



Medicines & Healthcare products  
Regulatory Agency



## **Coronavirus Vaccines - summary of Yellow Card reporting**

Data included: 9/12/2020 to 24/11/2021

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# Summary

At the time of this report, over 144,432 people across the UK have died within 28 days of a positive test for coronavirus (COVID-19). Vaccination is the single most effective way to reduce deaths and severe illness from COVID-19. A national immunisation campaign has been underway since early December 2020.

Three COVID-19 vaccines - the COVID-19 Pfizer/BioNTech Vaccine, COVID-19 Vaccine AstraZeneca and COVID-19 Vaccine Moderna – are currently being used in the UK. All have been authorised for supply by the Medicines and Healthcare products Regulatory Agency (MHRA) following a thorough review of safety, quality and efficacy information from clinical trials. In [clinical trials](#), the vaccines showed very high levels of protection against symptomatic infections with COVID-19. [Data](#) are available on the impact of the vaccination campaign in reducing infections and illness in the UK.

The MHRA confirmed on 9 September 2021 that the COVID-19 vaccines made by Pfizer and AstraZeneca can be used as safe and effective booster doses. Following review of data for the COVID-19 Vaccine Moderna vaccine, the MHRA and CHM experts also concluded that this vaccine can be used as a safe and effective booster dose. All vaccines and medicines have some side effects. These side effects need to be continuously balanced against the expected benefits in preventing illness.

The COVID-19 Pfizer/BioNTech Vaccine was evaluated in clinical trials involving more than 44,000 participants. The most [frequent adverse reactions](#) in these trials were pain at the injection site, fatigue, headache, myalgia (muscle pains), chills, arthralgia (joint pains), and fever; these were each reported in more than 1 in 10 people. These reactions were usually mild or moderate in intensity and resolved within a few days after vaccination. Adverse reactions were reported less frequently in older adults (over 55 years) than in younger people.

The COVID-19 Vaccine AstraZeneca was evaluated in clinical trials involving more than 23,000 participants. The most [frequently reported adverse reactions](#) in these trials were injection-site tenderness, injection-site pain, headache, fatigue, myalgia, malaise, pyrexia (fever), chills, and arthralgia, and nausea; these were each reported in more than 1 in 10 people. The majority of adverse reactions were mild to moderate in severity and usually resolved within a few days after vaccination. Adverse reactions were generally milder and reported less frequently in older adults (65 years and older) than in younger people.

The COVID-19 Vaccine Moderna was evaluated in clinical trials involving more than 30,000 participants. The most [frequent adverse reactions](#) in these trials were pain at the injection site, fatigue, headache, myalgia (muscle pains), arthralgia (joint pains), chills, nausea/vomiting, axillary swelling/tenderness (swelling/tenderness of glands in the armpit), fever, injection site swelling and redness; these were each reported in more than 1 in 10 people. These reactions were usually mild or moderate in intensity and resolved within a few days after vaccination. Adverse reactions were reported less frequently in older adults (over 65 years) than in younger people.

The MHRA continually monitors safety during widespread use of a vaccine. We have in place a [proactive strategy to do this](#). We also work closely with our public health partners in reviewing the effectiveness and impact of the vaccines to ensure the benefits continue to outweigh any possible side effects.

Part of our monitoring role includes reviewing reports of suspected side effects. Any member of the public or health professional can submit suspected side effects through the [Yellow Card scheme](#).

The nature of Yellow Card reporting means that reported events are not always proven side effects. Some events may have happened anyway, regardless of vaccination. This is particularly the case when millions of people are vaccinated, and especially when vaccines are being given to the most elderly people and people who have underlying illness.

This safety update report is based on detailed analysis of data up to 24 November 2021. As of 24 November 2021, an estimated 24.5 million first doses of the COVID-19 Pfizer/BioNTech Vaccine and 24.9 million first doses of the COVID-19 Vaccine AstraZeneca had been administered, and around 20.8 million and 24.1 million second doses of the COVID-19 Pfizer/BioNTech Vaccine and COVID-19 Vaccine AstraZeneca respectively. An approximate 1.5 million first doses and approximately 1.3 million second doses of the COVID-19 Vaccine Moderna have also now been administered.

As of 24 November 2021, for the UK, 136,582 Yellow Cards have been reported for the COVID-19 Pfizer/BioNTech Vaccine, 238,086 have been reported for the COVID-19 Vaccine AstraZeneca, 19,101 for the COVID-19 Vaccine Moderna and 1,280 have been reported where the brand of the vaccine was not specified.

For the COVID-19 Pfizer/BioNTech Vaccine, COVID-19 Vaccine AstraZeneca and COVID-19 Vaccine Moderna the overall reporting rate is around 3 to 7 Yellow Cards per 1,000 doses administered.

In the week since the previous summary for 17 November 2021 we have received a further 2,631 Yellow Cards for the COVID-19 Pfizer/BioNTech Vaccine, 599 for the COVID-19 Vaccine AstraZeneca, 985 for the COVID-19 Vaccine Moderna and 26 where the brand was not specified.

It is important to note that Yellow Card data cannot be used to derive side-effect rates or compare the safety profile of COVID-19 vaccines as many factors can influence ADR reporting.

For all COVID-19 vaccines, the overwhelming majority of reports relate to injection-site reactions (sore arm for example) and generalised symptoms such as 'flu-like' illness, headache, chills, fatigue (tiredness), nausea (feeling sick), fever, dizziness, weakness, aching muscles, and rapid heartbeat. Generally, these happen shortly after the vaccination and are not associated with more serious or lasting illness.

These types of reactions reflect the normal immune response triggered by the body to the vaccines. They are typically seen with most types of vaccine and tend to resolve within a day or two. The nature of reported suspected side effects is broadly similar across age groups, although, as was seen in clinical trials and as is usually seen with other vaccines, they may be reported more frequently in younger adults.

