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

The ADR (adverse drug reaction) reports do not provide a basis for revising the current recommendations regarding the use of the mRNA- vaccines.

Vaccination with the AstraZeneca COVID-19 vaccine has been suspended with effect from 11 March following reports of a number of cases in other European countries of a rare and serious picture of symptoms involving blood clotting, bleeding and low platelet counts following vaccination, which are now being investigated thoroughly. The Norwegian Medicines Agency has also received reports of cases concerning serious incidents following vaccination with the AstraZeneca vaccine which are now 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.

Amongst the reports that have been assessed, there were reported 119 deaths with a temporal link to vaccination. Most reports concern elderly nursing home residents in need of nursing care. The average age of those concerned is over 86 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)
- COVID-19 Vaccine AstraZeneca (AstraZeneca)
- COVID-19 Vaccine Janssen (Janssen Cilag International NV)

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

Comirnaty and COVID-19 Vaccine Moderna are mRNA vaccines, while 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 AstraZeneca COVID-19 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 16 March 2021

So far, a total of 7,702 reports of suspected adverse reactions following COVID-19 vaccination; of these, 3,923 have been assessed.

By 16 March 2021, over 451,000 people had received their first dose of COVID-19 vaccine, and over 257,000 people had received the second dose.

Distribution of reports by gender

Gender	Female	Male
Number	3216	706

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**
934	996	754	477	138	104	272	190	57

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	Date adopted	Total number of reports	Number of reports involving death	Serious reports other than death	Reports of non-serious events
Comirnaty (Pfizer/BioNTech)	27.12.2020	1755	116	164	1475
COVID-19 Vaccine Moderna (Moderna)	15.01.2021	93	1	8	84
COVID-19 Vaccine AstraZeneca (AstraZeneca)	08.02.2021	2075	2	70	2003

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

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, 119 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 two reports of deaths in younger people this week, which are referred to below.

Many people in this patient group who have so far been vaccinated are very frail or terminally ill patients. At this time of year, an average of around 50 people die every day in the age group 85 years or older, and around 35 people every day in the age group 75-85. It is therefore to be expected that deaths will in time relation after vaccination, without there necessarily being any causal link to the vaccine. The reported deaths have occurred within a period of up to 3 weeks following vaccination.

The reporters of several of these fatal cases state that no link with vaccination is suspected, and that the death is being reported for the sake of completeness. Many of the patients were also very frail prior to vaccination, and had many concomitant medical conditions and were taking many different medicines. Amongst this patient group, a number of factors often contribute to death, and the actual cause of death can be difficult to establish. It can be difficult to know whether the death was caused by the patient's underlying condition or another incidental, concomitant event. In the case of some of the frailest patients, there is always a possibility that relatively mild adverse reactions to the vaccine could have contributed to a serious course of their underlying illness.

These reports do not currently constitute a signal of an adverse reaction and do not provide a basis for revising the product information for the vaccines.

The Norwegian Medicines Agency has set up an external group of geriatricians 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, 242 reports have been assessed which meet one of the severity criteria listed above, but have not ended in death. The majority of these reports concern people over the age of 60 who were admitted to hospital. Any event that leads to hospital admission is routinely classified as serious, even when the patient is only kept under observation and subsequently makes a full recovery. In addition, there are a number of events that are always classified as serious, such as anaphylactic reactions, syncope (fainting) and hallucinations.

The most common adverse reactions in this group are fever, decreased general condition, shortness of breath, muscle pain, vomiting, diarrhoea and fatigue. These are largely the same symptoms which we see for the non-serious reports, but which have resulted in the patient being admitted for observation with a suspected more serious condition.

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 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)

