Substance abuse | 1 |
| Intentional self-injury | 1 |
| Suicide threat | 1 |
| Intrusive thoughts | 1 |
| Thought blocking | 1 |
| Bladder discomfort | 1 |
| Micturition frequency decreased | 1 |
| Mixed incontinence | 1 |
| Bladder dilatation | 1 |
| Cystitis interstitial | 1 |
| IgA nephropathy | 1 |
| Neurogenic bladder | 1 |
| Nephritis | 1 |
| Nephropathy | 1 |
| Renal disorder | 1 |
| Renal injury | 1 |
| Urethral spasm | 1 |
| Proteinuria | 1 |
| Haemorrhage urinary tract | 1 |
| Renal colic | 1 |
| Breast enlargement | 1 |
| Breast oedema | 1 |
| Breast swelling | 1 |
| Nipple pain | 1 |
| Erectile dysfunction | 1 |
| Menopausal symptoms | 1 |
| Postmenopausal haemorrhage | 1 |
| Polymenorrhoea | 1 |
| Penile oedema | 1 |
| Penis disorder | 1 |
| Prostatitis | 1 |
| Female genital tract fistula | 1 |
| Genital blister | 1 |
| Genital burning sensation | 1 |
| Genital discomfort | 1 |
| Pelvic discomfort | 1 |
| Scrotal pain | 1 |
| Sexual dysfunction | 1 |

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| Testicular swelling | 1 |
| Uterine haemorrhage | 1 |
| Uterine pain | 1 |
| Vulvovaginal rash | 1 |
| Apnoea | 1 |
| Dyspnoea at rest | 1 |
| Orthopnoea | 1 |
| Respiratory fatigue | 1 |
| Cough variant asthma | 1 |
| Obstructive airways disorder | 1 |
| Sputum discoloured | 1 |
| Pneumonitis | 1 |
| Rhinitis allergic | 1 |
| Rhinitis perennial | 1 |
| Nasal disorder | 1 |
| Nasal odour | 1 |
| Nasal oedema | 1 |
| Paranasal sinus haemorrhage | 1 |
| Sinonasal obstruction | 1 |
| Oropharyngeal swelling | 1 |
| Pharyngeal erythema | 1 |
| Pharyngeal oedema | 1 |
| Tonsillar erythema | 1 |
| Tonsillar inflammation | 1 |
| Pleurisy | 1 |
| Pleural effusion | 1 |
| Pneumothorax | 1 |
| Acute pulmonary oedema | 1 |
| Pulmonary infarction | 1 |
| Respiratory tract irritation | 1 |
| Tracheal pain | 1 |
| Throat clearing | 1 |
| Madarosis | 1 |
| Sweat discolouration | 1 |
| Sweat gland disorder | 1 |
| Blood blister | 1 |
| Pemphigoid | 1 |
| Pemphigus | 1 |
| Stevens-Johnson syndrome | 1 |
| Toxic epidermal necrolysis | 1 |
| Macule | 1 |
| Peau d'orange | 1 |
| Skin fissures | 1 |
| Skin lesion | 1 |
| Skin texture abnormal | 1 |
| Skin tightness | 1 |
| Sticky skin | 1 |
| Dyshidrotic eczema | 1 |
| Eczema asteatotic | 1 |
| Perioral dermatitis | 1 |

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| Seborrhoeic dermatitis | 1 |
| Fixed eruption | 1 |
| Dermatitis exfoliative generalised | 1 |
| Exfoliative rash | 1 |
| Lipohypertrophy | 1 |
| Erythema nodosum | 1 |
| Lichen planus | 1 |
| Pityriasis rosea | 1 |
| Hair growth abnormal | 1 |
| Guttate psoriasis | 1 |
| Ecchymosis | 1 |
| Henoch-Schonlein purpura | 1 |
| Systemic lupus erythematosus rash | 1 |
| Cutaneous symptom | 1 |
| Dermal cyst | 1 |
| Skin haemorrhage | 1 |
| Decubitus ulcer | 1 |
| Needle track marks | 1 |
| Cutaneous vasculitis | 1 |
| Hypersensitivity vasculitis | 1 |
| Urticaria papular | 1 |
| Urticarial vasculitis | 1 |
| Death of relative | 1 |
| Inadequate diet | 1 |
| Impaired driving ability | 1 |
| Water pollution | 1 |
| Breast feeding | 1 |
| Impaired quality of life | 1 |
| Tobacco user | 1 |
| COVID-19 treatment | 1 |
| Pericardial excision | 1 |
| Medical diet | 1 |
| Face lift | 1 |
| Prophylaxis against gastrointestinal ulcer | 1 |
| Hip surgery | 1 |
| Limb operation | 1 |
| Muscle relaxant therapy | 1 |
| Central nervous system stimulation | 1 |
| Prone position | 1 |
| Ileostomy | 1 |
| Mass excision | 1 |
| Blood pressure management | 1 |
| Hypertensive emergency | 1 |
| Hypertensive urgency | 1 |
| Tyramine reaction | 1 |
| Aortic aneurysm | 1 |
| Blood pressure fluctuation | 1 |
| Bloody discharge | 1 |
| Embolism | 1 |
| Thrombosis | 1 |

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| Arteriosclerosis | 1 |
| Blue toe syndrome | 1 |
| Pelvic venous thrombosis | 1 |
| Thrombophlebitis superficial | 1 |
| Varicophlebitis | 1 |
| Varicose vein | 1 |
| MAGIC syndrome | 1 |