

NOT FOR PUBLICATION

COMMISSION ON HUMAN MEDICINES

COVID-19 VBR EWG

Title of paper: Update on COVID-19 vaccine AstraZeneca safety Type of paper: Update
--

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]

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.

2. Data for 4th – 28th January 2021

Usage data

Rollout of COVID-19 Vaccine AstraZeneca began on 4th January 2021. Up to the end of 31st January 2021, an estimated 3,098,605 doses of COVID-19 Vaccine AstraZeneca have been given in the UK¹.

Summary of ADR reports

Between vaccine rollout on 4th January 2021 up to 28th January 2021, the MHRA has received a total of 9681 reports of suspected ADRs in association with COVID-19 Vaccine AstraZeneca.

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 1.

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

Reaction PT	Number of times reported
Headache	4194
Pyrexia	3758
Chills	2369
Fatigue	2146

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

Nausea	1893
Myalgia	1641
Arthralgia	1043
Dizziness	916
Pain	896
Pain in extremity	719
Vomiting	676
Malaise	474
Hyperhidrosis	454
Influenza like illness	451
Tremor	433
Diarrhoea	386
Decreased appetite	329
Back pain	321
Migraine	295
Influenza	285

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.

That being said, the reactions reported most frequently are common reactogenicity reactions seen with all vaccines as well as in the AstraZeneca clinical trials. These terms, or associated umbrella terms are labelled in the product information.

Onset times for cases reporting these reactions are short, usually the day of vaccination or the following day, which is consistent with established characteristics of reactogenicity reactions. The Yellow card data does indicate that reactogenicity reactions are more frequently reported in younger (patients aged under 65) vaccine recipients, for example, for the top 5 reaction PTs: Headache- 3556/4280 (83%) are reported in patients aged under 65; pyrexia 3217/3765 (85%), chills 1970/ 2369 (83%), fatigue 1770/2178 (81%) and for nausea 1563/1895 (82%) are reported in patients under 65. Case review through signal detection as well as analysis of seriousness criteria flagged in the cases identifies that in some recipients, the reactogenicity reactions are resulting in an interruption to usual daily activities, for example, requiring days off work. Reactogenicity reactions are further discussed in a separate paper.

Fatal cases

The MHRA has received 63 fatal cases associated with this vaccine. A review of fatal cases was provided at a recent EWG and broadly, the overview of the cases remains similar. The age of the patients, where reported, ranges from 57-101 years. This includes one death in a [REDACTED]

████████████████████ 4 patients in their 60s (again, these patients have been care home residents who were frail with end stage diseases. In many cases the reporting HCP states that the death was not suspected to be caused by the vaccine), 9 patients in their 70s and 26 cases in patients aged 80+. Age was not reported in the remaining cases.

45 cases report “death” or “sudden death” as the fatal term. In some cases, these reports are too sparse of detail to assess and so will be followed up for further information. In others, narrative descriptions describe death from an underlying or alternative disease, with this having been recorded as the cause of death. Often in these cases, the reporter states that they have submitted their report purely due to close temporality of the death to vaccination but without suspicion of an association. The majority of cases report patient frailty, serious co-morbidity (such as cardiac failure or other cardiovascular disease, cancer, dementia) and/ or the patient having been in declining health or palliative prior to vaccination.

In the remaining 18 cases, the fatal terms vary with 4 cases of cerebrovascular accident, 1 reporting cardiac arrest and another acute cardiac event, 2 stating malaise as the fatal term, and 1 case each of the following terms: dyspnoea, lower respiratory tract infection, cellulitis, pneumonia, COPD, allergic dermatitis, COVID-19, diabetic ketoacidosis, urosepsis and infection.

Safety topics under review

Anaphylaxis

Up to 28th January, the MHRA has received 21 cases reporting anaphylactic reaction and 2 reporting anaphylactoid reaction. Additional cases received since then do not change the overall assessment. The cases present a mixed picture with widely varying onset times and some cases more suggestive of anxiety or other types of non-severe allergic reaction. Furthermore, only a small proportion of cases report immediate onset following vaccination as would be typical of anaphylaxis. A conservative estimate of the reporting rate, taking into account all cases reported of anaphylaxis regardless of the level of evidence to support this classification, would be 0.8 cases per 100,000 doses; however it seems likely that the rate may be lower than this once all cases are adjudicated. With an adjudication of cases based on the Brighton Collaboration criteria, the rate lowers to 0.3 cases per 100,000 doses. This is a very rare occurrence and is lower than the reporting rate seen for the Pfizer vaccine (current estimate 1.8 per 100,000 doses) and is in line with rates for non-COVID-19 vaccinations found in the literature (between 0.1 and 1 per 100,000 doses).

