Norwegian
Medicines Agency

Reported suspected adverse reactions to coronavirus vaccines

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About the report

- A summary is presented below of all assessed reports concerning suspected adverse reactions following coronavirus vaccination from 27 December 2020, the date on which the first vaccine became available.

- The figures are taken from the Norwegian ADR Registry and include reports from healthcare professionals, the general population and Market Authorisation Holders in Norway.

- Only reports which have undergone quality assurance and been assessed in the Norwegian ADR Registry are included in the report. At any one time, there will be reports which are currently being assessed – these reports are not considered further in this summary.

- Reports of serious events are assessed first. The report therefore does not give a true picture of the distribution between serious and non-serious events.

- Symptoms or illnesses that occur after vaccination are reported if there is any *suspicion* of a possible link. As a result, it cannot be assumed that there is a causal relationship between the suspected adverse reaction and the vaccine.

- This report contains all suspected adverse reactions regardless of any possible causal link.

- Additional information from the reporter or new knowledge concerning the vaccine may become available at any time which alters the assessment of the reports.

- The Norwegian Medicines Agency, the European Medicines Agency (EMA), the World Health Organization (WHO) and pharmaceutical companies review the reports of adverse reactions and perform statistical calculations in order to identify unknown adverse reactions (i.e. signal detection). When a signal is identified, a more thorough analysis is carried out to assess whether it could be a new adverse reaction to the drug, or whether any other factors more likely explain the signal. Based on these analyses, it may be appropriate to update the product information with new adverse reactions or introduce measures aimed at minimising the risks.

- Weekly reports are published which summarise the adverse reactions reported following vaccination with the coronavirus vaccines.

Summary

This report is based on reports that are assessed until 11 May 2021. The assessed adverse reaction reports for this week do not provide a basis for revising the current recommendations regarding the use of the vaccines.

Vaccination with the Vaxzevria (the AstraZeneca COVID-19 vaccine) was suspended with effect from 11 March 2021 following reports of a number of cases of a rare and serious combination of symptoms involving blood clotting, bleeding and low blood platelet counts following vaccination in several European countries, including Denmark and Austria. Reports of similarly serious cases were also submitted in Norway. The cases were investigated thoroughly and the European Medicines Agency (EMA) has now concluded that there is a link between Vaxzevria (the AstraZeneca COVID-19 vaccine) and the rare cases.

An expert group appointed by the Norwegian Government have recommended that the vaccines from AstraZeneca and Janssen-Cilag is not used in the norwegian COVID-19 vaccination programme.

The government will follow the recommendation, and Vaxzevria (COVID-19 Vaccine AstraZeneca) is taken out of the Norwegian vaccination program. The Janssen vaccine will be stockpiled while the Norwegian Government considers how to offer this vaccine on a voluntary basis.

Common to all the vaccine types is that most adverse reaction reports following vaccination against COVID-19 concern transient adverse reactions such as headache, fatigue, malaise, fever, nausea and body pain. These usually appear on the first or second day after vaccination and last around 2-3 days. Most people tolerate these transient adverse reactions well, while others experience significant discomfort during the first few days after vaccination. The suspected adverse reactions which have been observed following vaccination are otherwise generally in line with what is described in the product information.

Amongst the reports that have been assessed, there were reported 160 deaths following vaccination. Six deaths concern persons under the age of 60, but most relate to elderly nursing home residents in need of nursing care. The average age of those concerned is over 84 years. Several of the reporters state that no causal link to vaccination is suspected. The fact that a person dies soon after being vaccinated does not mean that there is a causal relationship. In order to analyse whether there could be a causal relationship, other data sources and advanced analyses are normally required.

In the case of some patients, there is always a possibility that relatively mild adverse reactions following the vaccination of frail elderly people contributed to a deterioration in their underlying illness.

Coronavirus vaccines approved in Norway

Four coronavirus vaccines are approved for use in Norway:

- Comirnaty (BioNTech/Pfizer)

- COVID-19 Vaccine Moderna (Moderna)
- Vaxzevria (COVID-19 Vaccine AstraZeneca)
- COVID-19 Vaccine Janssen (Janssen Cilag International NV)

The Norwegian Government is following the recommendation of the Norwegian Institute of Public Health and the Vorland committee and is removing the AstraZeneca vaccine from the Norwegian vaccination programme. The Janssen vaccine will be stockpiled while the Norwegian Government considers how to offer this vaccine on a voluntary basis.