A number of detailed assessments of safety topics have been undertaken and we have updated our advice on these topics accordingly. Overall, our advice remains that the benefits of the vaccines outweigh the risks in the majority of people. Further comments on use in specific populations and details on the specific safety topics can be found within Section 3.

## **Conclusion**

Vaccines are the best way to protect people from COVID-19 and have already saved tens of thousands of lives. Everyone should continue to get their vaccination when invited to do so unless specifically advised otherwise.

- As with all vaccines and medicines, the safety of COVID-19 vaccines is being continuously monitored.

- The expected benefits of the vaccines in preventing COVID-19 and serious complications associated with COVID-19 far outweigh any currently known side effects in the majority of patients.

Further information on the type of suspected adverse reactions (ADRs) reported for the COVID-19 Pfizer/BioNTech Vaccine, the COVID-19 Vaccine AstraZeneca and the COVID-19 Vaccine Moderna is provided in Annex 1. It is important to read the attached guidance notes to ensure appropriate interpretation of the data.

# 1. Introduction

The Medicines and Healthcare products Regulatory Agency (MHRA) is the executive Agency of the Department of Health and Social Care that acts to protect and promote public health and patient safety, by ensuring that medicines and medical devices meet appropriate standards of safety, quality and efficacy.

The MHRA operates the [Yellow Card scheme](#) on behalf of the Commission on Human Medicines (CHM). The scheme collects and monitors information on suspected safety concerns or incidents involving vaccines, medicines, medical devices, and e-cigarettes. The scheme relies on voluntary reporting of suspected adverse incidents by healthcare professionals and members of the public (patients, users, or carers). The purpose of the scheme is to provide an early warning that the safety of a product may require further investigation. Further information about the Yellow Card scheme, including its contribution to identifying safety issues can be found on the [Yellow Card website](#).

The MHRA is playing an active role in responding to the coronavirus pandemic. In relation to COVID-19 vaccines, the MHRA has authorised their supply following a rigorous review of their safety, quality and efficacy. The clinical trials of COVID-19 vaccines have shown them to be effective and acceptably safe; however, as part of its statutory functions, the MHRA is responsible for monitoring these vaccines on an ongoing basis to ensure their benefits continue to outweigh any risks. This is a requirement for all authorised medicines and vaccines in the UK. This monitoring strategy is continuous, proactive and based on a wide range of information sources, with a dedicated team of scientists reviewing information daily to look for safety issues or unexpected rare events.

This report summarises information received via the Yellow Card scheme and will be published regularly to include other safety investigations carried out by the MHRA under the [COVID-19 Vaccine Surveillance Strategy](#).

## What is a Yellow Card?

The Yellow Card scheme is a mechanism by which anybody can voluntarily report any suspected adverse reactions or side effects to the vaccine. It is very important to note that a Yellow Card report does not necessarily mean the vaccine caused that reaction or event. We ask for any suspicions to be reported, even if the reporter isn't sure if it was caused by the vaccine. Reports to the scheme are known as suspected adverse drug reactions (ADRs).

Many suspected ADRs reported on a Yellow Card do not have any relation to the vaccine or medicine and it is often coincidental that symptoms occurred around the same time as vaccination. The reports are continually reviewed to detect possible new side effects that may require regulatory action, and to differentiate these from things that would have happened regardless of the vaccine or medicine being administered, for instance due to underlying or undiagnosed illness.

It is therefore important that the suspected ADRs described in this report are not interpreted as being proven side effects of COVID-19 vaccines. A list of the possible side effects of [COVID-19 Pfizer/BioNTech Vaccine](#), [COVID-19 Vaccine AstraZeneca](#) and [COVID-19 Vaccine Moderna](#) are provided in the product information document for healthcare professionals and the UK recipient information. These can also be found on the [Coronavirus Yellow Card](#) reporting site.

This public summary provides an overview of all UK suspected ADRs associated with the new COVID-19 vaccines (the COVID-19 Pfizer/BioNTech Vaccine, COVID-19 Vaccine AstraZeneca

and COVID-19 Vaccine Moderna), and the MHRA's analysis of the data, **between 9 December 2020 and 24 November 2021 (inclusive)**. A glossary of key terms is provided in Annex 2.

If identified, information on new and emerging safety concerns will be provided in future editions of this report together with details of any resulting regulatory action or changes to advice on use of the vaccines.



## 2. Yellow Card reports

### Vaccine doses administered

Data from the UK [Public Health agencies](#) show that at least 50,852,133 people have received their first vaccination in the UK by 24 November 2021, with 46,232,258 second doses administered. The priority groups of the immunisation campaign for this period included people aged 12 years and over, the clinically vulnerable, care home residents and workers, and frontline health and social care workers. Individuals are also being invited for their booster vaccination if it has been 152 days (5 months) since their second dose and they are either aged 40 and over or are aged 16 and over with a health condition that puts them at high risk from COVID-19.

**Table 1: Number of people who have received the first dose of a vaccination for COVID-19 in the UK between 8 December 2020 and end of 24 November 2021.**

Country	Number of doses
England	42,638,518
Wales	2,465,562
Northern Ireland	1,360,946
Scotland	4,342,107

**Table 2: Number of people who have received the second dose of a vaccination for COVID-19 in the UK between 8 December 2020 and end of 24 November 2021.**

Country	Number of doses
England	38,764,212
Wales	2,260,038
Northern Ireland	1,265,081
Scotland	3,942,927

As of 24 November 2021, an estimated 24.5 million first doses of the COVID-19 Pfizer/BioNTech Vaccine and 24.9 million first doses of the COVID-19 Vaccine AstraZeneca had been administered, and around 20.8 million and 24.1 million second doses of the COVID-19 Pfizer/BioNTech Vaccine and COVID-19 Vaccine AstraZeneca respectively. An approximate 1.5 million first doses and approximately 1.3 million second doses of the COVID-19 Vaccine Moderna have also now been administered. These figures are based on numbers of exposures reported individually by the individual nations which are extrapolated to produce an estimate of the total number of doses. Data are not always reported weekly and can be updated for historical dates when vaccinations are recorded on the relevant system. Therefore, data for this may be incomplete and the resulting estimates are approximate.