Additionally, the overall reporting rates for the COVID vaccines (3 reports per 1,000 doses administered) are much higher than other vaccines due to increased vigilance and awareness with these products which may also be reflected in the rates observed.

The description of events does not paint a picture of markedly severe, life-threatening allergic reactions and analysis of the cases does not highlight that these are occurring more frequently than we would expect with a vaccine. The course of the cases does not suggest that a specific waiting time after vaccination, as is in place for the Pfizer vaccine, is indicated. Furthermore,

the current evidence does not suggest that the presence of polysorbate as an excipient in the AstraZeneca vaccine is leading to an increase in the expected rate of anaphylaxis and clinical trial data did not identify any cases of anaphylaxis which were likely related to the vaccine.

An update on anaphylaxis was provided at the EWG meeting held on 29th January where it was decided that anaphylaxis should be included in section 4.8 of the Information for UK Healthcare Professionals. This is currently being implemented by AstraZeneca.

Bell's palsy

MHRA has received 10 cases reporting facial paralysis associated with this vaccine. [REDACTED]
[REDACTED] Ages reported include [REDACTED]
[REDACTED] 3 patients in their 70s and [REDACTED] (age not reported in 2 cases). The time to onset was 1 day in 5 cases, 2 days in 3 cases and 3 days in 2 cases. The facial paralysis as reported to have recovered in 2 cases, with the reaction recovering the same and following day, recovering in 2 cases and either not recovered or unknown in the remaining cases. Bell's Palsy is an Adverse Event of Special Interest and therefore observed vs expected analysis will be performed. More on this is presented in a separate paper.

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). This event is therefore monitored closely.

MHRA has received 1 post-authorisation report in [REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]

Transverse myelitis is an adverse event of special interest and as such, Observed vs Expected analysis will be performed when there are sufficient data for analysis, as well as Rapid Cycle Analysis of the rate within CPRD.

Conclusion

The ADR data received thus far are broadly in line with the safety profile seen in clinical trials, with the vast majority of reports reporting reactogenicity reactions. Review of the cumulative data does not identify any new safety signals.

Annex 1

Tabulation of all PTs reported with the COVID-19 vaccine AstraZeneca, DLP 28/01/2021

Reaction PT	Number of times reported
Headache	4194
Pyrexia	3758
Chills	2369
Fatigue	2146
Nausea	1893
Myalgia	1641
Arthralgia	1043
Dizziness	916
Pain	896
Pain in extremity	719
Vomiting	676
Malaise	474
Hyperhidrosis	454
Influenza like illness	451
Tremor	433
Diarrhoea	386
Decreased appetite	329
Back pain	321
Migraine	295
Influenza	285
Illness	254
Injection site pain	236
Lethargy	234
Feeling cold	226
Paraesthesia	225
Dyspnoea	208
Rash	207
Asthenia	205
Peripheral swelling	186
Abdominal pain	180
Pruritus	176
Abdominal pain upper	171
Palpitations	168
Insomnia	163
Eye pain	161
Oropharyngeal pain	160

Chest pain	156
Adverse drug reaction	154
Lymphadenopathy	145
Hypoaesthesia	137
Neck pain	128
Erythema	123
Tachycardia	122
Cough	121
Cold sweat	107
Swelling	99
Dizziness postural	97
Hot flush	96
Chest discomfort	94
Muscle spasms	92
Feeling abnormal	90
Feeling hot	86
Body temperature increased	85
Limb discomfort	84
Syncope	82
Body temperature	81
Tenderness	80
Musculoskeletal stiffness	80
Somnolence	79
Heart rate increased	78
Urticaria	78
Vaccination site pain	76
Night sweats	76
Dysgeusia	74
Confusional state	74
Ear pain	72
Feeling of body temperature change	71
Thirst	71
Muscular weakness	70
Pain of skin	64
Tension headache	63
Injection site mass	62
Dry mouth	54
Nasopharyngitis	52
Hallucination	51
Abdominal discomfort	50
Death	50
Bone pain	50