The mRNA vaccines and Vaxzevria (COVID-19 vaccine AstraZeneca) vaccine are given as two doses a few weeks apart, while the Janssen COVID-19 vaccine is given as a single dose.

Statistics concerning reports of suspected adverse reactions as of 11 May 2021

So far, a total of 12836 reports of suspected adverse reactions following COVID-19 vaccination; of these, 8858 (69 %) have been assessed.

By 11 May 2021, over 1,505,000 people had received their first dose of COVID-19 vaccine, and over 515,000 people had received the second dose.

Distribution of reports by gender

Gender	Female	Male	Unknown
Number	7410	1443	5

Table 1: Gender breakdown amongst patients in the reports

Distribution of reports by age

Age group										
	0-29	**30-39**	**40-49**	**50-59**	**60-69**	**70-79**	**80-89**	**90+**	**Unknown age**	**Total**
Serious reports	132	137	131	120	101	127	174	106	22	1050
Non serious reports	1928	2039	1661	1170	351	162	244	122	131	7808
Total	2060	2176	1792	1290	452	289	418	228	153	8858

Table 2: Age distribution of patients in the reports

The weekly report at FHI.no shows the number and proportion of persons vaccinated in different age groups and gender distribution nationwide.

Distribution of reports according to severity for each vaccine

Vaccine	Number vaccinated with first dose*	Number vaccinated with second dose*	Total number of reports	Number of reports involving death	Serious reports other than death	Reports of non-serious events

Comirnaty (Pfizer/BioNTech)	1 214 932	436 679	2 789	150	440	2 199
COVID-19 Vaccine Moderna (Moderna)	134 354	40933	370	5	77	288
COVID-19 Vaccine AstraZeneca (AstraZeneca)	132 069	9	5 699	5	373	5321
Total	**1 481 355**	**477 621**	**8858**	**160****	**890**	**7808**

Table 3: Distribution of reports of suspected adverse reactions according to severity
*** The fact that a person dies soon after being vaccinated does not necessarily mean there is a causal relationship. Read more on page 3.*

The data concerning the various coronavirus vaccines are not directly comparable. The vaccines have been administered to a different numbers of people with different disease profiles and ages.

*Per 9 May 2021 – *Weekly report from the Norwegian Institute of Public Health*

Reports on deaths

So far, 160 reports of deaths after vaccination have been assessed. Most deaths have occurred amongst elderly nursing home residents in need of nursing care, but the Norwegian Medicines Agency has also received six reports of deaths concerning persons under the age of 60.

Reports of deaths of persons under the age of 60

In a number of countries, there have been reports of a very rare but serious picture of symptoms involving a combination of blood clotting, low platelet count and haemorrhaging, now called Thrombosis with Thrombocytopenia Syndrome (TTS) or Vaccine-induced Immune Thrombotic Thrombocytopenia (VITT). The symptoms have in people 3-14 days following vaccination with the Vaxzevria (COVID-19 Vaccine Astra Zeneca). As of 11 May 2021, seven such cases had been reported in Norway, of which four had fatal outcomes. The Norwegian Medicines Agency and EMA believes that there is a probable link with the vaccine, but more research is needed to clarify exactly what is triggering this. Vaxzevria is now taken out of the Norwegian vaccination programme.

There have also been two fatal reports after vaccination with COVID-19 vaccine which has not been associated with this rare syndrome. The causal relationship in these cases is uncertain.

Reports concerning deaths in elderly persons

Many of the elderly nursing home residents who have been vaccinated are very frail or terminally ill patients. It is therefore to be expected that deaths will occur with a temporal link to vaccination, without there necessarily being any causal link to the vaccine. The reports on many of these deaths in the elderly state that no link with vaccination is suspected, and that the death is being reported for the sake of completeness. The Norwegian Medicines Agency has set up an external group of geriatric specialists to look into these incidents in order to give us a better insight into any causal relationships.

Reports classified as serious

Reports of adverse reactions are generally classified as serious when the event:

1. results in or extended a stay in hospital
2. results in a prolonged reduction in function level
3. results in life-threatening illness or death
4. results in birth defects/congenital malformations
5. is on the EMA's list of important medical events (the IME list)

In addition to the reports concerning deaths, 890 reports have so far been assessed which fulfil one of the other severity criteria listed above.

