Norwegian
Medicines Agency

Reported suspected adverse reactions to coronavirus vaccines

Table of contents

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 6 April 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 (COVID-19 vaccine AstraZeneca) was suspended with effect from 11 March following reports of a number of cases of a rare and serious picture of symptoms involving blood clotting, bleeding and low platelet counts following vaccination both in Norway and a number of other European countries. These cases are currently being investigated thoroughly.

Most reports 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 139 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 85 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 in use 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)

Vaccination with the Vaxzevria (COVID-19 vaccine AstraZeneca) has currently been suspended.

Comirnaty and COVID-19 Vaccine Moderna are mRNA vaccines, while Vaxzevria (COVID-19 Vaccine AstraZeneca) and COVID-19 Vaccine Janssen is virus vector vaccines. No doses of the Janssen COVID-19 vaccine have been given in Norway.

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 6 April 2021

So far, a total of 10,483 reports of suspected adverse reactions following COVID-19 vaccination; of these, 5635 have been assessed.

By 6 April 2021, over 722,000 people had received their first dose of COVID-19 vaccine, and over 287,000 people had received the second dose.

Distribution of reports by gender

Gender	Female	Male	Unknown
Number	4684	950	1

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	84	86	78	60	41	52	132	99	16	648
Non serious reports	1252	1345	1024	719	178	85	199	108	77	4987
Total	1336	1431	1102	779	219	137	331	207	93	5635

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)	521 014	270 330	2045	130	240	1675
COVID-19 Vaccine Moderna (Moderna)	66 058	16 931	132	3	18	111
COVID-19 Vaccine AstraZeneca (AstraZeneca)	134 623	0	3458	6	251	3201
Total	**722 648**	**287 412**	**5635**	**139**	**509**	**4987**

Table 3: Distribution of reports of suspected adverse reactions according to severity

**Per 6 April 2021 – sSYSVAK*

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.

Reports on deaths

So far, 139 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 which has occurred in people 3-14 days following vaccination with the Vaxzevria (COVID-19 Vaccine Astra Zeneca). As of 6 April, three such deaths had been reported in Norway. The Norwegian Medicines Agency believes that there is a probable link with the vaccine, but we need more research to clarify exactly what is triggering this.

There have also been reports of two deaths following a brain haemorrhage without blood clotting and one death linked to the deterioration of a previous medical condition following vaccination with the AstraZeneca COVID-19 vaccine with uncertain causality.

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.

Serious reports

Reported events following vaccination are classified as serious when:

- the event resulted in or extended a stay in hospital
- the event is considered to be a medically important event
- the event resulted in a prolonged reduction in function level
- the event resulted in a life-threatening illness (e.g. anaphylaxis) or death.
- the event resulted in birth defects/congenital malformations

So far, 509 reports have been assessed which meet one of the severity criteria listed above, but have not ended in death. The most frequent adverse reactions reported in serious reports are largely the same as those seen in non-serious reports, including fever, decreased general condition, shortness of breath, muscle pain, vomiting, diarrhoea and fatigue.

The most common reason why the reports have been classified as serious is because the event resulted in hospital admission. This applies to approx. 42% of all serious reports

(including deaths). Any event that leads to hospital admission is routinely classified as serious, even when the patient is only kept under observation and recover rapidly.

In addition, there are many events which are always classified as serious because they are on the EMA's Important Medical Events (IME) list, such as anaphylactic reactions, syncope (fainting) or hallucinations.

Other serious cases have also been observed following vaccination where no causal relationship has been established. Among other things, elevated blood sugar levels, high INR values in patients taking warfarin (Marevan), chest pain and difficulty breathing may be caused by blood clots, numbness, absence or reduction of sensation and paralysis. The Norwegian Medicines Agency wishes healthcare professionals to be aware of possible reactions after vaccination which could be associated with these conditions.

Some of these reactions were also seen in the studies that formed the basis for the conditional authorisations of the vaccines, but insufficient data is currently available to establish any link to the vaccine. However, a number of these reactions are included in the list of possible adverse reactions of particular interest which the pharmaceutical authorities in Europe are closely monitoring.

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.