The estimated number of doses administered differs from the estimated number of people vaccinated due to the different data sources used.

As of 24 November 2021, an estimated 16,383,575 people had received their booster or third vaccination in the UK. The priority groups being offered a booster dose of coronavirus (COVID-19) vaccine for this part of the vaccination campaign include people aged 40 years and over, health

and social care workers and the clinically vulnerable. On 29 November 2021 the JCVI announced those aged 18 to 39 will also be eligible for a booster when the NHS calls them forward.

**Table 3: Number of people who have received the third or booster dose of a vaccination for COVID-19 in the UK between 8 December 2020 and end of 24 November 2021.**

Country	Number of doses
England	13,697,204
Wales	806,297
Northern Ireland	344,451
Scotland	1,535,623

## Yellow Card reporting trends

A report of a suspected ADR to the Yellow Card scheme does not necessarily mean that it was caused by the vaccine, only that the reporter has a suspicion it may have been. Underlying or previously undiagnosed illness unrelated to vaccination can also be factors in such reports. **The relative number and nature of reports should therefore not be used to compare the safety of the different vaccines.** The MHRA may also refer to 'cases' as opposed to 'reports' within the analysis of the Yellow Card data; these typically refer to ADR reports that have undergone medical assessment and are considered to meet certain criteria for diagnosis of the reported event and have at least a plausible association with the vaccine. All cases and reports are kept under continual review in order to identify possible new risks.

Up to and including 24 November 2021, the MHRA received and analysed 136,582 UK Yellow Cards from people who have received the COVID-19 Pfizer/BioNTech Vaccine. These reports include a total of 388,618 suspected reactions (i.e. a single report may contain more than one symptom). The first report was received on 9 December 2020.

Up to and including 24 November 2021, the MHRA received and analysed a total of 238,086 UK reports of suspected ADRs to the COVID-19 Vaccine AstraZeneca. These reports include a total of 844,212 suspected reactions (a single report may contain more than one symptom). The first report was received on 4 January 2021.

Up to and including 24 November 2021, the MHRA received and analysed a total of 19,101 UK reports of suspected ADRs to the COVID-19 Vaccine Moderna. These include a total 62,126 suspected reactions (a single report may contain more than one symptom). The first report was received on 7 April 2021.

Additionally, up to and including 24 November 2021, the MHRA received 1,280 Yellow Card reports where the brand of vaccine was not specified by the reporter.

In the week since the previous summary for 17 November 2021 we have received a further 2,631 Yellow Cards for the COVID-19 Pfizer/BioNTech Vaccine, 599 for the COVID-19 Vaccine AstraZeneca, 985 for the COVID-19 Vaccine Moderna and 26 where the brand was not specified.

It is important to note that Yellow Card data cannot be used to derive side effect rates or compare the safety profile of COVID-19 vaccines as many factors can influence ADR reporting.

**Table 4: Number of suspected ADR reports received in the UK up to and including 24 November 2021.**

Country	Number of reports			
	COVID-19 Pfizer/ BioNTech Vaccine	COVID-19 Vaccine AstraZeneca	COVID-19 Vaccine Moderna	Brand unspecified
England	106,282	196,744	15,584	768
Wales	6,926	10,513	534	70
Northern Ireland	2,537	2,913	132	16
Scotland	10,423	16,966	2,019	140

The figures in Table 4 are based upon the postcode provided by the reporter. The sums of the reports in the table will not equal the total reports received for each vaccine as postcode may not have always been provided or may have been entered incorrectly. It is important to note that the number of reports received for each country does not directly equate to the number of people who may have experienced adverse reactions and therefore cannot be used to determine the incidence of reactions. ADR reporting rates are influenced by many aspects, including the extent of use.

We are working with public health bodies and encouraging all healthcare professionals and patients alike to report any suspected ADRs to the Yellow Card scheme. As expected, reports gradually increase in line with an increase in doses administered.

The overall reporting rate is in the order of 3 to 6 Yellow Cards per 1,000 doses administered for the COVID-19 Pfizer/BioNTech Vaccine, COVID-19 Vaccine AstraZeneca and COVID-19 Vaccine Moderna. It is known from the clinical trials that the more common side effects for all vaccines can occur at a rate of more than one in 10 doses (for example, local reactions or symptoms resembling transient flu-like symptoms).

### 3 Analysis of Data

One of the MHRA's main roles is to continually monitor the safety of medicines and vaccines during widespread use, and we have in place a [proactive strategy to do this for COVID-19 vaccines](#). We also work closely with our public health partners in reviewing the effectiveness and impact that the vaccines are having to ensure benefits continue to outweigh any possible side effects. In addition, we work with our international counterparts to gather information on the safety of vaccines in other countries.

Given the huge scale of the COVID-19 immunisation programme, with many millions of doses of vaccines administered over a relatively short time period, vigilance needs to be continuous, proactive and as near real-time as is possible. The importance of this is two-fold. First, we need to rapidly detect, confirm, and quantify any new risks and weigh these against the expected benefits. We can then take any necessary action to minimise risks to individuals.

Secondly, we need to very quickly establish if any serious medical events which are temporally related to vaccination are merely a coincidental association. These associations are likely while we are still in the midst of a major national vaccination programme, and because many of the millions of people offered the vaccine in the early phase of a vaccination campaign were elderly and/or had underlying medical conditions, which increases the likelihood of unrelated illnesses occurring soon after vaccination. As mentioned above, the nature of Yellow Card reporting means that reported events are not always proven adverse reactions, and some may have happened regardless of vaccination.