Rhinorrhoea	48
Photophobia	47
Rash erythematous	47
Peripheral coldness	43
Sweating fever	42
Vision blurred	41
Muscle fatigue	41
Renal pain	40
Paraesthesia oral	39
Lip swelling	38
Epistaxis	35
Disorientation	34
Rash pruritic	33
Balance disorder	32
Tinnitus	30
Swelling face	30
Presyncope	30
Cellulitis	29
COVID-19	29
Seizure	29
Ageusia	29
Neuralgia	29
Sensitive skin	29
Flushing	29
Pallor	29
Hypersensitivity	28
Injection site erythema	27
Contusion	27
Sinus headache	27
Hypertension	27
Heart rate	26
Nervousness	26
Restlessness	26
Injection related reaction	25
Restless legs syndrome	25
Poor quality sleep	25
Nightmare	25
Vertigo	24
Swollen tongue	24
Cluster headache	24
Taste disorder	24
Dyspepsia	23

Dehydration	23
Wheezing	23
Skin warm	23
Hypotension	23
Disturbance in attention	22
Nasal congestion	22
Eye swelling	21
Anaphylactic reaction	21
Pain in jaw	21
Sleep disorder	21
Skin burning sensation	21
Hypoaesthesia oral	20
Axillary pain	20
Vaccination site mass	20
Hyperaesthesia	20
Delirium	20
Abnormal dreams	20
Injection site warmth	19
Vaccination site erythema	19
Oral herpes	19
Pollakiuria	19
Injection site pruritus	18
Joint swelling	18
Flatulence	17
Local reaction	17
Body temperature fluctuation	17
Loss of consciousness	17
Anxiety	16
Sinus pain	16
Angioedema	16
Lymph node pain	15
Injection site swelling	15
Dry throat	15
Rash macular	15
Gastrointestinal pain	14
Muscle twitching	14
Musculoskeletal chest pain	14
Blister	14
Oral pain	13
Mouth ulceration	13
Joint stiffness	13
Burning sensation	13

Mental fatigue	13
Irritability	13
Injection site rash	12
Herpes zoster	12
Skin temperature	12
Facial paralysis	12
Anosmia	12
Parosmia	12
Agitation	12
Sneezing	12
Skin reaction	12
Dermatitis allergic	12
Visual impairment	11
Gait disturbance	11
Vaccination site swelling	11
Spinal pain	11
Head discomfort	11
Vaginal haemorrhage	11
Photosensitivity reaction	11
Eye pruritus	10
Body temperature decreased	10
Injection site reaction	9
Discomfort	9
Maternal exposure during pregnancy	9
Oxygen saturation decreased	9
Dysarthria	9
Panic attack	9
Lacrimation increased	8
Eye irritation	8
Gingival pain	8
Retching	8
Hyperpyrexia	8
Gait inability	8
Inflammation	8
Infection	8
Body temperature abnormal	8
Tension	8
Asthma	8
Throat irritation	8
Dermatitis	8
COVID-19 immunisation	8
Dry eye	7

Ocular hyperaemia	7
Asthenopia	7
Gastrooesophageal reflux disease	7
Vaccination site warmth	7
Vaccination complication	7
Blood pressure increased	7
Cerebrovascular accident	7
Migraine with aura	7
Hypersomnia	7
Depressed mood	7
Breast pain	7
Menorrhagia	7
Tachypnoea	7
Hypoxia	7
Pulmonary pain	7
Pharyngeal swelling	7
Throat tightness	7
Skin sensitisation	7
Cyanosis	7
Angina pectoris	6
Bradycardia	6
Sinus tachycardia	6
Periorbital swelling	6
Blindness	6
Abdominal distension	6
Mouth swelling	6
Glossodynia	6
Injection site inflammation	6
Q fever	6
Heart rate irregular	6
Trismus	6
Dysstasia	6
Memory impairment	6
Unresponsive to stimuli	6
Allodynia	6
Hypopnoea	6
Miliaria	6
Skin irritation	6
Neutropenia	5
Diplopia	5
Photopsia	5
Toothache	5