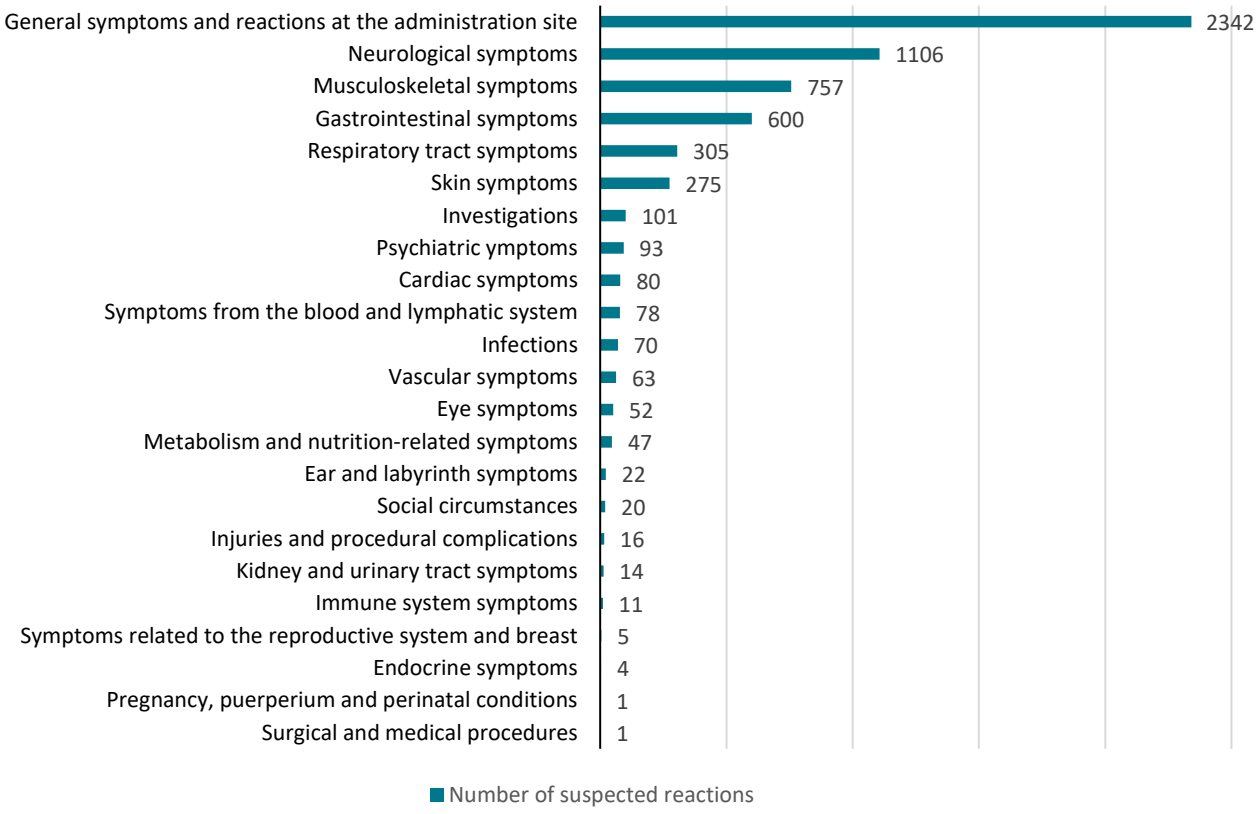

Figure 1: Reported suspected adverse reactions by category for mRNA vaccines (Comirnaty and COVID-19 Vaccine Moderna)

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	2342
Neurological symptoms E.g.: Headache, dizziness, drowsiness, syncope	1106
Musculoskeletal symptoms E.g.: Muscle pain, joint pain, muscle stiffness, pain in the extremities	757
Gastrointestinal symptoms E.g.: Stomach pain, nausea, vomiting, diarrhoea	600
Respiratory tract symptoms E.g.: Difficulty breathing, shortness of breath, cough, irritation of the respiratory	305
Skin symptoms E.g.: Rash, itching, redness, cold sweats	275
Examinations E.g.: Abnormal and raised heart rate, decreased blood pressure, decrease in oxygen saturation	101
Psychiatric symptoms E.g.: Sleep abnormalities, restlessness, lethargy, hallucination	93
Cardiac symptoms E.g.: Bradycardia, tachycardia	80
Symptoms from the blood and lymphatic system E.g.: Swollen lymph nodes	78
Vascular symptoms E.g.: Flushes, pallor, low blood pressure	70
Infections E.g.: Pneumonia, cold symptoms	63
Metabolic and nutrition-related symptoms E.g.: Reduced appetite	52
Eye symptoms E.g.: Blurred vision, twitch	47
Ear and labyrinth symptoms E.g.: Discomfort in the ear	22
Social circumstances E.g.: Bedridden	20
Kidney and urinary tract symptoms E.g.: Urinary tract infection	16
Injuries and procedural complications E.g.: Fall	14
Immune system symptoms E.g.: Allergic reaction	11
Symptoms relating to the reproductive organs and breast E.g.: Breast pain	5
Endocrine symptoms	4
Pregnancy, puerperium and perinatal conditions	1
Surgical and medical procedures	1

Table 4: Reported suspected adverse reactions by category for mRNA vaccines (Comirnaty and COVID-19 Vaccine Moderna)

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

- COVID-19 Vaccine AstraZeneca (AstraZeneca)