Yellow Card reports of suspected ADRs are evaluated, together with additional sources of evidence, by a team of safety experts to identify any new safety issues or side effects. We apply statistical techniques that can tell us if we are seeing more events than we would expect to see, based on what is known about background rates of illness in the absence of vaccination. This aims to account for factors such as coincidental illness. We also look at the clinical characteristics to see if new patterns of illness are emerging that could indicate a new safety concern.

We supplement this form of safety monitoring with other epidemiology studies including analysis of data on national vaccine usage, anonymised GP-based electronic healthcare records and other healthcare data to proactively monitor safety. We also take into account the international experience based on data from other countries using the same vaccines. These combined safety data enables the MHRA to detect side effects or safety issues associated with COVID-19 vaccines. As well as confirming new risks, an equally important objective of monitoring will be to quickly rule out risks – in other words to confirm that the vaccine is not responsible for a suspected side effect and to provide reassurance on its safety.

#### Overall safety

As with any vaccine, COVID-19 vaccines will cause side effects in some people. The total number and the nature of the majority of Yellow Cards reports received so far is not unusual for a new vaccine for which members of the public and healthcare professionals are encouraged to report any suspected adverse reaction.

As highlighted above, it is known from the clinical trials that the most common side effects for all vaccines can occur at a rate of more than one per 10 doses (such as local reactions, symptoms resembling transient flu-like symptoms). Overall, Yellow Card reporting is therefore lower than the reporting rate of possible side effects from the clinical trials, although we generally do not expect all

suspected side effects to be reported on Yellow Cards. The primary purpose of Yellow Card reporting is to detect new safety concerns.

For all COVID-19 vaccines, detailed review of all reports has found that the overwhelming majority relate to injection-site reactions (sore arm for example) and generalised symptoms such as a 'flu-like' illness, headache, chills, fatigue (tiredness), nausea (feeling sick), fever, dizziness, weakness, aching muscles, and rapid heartbeat. Generally, these happen shortly after the vaccination and are not associated with more serious or lasting illness. These types of reaction reflect the acute immune response triggered by the body to the vaccines, are typically seen with most types of vaccine and tend to resolve within a day or two. The nature of reported suspected ADRs across all ages is broadly similar, although, as seen in the clinical trials and as is usually seen with other vaccines, they may be reported more frequently in younger adults.

As we receive more reports of these types of reactions with more exposure to the COVID-19 vaccines, we are building a picture of how individuals are experiencing them and the different ways that side effects may present in people. Some people have reported a sudden feeling of cold with shivering/shaking accompanied by a rise in temperature, often with sweating, headache (including migraine-like headaches), nausea, muscle aches and feeling unwell, starting within a day of having the vaccine. Similar to the flu like illness reported in clinical trials, these effects may last a day or two.

It is important to note that it is possible to have caught COVID-19 and not realise until after vaccination. If other COVID symptoms are experienced or fever is high and lasts longer than two or three days, vaccine recipients should stay at home and arrange to have a test.

A number of detailed assessments of safety topics have been undertaken and we have updated our advice on these topics accordingly. Overall, our advice remains that the benefits of the vaccines outweigh the risks in the majority of people. Further comments on use in specific populations and details on the following safety topics can be found below.

## **Comments on safety in specific populations**

### **Safety of COVID-19 vaccines in pregnancy**

The MHRA closely monitors the safety of COVID-19 vaccine exposures in pregnancy, including published information as well as Yellow Card reports for COVID-19 vaccines used in pregnancy. These reports have been reviewed by the independent experts of the Commission on Human Medicines' COVID-19 Vaccines Benefit Risk Expert Working Group and by the Medicines for Women's Health Expert Advisory Group (MWHEAG).

Pregnant women have the same risk of getting COVID-19 as non-pregnant women but they may be at an increased risk of becoming severely ill, particularly if they get infected in the third trimester or if they also have underlying medical problems, compared to non-pregnant women. The current advice of the Joint Committee on Vaccination and Immunisation (JCVI) is that the COVID-19 vaccines, including booster doses, should be offered to those who are pregnant at the same time as non-pregnant individuals based on their age and clinical risk group. The COVID-19 Pfizer/BioNTech Vaccine and COVID-19 Vaccine Moderna vaccines are currently the preferred vaccines for use during pregnancy and can be given at any stage in pregnancy.

The numbers of Yellow Card reports for pregnant women are low in relation to the number of pregnant women who have received COVID-19 vaccines to date (more than 104,000 up to end of September 2021 in England, Scotland and Wales). Pregnant women have reported similar suspected reactions to the vaccines as people who are not pregnant. Reports of miscarriage and stillbirth are also low in comparison to how commonly these events occur in the UK outside of the

pandemic. A few reports of commonly occurring congenital anomalies and obstetric events have also been received. There is no pattern from the reports to suggest that any of the COVID-19 vaccines used in the UK, or any reactions to these vaccines, increase the risk of miscarriage, stillbirths, congenital anomalies or birth complications.

Sadly, miscarriage is estimated to occur in about 20 to 25 in 100 pregnancies in the UK and most occur in the first 12 to 13 weeks of pregnancy (the first trimester). Newly published studies from the USA and Norway have compared miscarriage rates for vaccinated and unvaccinated women who were pregnant over the same time periods. The studies included data from a large number of women (more than 15,000) who received the Pfizer-BioNTech or Moderna vaccines. Both studies found that miscarriage was equally likely to occur amongst women vaccinated in the previous 3 to 5 weeks as amongst unvaccinated women at the same stage of pregnancy. These studies provide strong evidence for no increased risk of miscarriage in association with the mRNA vaccines in current use. Data on the Oxford-AZ vaccine is less extensive but is consistent with these findings.