Constipation	5
Dysphagia	5
Hypothermia	5
Sudden death	5
Facial pain	5
No reaction on previous exposure to drug	5
Vaccination site joint pain	5
Sinusitis	5
Fall	5
Respiratory rate increased	5
Weight decreased	5
Hypoglycaemia	5
Arthritis	5
Mobility decreased	5
Musculoskeletal discomfort	5
Musculoskeletal pain	5
Mental impairment	5
Epilepsy	5
Tearfulness	5
Dysmenorrhoea	5
Pelvic pain	5
Respiration abnormal	5
Dry skin	5
Cardiac flutter	4
Deafness	4
Hyperacusis	4
Abdominal pain lower	4
Irritable bowel syndrome	4
Vomiting projectile	4
Lip pain	4
Oral discomfort	4
Sensation of foreign body	4
Loss of control of legs	4
General physical health deterioration	4
Injection site joint pain	4
Injection site oedema	4
Adverse reaction	4
Drug hypersensitivity	4
Localised infection	4
Lower respiratory tract infection	4
Post procedural complication	4

Oxygen saturation	4
Feeding disorder	4
Hyperglycaemia	4
Neurological symptom	4
Paralysis	4
Freezing phenomenon	4
Sensory loss	4
Transient ischaemic attack	4
Depression	4
Bradyphrenia	4
Micturition urgency	4
Hyperventilation	4
Productive cough	4
Tonsillar hypertrophy	4
Skin exfoliation	4
Piloerection	4
Bedridden	4
Myocardial infarction	3
Cardiac arrest	3
Ear discomfort	3
Motion sickness	3
Gastritis	3
Abdominal rigidity	3
Gingival bleeding	3
Rectal haemorrhage	3
Lip dry	3
Salivary hypersecretion	3
Aphthous ulcer	3
Hunger	3
Temperature intolerance	3
Vaccination site pruritus	3
Vaccination site rash	3
Serum sickness-like reaction	3
Allergy to vaccine	3
Sepsis	3
Tonsillitis	3
Urinary tract infection	3
Gastroenteritis viral	3
Maternal exposure during breast feeding	3
Blood glucose increased	3

International normalised ratio increased	3
Heart rate decreased	3
Urine output	3
Increased appetite	3
Muscle tightness	3
Flank pain	3
Aphasia	3
Clumsiness	3
Amnesia	3
Muscle contractions involuntary	3
Hemiparesis	3
Febrile convulsion	3
Sensory disturbance	3
Sleep deficit	3
Pregnancy	3
Apathy	3
Listless	3
Autoscopy	3
Head banging	3
Thinking abnormal	3
Dysuria	3
Polyuria	3
Yawning	3
Skin discolouration	3
Rash papular	3
Giant cell arteritis	3
Haematoma	3
Extrasystoles	2
Supraventricular tachycardia	2
Ear swelling	2
Vertigo positional	2
Eye movement disorder	2
Blindness transient	2
Pancreatitis	2
Eructation	2
Faeces soft	2
Defaecation urgency	2
Gingival blister	2
Oral pruritus	2
Salivary gland pain	2
Stomatitis	2

Tongue blistering	2
Temperature regulation disorder	2
Feeling drunk	2
Condition aggravated	2
Crying	2
Injected limb mobility decreased	2
Injection site papule	2
Oedema peripheral	2
Adverse event	2
Vaccination site discomfort	2
Vaccination site induration	2
Vaccination site inflammation	2
Hepatic pain	2
Serum sickness	2
Anaphylactoid reaction	2
Vaccination site cellulitis	2
Suspected COVID-19	2
Conjunctivitis	2
Herpes simplex	2
Urosepsis	2
Rhinitis	2
Chillblains	2
Procedural nausea	2
Thermal burns of eye	2
Magnetic resonance imaging brain	2
Grip strength decreased	2
Analgesic drug level	2
Urine output decreased	2
Hypophagia	2
Joint lock	2
Periarthritis	2
Joint noise	2
Joint warmth	2
Muscle rigidity	2
Coordination abnormal	2
Dyskinesia	2
Vascular headache	2
Cognitive disorder	2
Migraine without aura	2
Myelitis transverse	2
Dizziness exertional	2
Formication	2

Monoparesis	2
Trigeminal neuralgia	2
Abortion spontaneous	2
Morning sickness	2
Delusion	2
Dissociation	2
Emotional disorder	2
Mood altered	2
Factitious disorder	2
Hallucination, visual	2
Panic reaction	2
Suicidal ideation	2
Tachyphrenia	2
Urinary incontinence	2
Acute kidney injury	2
Chromaturia	2
Breast mass	2
Menstruation irregular	2
Menstruation delayed	2
Genital ulceration	2
Uterine spasm	2
Vaginal discharge	2
Stridor	2
Nasal dryness	2
Pharyngeal paraesthesia	2
Pulmonary embolism	2
Aphonia	2
Rhinalgia	2
Skin swelling	2
Yellow skin	2
Drug eruption	2
Petechiae	2
Livedo reticularis	2
Immobile	2
Immunisation	2
Shock	2
Raynaud's phenomenon	2
Bone marrow oedema	1
Leukopenia	1
Lymphadenitis	1
Thrombocytopenia	1
Acute cardiac event	1