What types of events are classified as "serious" following COVID-19 vaccination?
Hospital admission is the most common reason why an event is classified as serious, and this applies to 45% of serious reports. In these cases, the descriptions provided by the person submitting the report cover everything from patients who are only kept under observation for a short period of time and go on to recover quickly, to patients with a life-threatening illness which results in permanent injury.

Most of the serious suspected adverse reactions which have been reported concern medical conditions which are relatively common amongst the population and the timing following vaccination may therefore simply be coincidental.

The EMA has compiled a list of important medical events (5) which are always to be classified as serious (the IME list). The summary below lists the conditions on the IME list which are most frequently reported following COVID-19 vaccination.

The most frequently reported conditions on the IME list for all vaccines in descending order

- Fainting (syncope)
- Blood clot in the lungs
- Anaphylactic reaction
- Deep vein thrombosis
- Pneumonia
- Low blood platelet count (thrombocytopenia)
- Blood clots or bleeding in the brain
- Hallucinations
- Cerebral stroke
- Loss of consciousness

The list shows that numerous serious suspected adverse effects have been reported following COVID-19 vaccination. The challenge is to respond if new combinations of symptoms following vaccination become apparent – or if common medical conditions occur

more frequently following vaccination than we would expect. We have a three-pronged approach to identifying these links:

1. **Both health professionals and the government authorities assess individual cases of medical conditions and reports in order to look for unknown combinations of symptoms or to determine whether there are any factors associated with the progression of the conditions which would indicate a link with vaccination.**

   It was a combination of observant doctors at Oslo University Hospital, a robust and fast electronic monitoring system and analyses by the University Hospital of Northern Norway and the Preparedness Register which enabled Norway to help reveal that, in rare cases, Vaxzevria can give rise to a serious combination of symptoms involving blood clotting and low blood platelet counts.

2. **We carry out statistical analyses where we investigate whether the number of reports of a combination of symptoms is higher than expected.**

   Such statistical analyses of reported adverse reactions have shown that serious allergic reactions occur more frequently following COVID-19 vaccination than with vaccination with influenza vaccines. It also forms the basis for the EMA's current investigations aimed at determining whether indications of an increase in the prevalence of immune thrombocytopenia (ITP) are linked to the vaccine.

3. **Health registers are used to assess and investigate further, and to confirm or disprove possible links between vaccination and reported symptoms or diagnoses. This is done in partnership with the Norwegian Institute of Public Health.**

   Further investigation of possible links concerning symptoms reported via the spontaneous reporting system can be carried out by linking the Norwegian Immunisation Register (SYSVAK) to other health registers, such as the Norwegian Patient Registry (NPR) or the Municipal Patient and User Registry (KPR), to see whether any diagnoses occur more frequently following vaccination than is otherwise the case.

   The Norwegian Institute of Public Health and research institutions in many countries are also conducting registry studies to see whether there is any increase in the prevalence of diseases amongst vaccinated people that are not necessarily identified through the adverse reaction reports.

Reactions which health professionals should be aware of

Other serious events have also been observed following vaccination where no causal relationship has been established. The Norwegian Medicines Agency wishes healthcare professionals to be aware of the following conditions in persons who are vaccinated:

- elevated blood sugar levels in people with diabetes
- high INR values in patients taking warfarin (Marevan)
- chest pain and breathing difficulties suspected as being due to blood clots
- numbness
- absence or reduced sensation and paralysis

- exacerbation of autoimmune diseases
- persistent headache
- inflammation of the pericardium (pericarditis)

Some of these symptoms were also observed in studies which formed the basis for the temporary authorisation of the vaccines, but insufficient data is currently available to establish any link to the vaccine. A number of the reactions have been included in the list of possible adverse reactions of particular interest which the pharmaceutical authorities in Europe are closely monitoring.

Reports of severly elevated blood pressure after vaccination with mRNA-vaccine

A total of 17 cases of high blood pressure have been reported as suspected adverse reactions following vaccination with the mRNA COVID-19 vaccines, 16 following vaccination with the Comirnaty vaccine and one following vaccination with the Moderna vaccine. The patients were aged between 28 and 98, two of whom were men. At the time of the reports, the vast majority of patients either had recovered or were recovering.

These reports include two cases of severely elevated blood pressure following vaccination. These concerned two elderly patients who had underlying risk factors for high blood pressure, with one patient being admitted for assessment and monitoring. Both patients stabilised within two days and they are reported to be recovering. These cases have been reported to the European Medicines Agency (EMA).