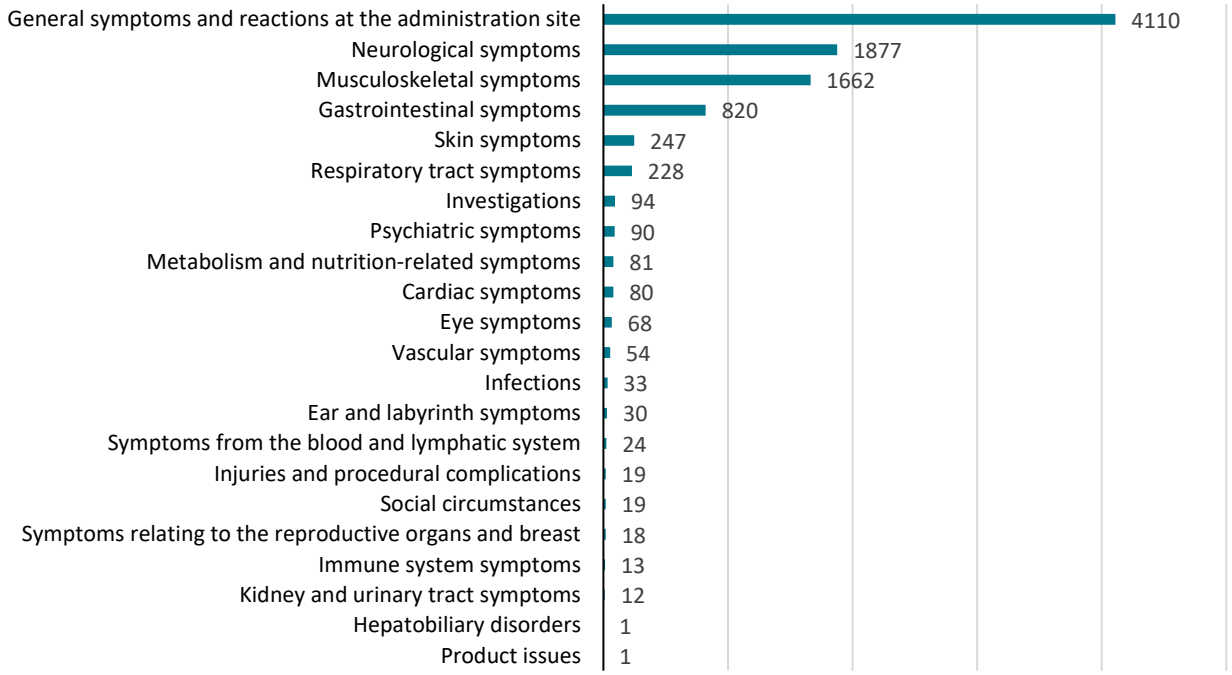

Figure 2: Number of reported suspected adverse reactions by category for viral vector vaccines (COVID-19 Vaccine AstraZeneca)

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	4110
Neurological symptoms E.g.: Headache, dizziness, drowsiness, numbness	1877

Musculoskeletal symptoms E.g.: Muscle pain, joint pain, back pain	1662
Gastrointestinal symptoms E.g.: Stomach pain, nausea, vomiting, diarrhoea	820
Skin symptoms E.g.: Rash, skin pain, cold sweats	247
Respiratory tract symptoms E.g.: Difficulty breathing, hyperventilation, nasal congestion, pain and swelling of pharynx	228
Examinations E.g.: Abnormal and raised heart rate	94
Psychiatric symptoms E.g.: Sleep abnormalities, insomnia	90
Metabolic and nutrition-related symptoms E.g.: Reduced appetite	81
Cardiac symptoms E.g.: Palpitations	80
Eye symptoms E.g.: Blurred vision, twitch	68
Vascular symptoms E.g. Flushing	54
Infections E.g. Sinus infection, cold symptoms	33
Ear and labyrinth symptoms E.g.: Discomfort in the ear	30
Symptoms from the blood and lymphatic system E.g.: Swollen lymph nodes	24
Injuries and procedural complications E.g. Contusion	19
Social circumstances E.g.: Bedridden	19
Symptoms relating to the reproductive organs and breast: E.g. Pain in reproductive organs and nipples	18
Immune system symptoms E.g.: anaphylactic reaction, allergic reaction	13
Kidney and urinary tract symptoms E.g.: Frequent urination	12
Hepatobiliary disorders	1
Product issues	1

Table 4: Reported suspected adverse reactions by category for viral vector vaccines (COVID-19 Vaccine 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.

Reports that the Norwegian Medicines Agency has specifically looked at in this week's report

Report of blood clotting and brain haemorrhage following vaccination with the AstraZeneca COVID-19 vaccine

Several countries have reported an unusual clinical picture involving a combination of blood clotting, low platelet count and haemorrhaging which has occurred in people 3-14 days following vaccination with the AstraZeneca COVID-19 vaccine. As of 16 March, three such cases had been reported in Norway, one of which concerns a death, the other two are being treated in hospital.

One death following a brain haemorrhage has also been reported.

Typical cases have involved blood clotting in a vein which transports blood from the brain (venous sinus thrombosis), a low platelet count and bleeding in the brain. In other cases, blood clotting has been observed in other small or large veins.

The Norwegian Medicines Agency cannot rule out the possibility that this clinical picture is linked to the vaccination.