Reactions to mRNA vaccines

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

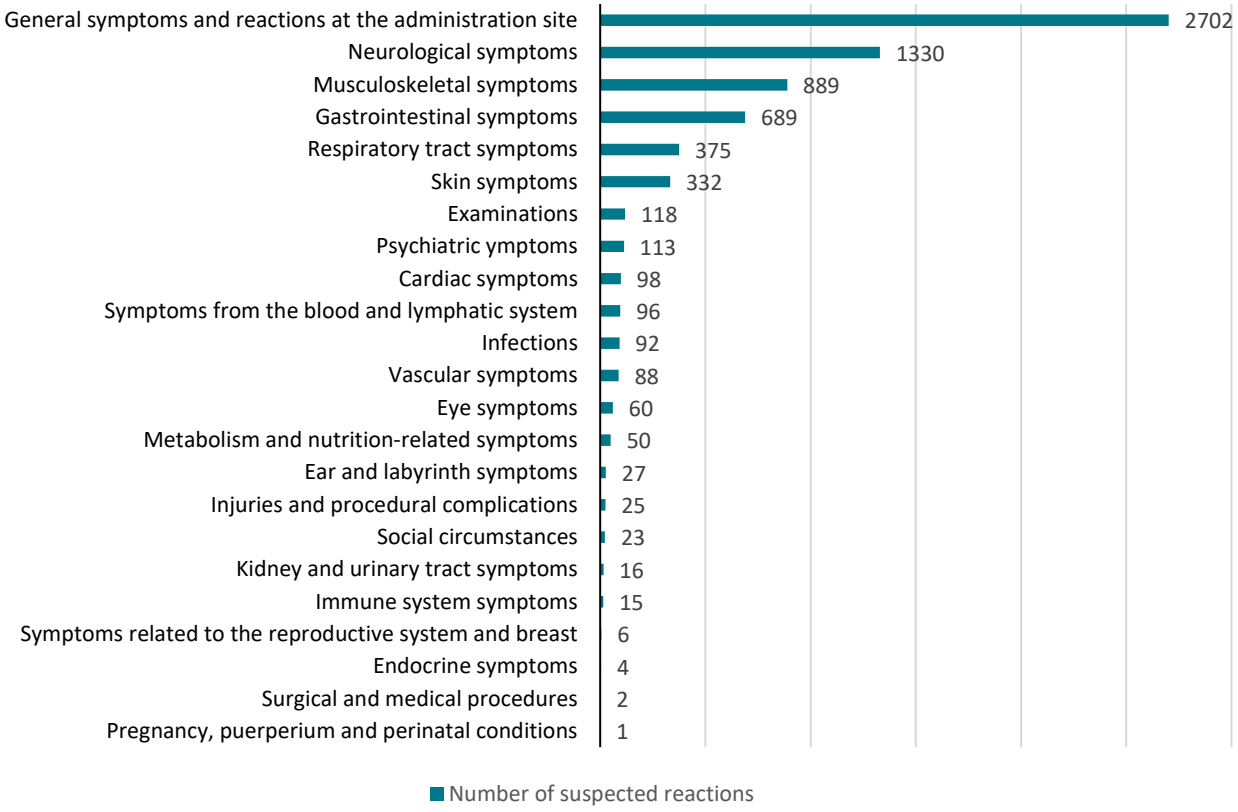

Figure 1: Reported suspected adverse reactions by category for mRNA vaccines (Comirnaty and COVID-19 Vaccine Moderna)

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	2702
Neurological symptoms E.g.: Headache, dizziness, drowsiness, syncope	1330

Musculoskeletal symptoms E.g.: Muscle pain, joint pain, muscle stiffness, pain in the extremities	889
Gastrointestinal symptoms E.g.: Stomach pain, nausea, vomiting, diarrhoea	689
Respiratory tract symptoms E.g.: Difficulty breathing, shortness of breath, cough, irritation of the respiratory	375
Skin symptoms E.g.: Rash, itching, redness, cold sweats	332
Examinations E.g.: Abnormal and raised heart rate, decreased blood pressure, decrease in oxygen saturation	118
Psychiatric symptoms E.g.: Sleep abnormalities, restlessness, lethargy, hallucination	113
Cardiac symptoms E.g.: Bradycardia, tachycardia	98
Symptoms from the blood and lymphatic system E.g.: Swollen lymph nodes	96
Infections E.g.: Pneumonia, cold symptoms	92
Vascular symptoms E.g.: Flushes, pallor, low blood pressure	88
Eye symptoms E.g.: Blurred vision, twitch	60
Metabolic and nutrition-related symptoms E.g.: Reduced appetite	50
Ear and labyrinth symptoms E.g.: Discomfort in the ear	27
Injuries and procedural complications E.g.: Fall	25
Social circumstances E.g.: Bedridden	23
Kidney and urinary tract symptoms E.g.: Urinary tract infection	16
Immune system symptoms E.g.: Allergic reaction	15
Symptoms relating to the reproductive organs and breast E.g.: Breast pain	6
Endocrine symptoms	4
Surgical and medical procedures	2
Pregnancy, puerperium and perinatal conditions	1

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.

The most frequently reported symptoms 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.