It has not been ascertained whether these cases of high blood pressure could be linked to the vaccine, but the Norwegian Medicines Agency distributes information about them to ensure that doctors and patients are aware of the possibility of severly elevated blood pressure in persons who have recently been vaccinated.

Patients who experience severely elevated blood pressure may have symptoms such as headaches, difficulty breathing, chest pain, visual disturbances, coughing and general malaise.

High blood pressure in general is not a reason to advise against vaccination, and it is recommended that these patients be vaccinated in order to protect them against COVID-19 disease

Number of suspected adverse reactions according to category

A single adverse reaction report can include a number of suspected adverse reactions or symptoms. Suspected adverse reactions are presented below, grouped according to the category to which they belong for each vaccine type and the types of suspected adverse reactions which have been reported most frequently. The categories are the highest level in a hierarchical, standardised medical terminology which is used internationally (MedDRA). Using this terminology makes it possible compare reports internationally.

Suspected adverse reactions to mRNA vaccines

- Comirnaty (Pfizer/BioNTech)
- COVID-19 Vaccine Moderna (Moderna)

The most frequently reported symptoms following vaccination with the mRNA vaccines primarily consist of known adverse reactions within the general symptoms category, and include reactions at the vaccine injection site, decreased general condition, fever and general malaise. Headache, dizziness and drowsiness after vaccination are also frequently reported, as well as gastrointestinal symptoms such as diarrhoea, nausea and vomiting. The symptoms have arisen within 1-2 days after vaccination and have generally disappeared within a few days. Some reports have been received where the patient has developed infections such as pneumonia and influenza. As the mRNA vaccines are not live, they cannot cause conditions which are being vaccinated against or other infections.