Evidence for pregnancy outcomes other than miscarriage is accumulating as more pregnancies reach full term. Currently available evidence does not suggest any increased risks of pregnancy complications, stillbirths, preterm births or adverse neonatal outcomes following vaccination in later pregnancy.

Stillbirths are sadly estimated to occur in about 1 in 200 pregnancies in the UK. Information from surveillance by UKHSA (formerly Public Health England) has found similar rates of stillbirth amongst (more than 24,000) women who were vaccinated during pregnancy and those who gave birth over the same period and were unvaccinated. Likewise, surveillance by Public Health Scotland has found similar rates of perinatal mortality (including stillbirths) amongst (more than 3,800) women who were vaccinated during pregnancy and those who gave birth over the same period and were unvaccinated.

Although, like most vaccines and medicines, clinical trials of COVID-19 vaccines in pregnant women were not carried out prior to use of the vaccines in the general population, there is now growing evidence from real world data which provides reassurance on the safety of the vaccines in pregnancy. This adds to the evidence from non-clinical studies of the COVID-19 vaccines which have not raised any concerns about safety in pregnancy. The COVID-19 vaccines do not contain organisms that can multiply in the body, so they cannot infect an unborn baby in the womb.

The MHRA will continue to closely monitor safety data for use of the COVID-19 vaccines in pregnancy, including through evaluation of electronic healthcare record data.

### **Safety of COVID-19 vaccines in those breastfeeding**

The MHRA closely monitors the safety of COVID-19 vaccines during breastfeeding, including evaluation of Yellow Card reports for COVID-19 vaccines from breastfeeding women. These reports have been reviewed by the independent experts of the Commission on Human Medicines' COVID-19 Vaccines Benefit Risk Expert Working Group, by paediatric and breastfeeding experts.

There is no current evidence that COVID-19 vaccination while breastfeeding causes any harm to breastfed children or affects the ability to breastfeed.

COVID-19 vaccines do not contain live components and there is no known risk associated with being given a non-live vaccine whilst breastfeeding. The current advice of the Joint Committee on Vaccination and Immunisation (JCVI) is that breastfeeding parents may be offered any suitable COVID-19 vaccine depending on their age.

We have received about 3,500 Yellow card reports from women breastfeeding at the time of vaccination. Most of these women reported only suspected reactions in themselves which were similar to reports for the general population, with no effects reported on their milk supply or in their breastfed children.

A small number of women have reported decreases in their milk supply, most of which were transient, or possible reactions in their breastfed child. A number of factors can affect milk supply and infant behaviour, including general maternal health, amount of sleep, and anxiety. The symptoms reported for the children (high temperature, rash, diarrhoea, vomiting and general irritability) are common conditions in children of this age, so some of the effects reported may have occurred by coincidence.

A small number of women may experience a reduction in their breast milk production and it may be helpful for breastfeeding women to know how to maintain their breast milk supply, particularly if they are feeling unwell. The NHS website has a good resource for this: <https://www.nhs.uk/start4life/baby/breastfeeding/>.

### **Suspected side effects reported in individuals under 18 years old**

The MHRA closely monitors the safety of COVID-19 vaccine exposures in individuals under 18 years old, including Yellow Card reports for COVID-19 vaccines used in this age group.

To date there have been an estimated 2.6 million first doses and 417,500 second doses of the COVID-19 Pfizer/BioNTech Vaccine given to under 18s, approximately 11,500 first doses and 10,000 second doses of the COVID-19 Vaccine AstraZeneca given to this population and 17,800 first doses and 13,600 second doses of the COVID-19 Vaccine Moderna given to individuals under 18.

The MHRA has received 1,873 UK reports of suspected ADRs for the COVID-19 Pfizer/BioNTech Vaccine in which the individual was reported to be under 18, 243 reports for the COVID-19 Vaccine AstraZeneca, 6 for the COVID-19 Vaccine Moderna and 8 where the brand of vaccine was unspecified.

The experience reported in under 18s is similar to that identified in the general population and a review of these reports does not raise any additional safety topics specific to this age group.

There has been a small number of reports for myocarditis and pericarditis (inflammation of the heart) in individuals under 18 years both in the UK and internationally. This is a recognised potential risk with the COVID-19 Pfizer/BioNTech Vaccine and COVID-19 Vaccine Moderna and the MHRA is closely monitoring these events. Further information surrounding these very rare reports of myocarditis and pericarditis within this population can be found within the specific section on this safety topic later in the summary. We will continue to closely monitor the safety of the COVID-19 vaccines in those under 18 years old.

### **Suspected side effects reported in individuals receiving a booster vaccination**

Safety monitoring plans have been agreed to ensure action can be taken on any emerging safety concerns from supplementary or booster doses. The MHRA has received 10,460 UK reports of suspected ADRs where the COVID-19 Pfizer/BioNTech Vaccine was reported to be the booster dose, 145 reports where the COVID-19 Vaccine AstraZeneca was reported to be the booster dose, 1,575 reports where the COVID-19 Vaccine Moderna was reported to be the booster dose and 68 reports where the brand of vaccine booster was unspecified.

In the context of over 16 million COVID-19 third doses and boosters in the UK up to the 24 November 2021, this gives an overall reporting rate of 0.7 reports per 1,000 booster or third doses. This is lower than the reporting rate for COVID-19 vaccines for all doses, which is between 3-7 reports per 1,000 doses.

The nature of events reported with booster and third doses is similar to that reported for the first two doses of the COVID-19 vaccines, and in the vast majority relate to expected reactogenicity events. Review of booster and third dose reports does not raise any new safety concerns. . As part of the MHRA's booster safety monitoring strategy, reports of suspected adverse events following COVID-19 boosters given at the same time as seasonal flu vaccines have been closely monitored, and no new safety concerns have been identified in this data either.