Cardiac disorder	1
Cardiac discomfort	1
Pericarditis	1
Tachyarrhythmia	1
Atrial fibrillation	1
Ventricular tachycardia	1
Deafness unilateral	1
Hypoacusis	1
Sudden hearing loss	1
Adrenocortical insufficiency acute	1
Diabetes insipidus	1
Vitreous floaters	1
Eyelid ptosis	1
Erythema of eyelid	1
Eye disorder	1
Eye allergy	1
Abnormal sensation in eye	1
Foreign body sensation in eyes	1
Miosis	1
Pupils unequal	1
Episcleritis	1
Metamorphopsia	1
Visual snow syndrome	1
Visual acuity reduced	1
Anal hypoaesthesia	1
Colitis	1
Colitis ischaemic	1
Hyperaesthesia teeth	1
Epigastric discomfort	1
Faeces discoloured	1
Reflux gastritis	1
Abdominal tenderness	1
Gastric dilatation	1
Gastrointestinal disorder	1
Acute abdomen	1
Oesophageal spasm	1
Gingival oedema	1
Gingival pruritus	1
Gingival swelling	1
Small intestinal haemorrhage	1
Discoloured vomit	1
Haematemesis	1

Haematochezia	1
Cheilitis	1
Lip blister	1
Lip disorder	1
Lip pruritus	1
Palatal swelling	1
Tongue dry	1
Tongue pruritus	1
Puncture site bruise	1
Puncture site pain	1
Puncture site reaction	1
No adverse event	1
Application site bruise	1
Application site erythema	1
Sluggishness	1
Masked fever	1
Feeling jittery	1
Hangover	1
Fibrosis	1
Energy increased	1
Multiple organ dysfunction syndrome	1
Secretion discharge	1
Implant site warmth	1
Infusion site pain	1
Injection site bruising	1
Injection site hypoaesthesia	1
Injection site induration	1
Injection site paraesthesia	1
Drug interaction	1
Mass	1
Mucosal pain	1
Face oedema	1
Localised oedema	1
Oedema	1
Facial discomfort	1
Non-cardiac chest pain	1
Drug ineffective	1
Extensive swelling of vaccinated limb	1
Vaccination site bruising	1
Vaccination site joint movement impairment	1
Vaccination site joint swelling	1

Vaccination site nodule	1
Reaction to excipient	1
Bacille Calmette-Guerin scar reactivation	1
Immune system disorder	1
Sensitisation	1
Gastroenteritis	1
Administration site cellulitis	1
Mastitis	1
Encephalitis	1
Abscess oral	1
Gingival abscess	1
Gingivitis	1
Ear infection	1
Labyrinthitis	1
Eye infection	1
Eyelid infection	1
Fungal infection	1
Abscess	1
Abscess limb	1
Pneumonia	1
Pneumocystis jirovecii pneumonia	1
Skin infection	1
Furuncle	1
Staphylococcal scalded skin syndrome	1
Acute sinusitis	1
Kidney infection	1
Infected lymphocele	1
Viral pharyngitis	1
Viral rash	1
Exposure via breast milk	1
Maternal exposure timing unspecified	1
Exposure to SARS-CoV-2	1
Medication error	1
Nerve injury	1
Cortisol increased	1
Cold agglutinins positive	1
Blood glucose decreased	1
Blood glucose fluctuation	1
Glycosylated haemoglobin increased	1