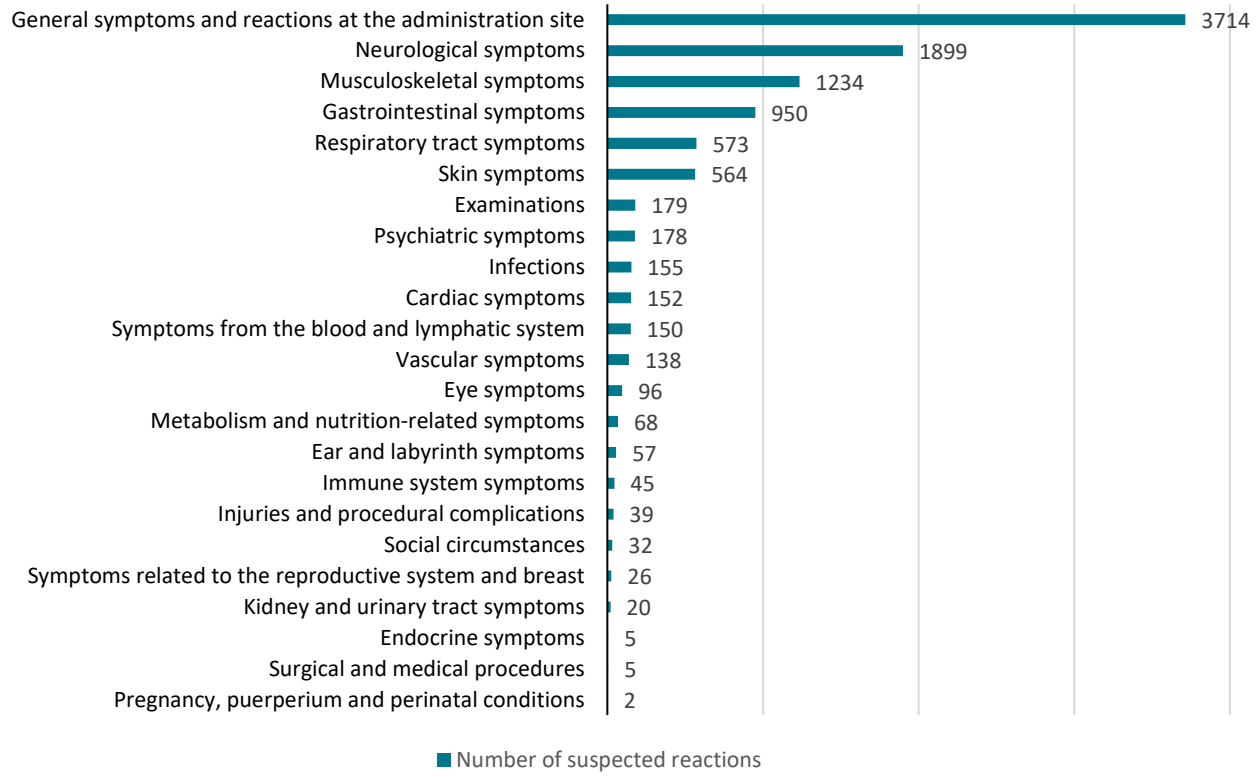

Figure 1: Reported suspected adverse reactions by category for mRNA vaccines (Comirnaty and COVID-19 Vaccine Moderna)

Category	Number of suspected adverse reactions
General symptoms and reactions at the vaccine administration site E.g.: Pain and reactions at the injection site, discomfort, fever, fatigue, decreased general condition	3714
Neurological symptoms E.g.: Headache, dizziness, drowsiness, syncope	1899
Musculoskeletal symptoms E.g.: Muscle pain, joint pain, muscle stiffness, pain in the extremities	1234
Gastrointestinal symptoms E.g.: Stomach pain, nausea, vomiting, diarrhoea	950

Respiratory tract symptoms E.g.: Difficulty breathing, shortness of breath, cough, irritation of the respiratory	573
Skin symptoms E.g.: Rash, itching, redness, cold sweats	564
Examinations E.g.: Abnormal and raised heart rate, decreased blood pressure, decrease in oxygen saturation	179
Psychiatric symptoms E.g.: Sleep abnormalities, restlessness, lethargy, hallucination	178
Infections E.g.: Pneumonia, cold symptoms	155
Cardiac symptoms E.g.: Bradycardia, tachycardia, pericarditis	152
Symptoms from the blood and lymphatic system E.g.: Swollen lymph nodes	150
Vascular symptoms E.g.: Flushes, pallor, low blood pressure	138
Eye symptoms E.g.: Blurred vision, twitch	96
Metabolic and nutrition-related symptoms E.g.: Reduced appetite	68
Ear and labyrinth symptoms E.g.: Discomfort in the ear	57
Immune system symptoms E.g.: Allergic reaction	3645
Injuries and procedural complications E.g.: Fall	39
Social circumstances E.g.: Bedridden	32
Symptoms relating to the reproductive organs and breast E.g.: Breast pain	26
Kidney and urinary tract symptoms E.g.: Urinary tract infection	20
Endocrine symptoms	5
Surgical and medical procedures	5
Pregnancy, puerperium and perinatal conditions	2

Table 4: Reported suspected adverse reactions by category for mRNA vaccines (Comirnaty and COVID-19 Vaccine Moderna). A report can cover several adverse reactions and there will therefore be many more adverse reactions than reports.

Suspected adverse reactions to viral vector vaccines

- Vaxzevria (COVID-19 Vaccine AstraZeneca)(AstraZeneca)

Suspected adverse reactions reported following vaccination with viral vector vaccines reflect the reactions observed during the studies and described in the summary of product characteristics for the AstraZeneca vaccine. Many people experience severe reactions after the first dose, but only minor reactions after the second, and most reports concern known adverse reactions, such as reactions around the injection site, headache, fever, fatigue and deterioration in general condition.