There have been a small number of reports of suspected myocarditis and pericarditis (inflammation of the heart) following booster doses with Pfizer/BioNTech and Moderna COVID-19 vaccines. This is a recognised potential risk with the COVID-19 Pfizer/BioNTech Vaccine and COVID-19 Vaccine Moderna and the MHRA is closely monitoring these events. The reports after booster doses are extremely rare and there is no indication that these events are more serious after boosters. Further information surrounding these very rare reports of suspected myocarditis and pericarditis can be found within the specific section on this safety topic later in the summary.

We will continue to closely monitor the safety of booster and third doses of the COVID-19 vaccines.

## **Comments on specific safety topics**

The following reports reflect data up to 24 November 2021. The glossary provides an explanation of the clinical terms used.

### **Anaphylaxis (severe allergic reactions)**

On 9 December 2020, the MHRA issued preliminary guidance on severe allergic reactions after administration of the COVID-19 Pfizer/BioNTech Vaccine due to early reports of anaphylaxis. Following further detailed review, this advice was amended on 30 December to the current advice. The advice is that people with a previous history of severe allergic reactions to any ingredients of the vaccine should not receive it. People who receive the vaccine should be monitored for at least 15 minutes afterwards. Similar advice was introduced for the Covid-19 Vaccine Moderna as it uses a similar technology to the Pfizer vaccine.

Widespread use of the vaccine now suggests that severe allergic reactions to the COVID-19 Pfizer/BioNTech Vaccine and COVID-19 Vaccine Moderna are very rare. Anaphylaxis can also be a very rare side effect associated with most other vaccines.

The MHRA continues to monitor reports of severe allergic reactions with the COVID-19 Pfizer/BioNTech Vaccine and has received 562 UK spontaneous adverse reactions associated with anaphylaxis or anaphylactoid reactions. Severe allergic reactions to the COVID-19 Pfizer/BioNTech Vaccine remain very rare. The MHRA's guidance remains that those with a previous history of allergic reactions to the ingredients of the vaccine should not receive it.

The MHRA is closely monitoring reports of anaphylaxis with the COVID-19 Vaccine Moderna and has received 47 reports of anaphylaxis in association with the vaccine. Anaphylaxis is a potential side effect of the vaccine, and it is recommended that those with known hypersensitivity to the ingredients of the vaccine should not receive it.



The MHRA also closely monitors reports of anaphylaxis or anaphylactoid reactions with the COVID-19 Vaccine AstraZeneca and has received 845 UK spontaneous adverse reactions associated with anaphylaxis or anaphylactoid reactions reported and such reports are very rare. The product information reflects the fact that reports of anaphylaxis have been received for the COVID-19 Vaccine AstraZeneca.

### **Bell's Palsy**

MHRA continues to review reports of suspected Bell's Palsy and to analyse them against the number expected to occur by chance in the absence of vaccination (the 'natural rate'). The number of reports of facial paralysis received so far is similar to the expected natural rate and does not currently suggest an increased risk following the vaccines. We will continue to monitor these events, including through evaluation of electronic healthcare record data.

### **Thrombo-embolic (blood clotting) events with concurrent low platelets**

The MHRA has undertaken a thorough review into UK cases of an extremely rare and unlikely to occur specific type of blood clot in the brain, known as cerebral venous sinus thrombosis (CVST) occurring together with low levels of platelets (thrombocytopenia) following vaccination with the COVID-19 Vaccine AstraZeneca. It has also considered other blood clotting reports (thromboembolic events) alongside low platelet levels.

This scientific review concluded that the evidence of a link with COVID-19 Vaccine AstraZeneca is likely and [an announcement](#) was made on 7 April 2021 with a further statement on 7 May 2021. We have continued to publish the latest breakdown of all cases of these extremely rare side effects on a weekly basis.

Anyone who experienced cerebral or other major blood clots occurring with low levels of platelets after their first vaccine dose of COVID-19 Vaccine AstraZeneca should not have further doses. Anyone who did not have these side effects should come forward for their second dose when invited.

The MHRA has also confirmed that the evidence to date does not suggest that the COVID-19 Vaccine AstraZeneca causes venous thromboembolism which occurred in the absence of a low platelet count.

Anyone who experiences any of the following from around 4 days after vaccination should seek medical advice urgently:

- a severe headache that is not relieved with simple painkillers or gets worse or feels worse when you lie down or bend over
- an unusual headache that may be accompanied by blurred vision, confusion, difficulty with speech, weakness, drowsiness or seizures (fits)
- rash that looks like small bruises or bleeding under the skin beyond the injection site
- shortness of breath, chest pain, leg swelling or persistent abdominal (tummy) pain.

Up to 26 November 2021, the MHRA had received Yellow Card reports of 427 cases of major thromboembolic events (blood clots) with concurrent thrombocytopenia (low platelet counts) in the UK following vaccination with COVID-19 Vaccine AstraZeneca. Forty-seven of the 426 reports have been reported after a second dose. Of the 427 reports, 215 occurred in females, and 208

occurred in males aged from 18 to 93 years. The overall case fatality rate was 17% with 74 deaths, six of which occurred after the second dose.

Cerebral venous sinus thrombosis was reported in 155 cases (average age 46 years) and 272 had other major thromboembolic events (average age 54 years) with concurrent thrombocytopenia. The estimated number of first doses of COVID-19 Vaccine AstraZeneca administered in the UK by 24 November 2021 was 24.9 million and the estimated number of second doses was 24.1 million.