Gastrointestinal stoma output increased	1
Maximum heart rate decreased	1
Orthostatic heart rate response increased	1
Pulse abnormal	1
Allergy alert test	1
Blood ketone body	1
Respiratory rate decreased	1
Peak expiratory flow rate	1
Cells in urine	1
Blood pressure decreased	1
SARS-CoV-2 test	1
SARS-CoV-2 test positive	1
Food refusal	1
Salt craving	1
Diabetic ketoacidosis	1
Polydipsia	1
Food aversion	1
Starvation	1
Ketosis	1
Polymyalgia rheumatica	1
Myositis	1
Fibromyalgia	1
Myofascial pain syndrome	1
Muscle mass	1
Muscle oedema	1
Muscle swelling	1
Limb mass	1
Growing pains	1
Myopathy	1
Osteoarthritis	1
Rheumatoid arthritis	1
Still's disease	1
Groin pain	1
Neck mass	1
Arthritis reactive	1
Tendonitis	1
Uterine leiomyoma	1
Sleep paralysis	1
Brain stem stroke	1
Haemorrhagic stroke	1

Ischaemic stroke	1
Cervicobrachial syndrome	1
Senile dementia	1
Altered state of consciousness	1
Consciousness fluctuating	1
Depressed level of consciousness	1
Bradykinesia	1
Extrapyramidal disorder	1
Hypokinesia	1
Movement disorder	1
Psychomotor hyperactivity	1
Dystonia	1
Noninfective encephalitis	1
Facial paresis	1
Facial spasm	1
Cold-stimulus headache	1
Drug withdrawal headache	1
Exertional headache	1
External compression headache	1
Thunderclap headache	1
Tongue paralysis	1
Multiple sclerosis	1
Hypotonia	1
Tunnel vision	1
Visual field defect	1
Drooling	1
Myoclonus	1
Muscle spasticity	1
Hyposmia	1
Burning feet syndrome	1
Lhermitte's sign	1
Monoplegia	1
Neuropathy peripheral	1
Seizure like phenomena	1
Tonic convulsion	1
Aura	1
Hypogeusia	1
Slow speech	1
Speech disorder	1
Intention tremor	1
Premature labour	1
Premature rupture of membranes	1

Patient-device incompatibility	1
Oversensing	1
Inappropriate affect	1
Aggression	1
Indifference	1
Social avoidant behaviour	1
Daydreaming	1
Major depression	1
Depersonalisation/derealisation disorder	1
Middle insomnia	1
Eating disorder	1
Euphoric mood	1
Fear of disease	1
Mood swings	1
Hallucination, auditory	1
Hallucinations, mixed	1
Anhedonia	1
Decreased interest	1
Negative thoughts	1
Sense of a foreshortened future	1
Mania	1
Sleep talking	1
Sleep terror	1
Illusion	1
Loss of libido	1
Conversion disorder	1
Somatic symptom disorder	1
Logorrhoea	1
Bruxism	1
Hyperarousal	1
Bladder discomfort	1
Incontinence	1
Urinary hesitation	1
Urinary retention	1
Bladder disorder	1
Urethral spasm	1
Urine odour abnormal	1
Nocturia	1
Breast swelling	1
Breast tenderness	1
Nipple pain	1

Postmenopausal haemorrhage	1
Menstrual disorder	1
Metrorrhagia	1
Hypomenorrhoea	1
Fallopian tube spasm	1
Scrotal pain	1
Scrotal swelling	1
Testicular pain	1
Uterine pain	1
Vaginal lesion	1
Vulvovaginal pain	1
Dyspnoea at rest	1
Orthopnoea	1
Respiratory arrest	1
Sleep apnoea syndrome	1
Bronchospasm	1
Chronic obstructive pulmonary disease	1
Haemoptysis	1
Pneumonitis	1
Pleuritic pain	1
Sinonasal obstruction	1
Pharyngeal erythema	1
Pharyngeal hypoaesthesia	1
Pharyngeal oedema	1
Tonsillar erythema	1
Pleurisy	1
Pulmonary oedema	1
Respiratory symptom	1
Aspiration	1
Lung disorder	1
Respiratory tract irritation	1
Catarrh	1
Nasal discomfort	1
Paranasal sinus discomfort	1
Throat clearing	1
Upper-airway cough syndrome	1
Alopecia	1
Scar pain	1
Skin odour abnormal	1
Eczema	1
Eczema asteatotic	1

Lipohypertrophy	1
Butterfly rash	1
Rosacea	1
Skin mass	1
Skin erosion	1
Skin ulcer	1
Needle track marks	1
Sight disability	1
Retirement	1
Limb immobilisation	1
Muscle relaxant therapy	1
Bed rest	1
Hospitalisation	1
Injection	1
Circulatory collapse	1
Lymphoedema	1
Thrombosis	1
Deep vein thrombosis	1
Ischaemic limb pain	1