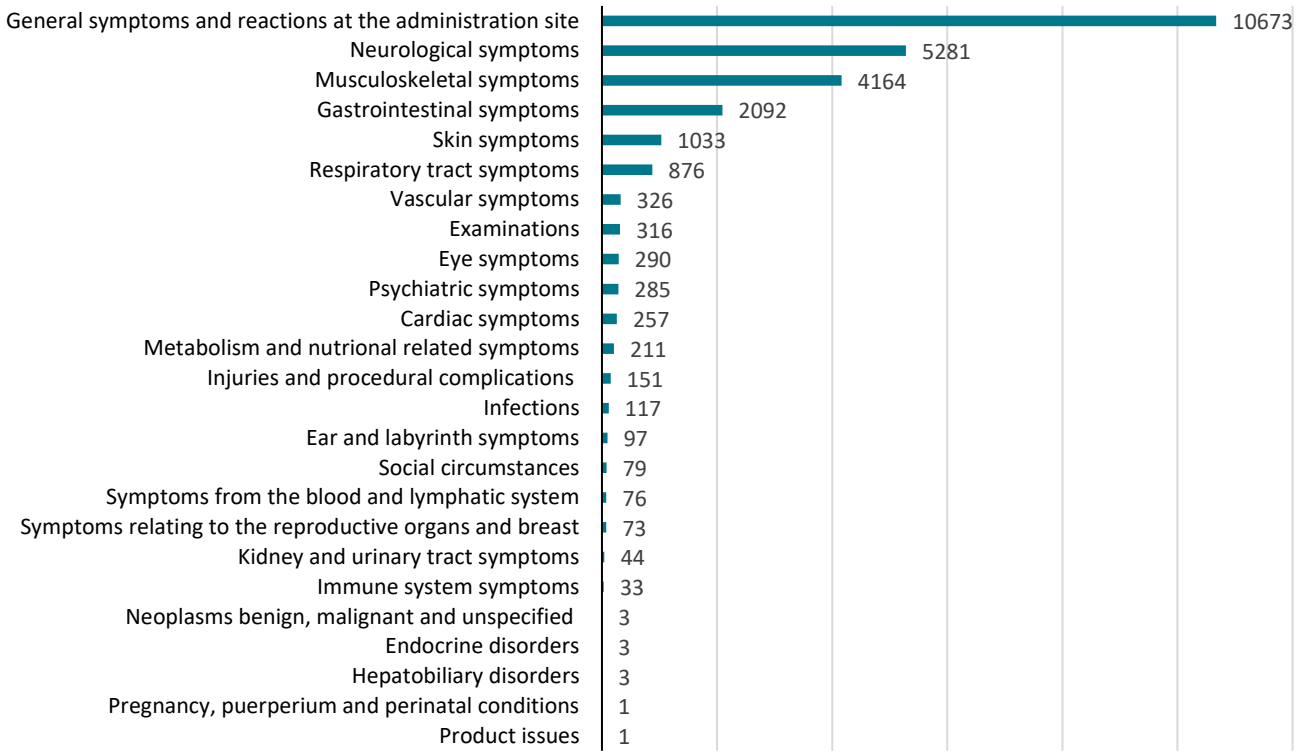

Figure 2: Number of reported suspected adverse reactions by category for viral vector vaccines (COVID-19 Vaccine AstraZeneca)

Category	Number of reported adverse reactions
General symptoms and reactions at the vaccine administration site E.g.: Pain and reactions at the injection site, discomfort, fever, fatigue, decreased general condition	10673
Neurological symptoms E.g.: Headache, dizziness, drowsiness, numbness	5281

Musculoskeletal symptoms E.g.: Muscle pain, joint pain, back pain	4164
Gastrointestinal symptoms E.g.: Stomach pain, nausea, vomiting, diarrhoea	2092
Skin symptoms E.g.: Rash, skin pain, cold sweats	1033
Respiratory tract symptoms E.g.: Difficulty breathing, hyperventilation, nasal congestion, pain and swelling of pharynx	876
Vascular symptoms E.g. Flushing	326
Examinations E.g.: Abnormal and raised heart rate	316
Psychiatric symptoms E.g.: Sleep abnormalities, insomnia	290
Eye symptoms E.g.: Blurred vision, twitch, eye pain	285
Cardiac symptoms E.g.: Palpitations	257
Metabolic and nutrition-related symptoms E.g.: Reduced appetite	211
Injuries and procedural complications E.g. Contusion	151
Infections E.g. Sinus infection, cold symptoms	117
Ear and labyrinth symptoms E.g.: Discomfort in the ear, sound sensitivity	97
Symptoms from the blood and lymphatic system E.g.: Swollen lymph nodes	79
Social circumstances E.g.: Bedridden	76
Symptoms relating to the reproductive organs and breast: E.g. Pain in reproductive organs and nipples	73
Kidney and urinary tract symptoms E.g.: Frequent urination	44
Immune system symptoms E.g.: anaphylactic reaction, allergic reaction	33
Hepatobiliary disorders	3
Neoplasms, benign, malignant and unspecified	3
Endocrine disorders	3
Pregnancy, puerperium and perinatal conditions	1
Product issues	1

Table 4: Reported suspected adverse reactions by category for viral vector vaccines (COVID-19 Vaccine AstraZeneca). A report can cover several adverse reactions and there will therefore be many more adverse reactions than reports.