The overall incidence after first or unknown doses was 15.3 per million doses. Considering the different numbers of patients vaccinated with COVID-19 Vaccine AstraZeneca in different age groups, the data indicates that there is a higher reported incidence rate in the younger adult age groups following the first dose compared to the older groups (21.1 per million doses in those aged 18-49 years compared to 11.0 per million doses in those aged 50 years and over). The number of first doses given to those in the 18-49 years age group is estimated to be 8.5 million while an estimated 16.3 million first doses have been given to patients aged 50+ years. The MHRA advises that this evidence should be taken into account when considering the use of the vaccine. There is some evidence that the reported incidence rate is higher in females compared to men although this is not seen across all age groups and the difference remains small.

The overall incidence of thromboembolic events with concurrent low platelets after second doses was 2.0 cases per million doses. Taking into account the different numbers of patients vaccinated with COVID-19 Vaccine AstraZeneca in different age groups, the data indicates that there is a lower reported incidence rate in younger adult age groups following the second dose compared to the older groups (1.0 per million doses in those aged 18-49 years compared to 2.0 per million doses in those aged 50 years and over). The number of second doses given to those in the 18-49 years age group is estimated to be 8.2 million while an estimated 15.9 million second doses have been given to patients aged 50+ years. These rates after second doses should not be directly compared to the incidence rates reported after the first dose as the time for follow-up and identification of cases after second doses is more limited and differs across age groups. However, the data are reassuring, particularly regarding younger recipients where there is a significantly lower incidence after the second dose compared to the first, and there is overall no indication of an increased risk of these events after the second dose in any age group. Anyone who did not have these side effects should come forward for their second dose when invited.

These cases have also been analysed by the government's independent advisory body, the COVID-19 Vaccines Benefit Risk Expert Working Group, which includes lay representatives and advice from leading haematologists.

On the basis of this ongoing review, the advice remains that the benefits of the vaccine outweigh the risks in the majority of people.

**Table 5: Number of suspected thrombo-embolic events with concurrent thrombocytopenia ADR cases received for the COVID-19 Vaccine AstraZeneca in the UK up to and including 24 November 2021.**

Country	Number of cases
England	331
Wales	13
Northern Ireland	10
Scotland	35
Unknown	38

**Table 6: Number of UK suspected thrombo-embolic events with concurrent thrombocytopenia ADR cases received for the COVID-19 Vaccine AstraZeneca by patient age up to and including 24 November 2021.**

Age range (years)	Number of cases	Number of fatal cases
18-29	30	7
30-39	50	11
40-49	108	13
50-59	101	19
60-69	61	10
70-79	40	7
80-89	6	3
90-99	2	1
Unknown	29	3
<b>Total</b>	<b>427</b>	<b>74</b>

**Table 7: Number of UK suspected thrombo-embolic events with concurrent thrombocytopenia ADR cases received for the COVID-19 Vaccine AstraZeneca by patient sex up to and including 24 November 2021.**

Sex	Number of cases	Number of fatal cases
Male	208	33
Female	215	41
Unknown	4	0
<b>Total</b>	<b>427</b>	<b>74</b>

Up to 24 November 2021, the MHRA had received Yellow Card reports of 28 cases of major thromboembolic events (blood clots) with concurrent thrombocytopenia (low platelet counts) in the UK following use of the COVID-19 Pfizer/BioNTech Vaccine. These events occurred in 10 females, and 18 males aged from 18 to 91 years, and the overall case fatality rate was 14% with four deaths reported.

Up to 24 November 2021, the MHRA had received Yellow Card reports of 3 cases of major thromboembolic events (blood clots) with concurrent thrombocytopenia (low platelet counts) in the UK following the use of COVID-19 vaccine Moderna. The 3 events occurred in adult males under the age of 60, and there have been no fatal cases reported.

To note, direct comparison of the summary provided here, and the analysis prints is not possible. This review includes reports of CVST or other thrombo-embolic events with concurrent thrombocytopenia. Yellow Card reports may contain more than one reported reaction and the analysis prints are listed by individual reactions rather than whole reports. Therefore, summing the reactions listed in the prints will not equate to the total cases included within this summary.

### Capillary Leak Syndrome

The MHRA has received 14 reports of suspected capillary leak syndrome (a condition where fluid leaks from the small blood vessels into the body) in the context of more than 48.9 million doses of COVID-19 Vaccine AstraZeneca given. Of these reports, 3 people had a history of capillary leak syndrome. This is an extremely rare relapsing-remitting condition and triggers for relapses are not

well understood. As a precautionary measure, the MHRA is advising that COVID-19 Vaccine AstraZeneca is not used in people who have previously experienced episodes of capillary leak syndrome. The product information has been updated to reflect this advice.

### **Menstrual disorders (period problems) and unexpected vaginal bleeding**

The MHRA is reviewing reports of suspected side effects of menstrual disorders (period problems) and unexpected vaginal bleeding following vaccination against COVID-19 in the UK. These reports are also being reviewed by the independent experts of the Commission on Human Medicines' COVID-19 Vaccines Benefit Risk Expert Working Group and the Medicines for Women's Health Expert Advisory Group. The rigorous evaluation completed to date does not support a link between changes to menstrual periods and related symptoms and COVID-19 vaccines.

A total of 42,325 suspected reactions relating to a variety of menstrual disorders have been reported after all three of the COVID-19 vaccines including heavier than usual periods, delayed periods and unexpected vaginal bleeding. These suspected reactions have been reported in 33,006 individual Yellow Card reports (as each report may contain more than one suspected reaction). This is following approximately 50.2 million COVID-19 vaccine doses administered to women up to 24 November 2021. The number of reports of menstrual disorders and vaginal bleeding is low in relation to both the number of people who have received COVID-19 vaccines to date and how common menstrual disorders are generally.

The menstrual changes reported are mostly transient in nature. There is no evidence to suggest that COVID-19 vaccines will affect fertility and your ability to have children.