Reactions to viral vector vaccines

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

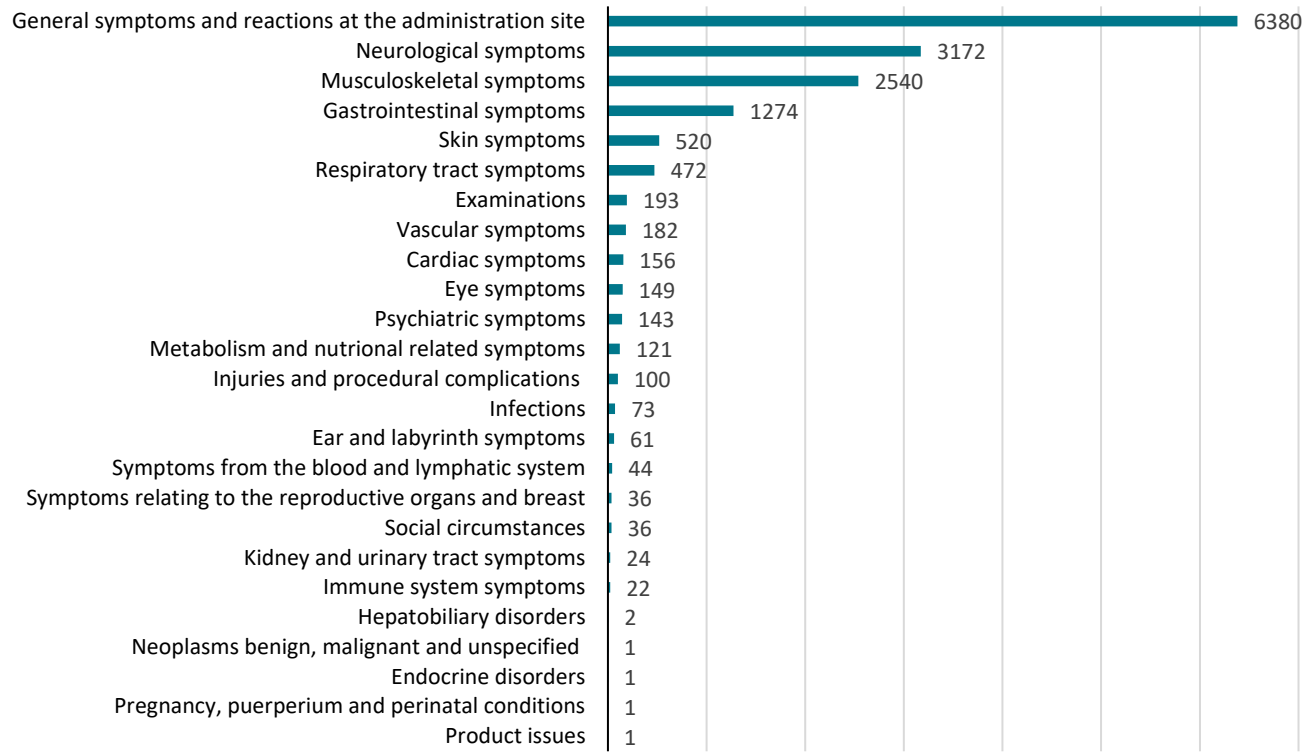

Figure 2: Number of reported suspected adverse reactions by category for viral vector vaccines (COVID-19 Vaccine AstraZeneca)

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	6380
Neurological symptoms E.g.: Headache, dizziness, drowsiness, numbness	3172
Musculoskeletal symptoms E.g.: Muscle pain, joint pain, back pain	2540
Gastrointestinal symptoms E.g.: Stomach pain, nausea, vomiting, diarrhoea	1274

Skin symptoms E.g.: Rash, skin pain, cold sweats	520
Respiratory tract symptoms E.g.: Difficulty breathing, hyperventilation, nasal congestion, pain and swelling of pharynx	472
Examinations E.g.: Abnormal and raised heart rate	193
Vascular symptoms E.g. Flushing	182
Cardiac symptoms E.g.: Palpitations	156
Eye symptoms E.g.: Blurred vision, twitch, eye pain	149
Psychiatric symptoms E.g.: Sleep abnormalities, insomnia	143
Metabolic and nutrition-related symptoms E.g.: Reduced appetite	121
Injuries and procedural complications E.g. Contusion	100
Infections E.g. Sinus infection, cold symptoms	73
Ear and labyrinth symptoms E.g.: Discomfort in the ear, sound sensitivity	61
Symptoms from the blood and lymphatic system E.g.: Swollen lymph nodes	44
Symptoms relating to the reproductive organs and breast: E.g. Pain in reproductive organs and nipples	36
Social circumstances E.g.: Bedridden	36
Kidney and urinary tract symptoms E.g.: Frequent urination	24
Immune system symptoms E.g.: anaphylactic reaction, allergic reaction	22
Hepatobiliary disorders	2
Neoplasms, benign, malignant and unspecified	1
Endocrine disorders	1
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.

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.