Whilst uncomfortable or distressing, period problems are extremely common and stressful life events can disrupt menstrual periods. Changes to the menstrual cycle have also been reported following infection with COVID-19 and in people affected by long-COVID. General advice about period problems and/or unexpected vaginal bleeding is available from the [NHS website](#). It is important that anyone experiencing changes to their periods that are unusual for them, persist over time, or has any new vaginal bleeding after the menopause, following COVID-19 vaccination, should contact their doctor. Anyone presenting with menstrual disorders and/or unexpected vaginal bleeding following COVID-19 vaccination should be treated according to clinical guidelines for these conditions, as usual.

The MHRA continues to closely review reports of suspected side effects of menstrual disorders and unexpected vaginal bleeding.

### **Myocarditis and pericarditis (Inflammation of the heart)**

The MHRA has undertaken a thorough review of both UK and international reports of suspected myocarditis and pericarditis following vaccination against COVID-19. There has been a consistent pattern of higher reporting of these suspected events with the COVID-19 Pfizer/BioNTech and COVID-19 Vaccine Moderna, and of these occurring more frequently in males. In the UK the body of evidence shows that for Pfizer in particular, there is similar frequency of reporting after the first and second dose, with suspected events typically occurring within a short time after vaccination. These reports have also been analysed by the government's independent advisory body, the Commission on Human Medicines (CHM) and its COVID-19 Vaccines Benefit Risk Expert Working Group. Following their advice, the product information for the COVID-19 Vaccine Moderna and COVID-19 Pfizer/BioNTech Vaccines was updated to inform of these reports and advise healthcare professionals and patients to be aware of important symptoms for myocarditis and pericarditis.

These reports are extremely rare, and the events reported are typically mild with individuals usually recovering within a short time with standard treatment and rest. People should come forward for their first and second vaccination when invited to do so, unless advised otherwise.

It is important that anyone who experiences new onset of symptoms such as chest pain, shortness of breath or feelings of having a fast-beating, fluttering, or pounding heart seeks medical attention.

Up to and including 24 November 2021, we have received 450 reports of myocarditis and 341 reports of pericarditis following use of the COVID-19 Pfizer/BioNTech Vaccine, as well as four reports of carditis, three reports each of viral pericarditis and viral myocarditis, two reports for infective pericarditis, and one report each of constrictive pericarditis, non-infective endocarditis and streptococcal endocarditis. For COVID-19 Vaccine AstraZeneca there have been 161 reports of myocarditis and 192 reports of pericarditis following vaccination up to and including 24 November 2021 as well as eight reports for endocarditis, five reports for viral pericarditis, two reports each for endocarditis bacterial, carditis, viral myocarditis and acute endocarditis, and one report each for infectious myocarditis and autoimmune myocarditis. There have been 103 reports of myocarditis, 59 reports of pericarditis and one report each of hypersensitivity myocarditis and endocarditis following use of COVID-19 Vaccine Moderna up to the same date. Three fatal events have been reported with the COVID-19 Pfizer/BioNTech Vaccine and two fatal events with the COVID-19 Vaccine AstraZeneca. There have been no fatal myocarditis or pericarditis events reported with the COVID-19 Vaccine Moderna to date. Fatal events are being monitored closely and are carefully followed up to gather relevant information. The majority of fatal reports describe underlying illnesses in these patients that could provide alternative explanations for the events reported.

Based on reports of suspected ADRs in the UK, the overall reporting rate across all age groups for suspected myocarditis (including viral myocarditis), after both first and second dose, is 10 reports per million doses of COVID-19 Pfizer/BioNTech Vaccine and for suspected pericarditis (including viral pericarditis and infective pericarditis) the overall reporting rate is 8 reports per million doses. For COVID-19 Vaccine Moderna, the overall reporting rate for suspected myocarditis is 37 per million doses and for suspected pericarditis is 21 per million doses. For COVID-19 Vaccine AstraZeneca the overall reporting rate for suspected myocarditis (including viral myocarditis and infectious myocarditis) is 3 per million doses and for suspected pericarditis (including viral pericarditis) is 4 per million doses. It should be noted that more than one event can be included in each report.

When the reporting rate is calculated by age group (see Table 8) the reporting rate for suspected myocarditis and pericarditis is highest in the 18-29-year age group for the Pfizer/BioNTech and Moderna COVID-19 vaccines. A more even spread in reporting rates across the age groups is seen for AstraZeneca COVID-19 vaccine. For all vaccines there is a trend for decreased reporting in the older age groups. Pfizer/BioNTech is currently the preferred COVID-19 vaccine for the under 18s age group in the UK vaccination programme, and for this vaccine there is no indication in the current data that there is an increased reporting rate of suspected myocarditis and pericarditis in this age group compared to young adults. There are largely similar reporting rates between the first and second doses of the Pfizer/BioNTech and AstraZeneca COVID-19 vaccines. There is greater variability between first and second dose reporting rates with Moderna however the reporting rate estimates for Moderna may lack precision due to the more limited experience with Moderna in the UK and small numbers of suspected reports. This introduces more uncertainty into the data.

It is important not to compare the reporting rates between the different COVID-19 vaccines as many factors can influence ADR reporting. These reporting rates may also be subject to change as more experience is gathered in the UK.

**Table 8: Reporting rates per million doses for UK ADR reports of suspected myocarditis and pericarditis associated with COVID-19 Vaccines, by patient age and dose, up to and including 24 November 2021.**

Age range (years)	COVID-19 Pfizer/BioNTech Vaccine First or unknown dose	COVID-19 Pfizer/BioNTech Vaccine Second dose	COVID-19 Vaccine Moderna First or unknown dose	COVID-19 Vaccine Moderna Second dose	COVID-19 Vaccine AstraZeneca First or unknown dose	COVID-19 Vaccine AstraZeneca Second dose
<18 years	11	Not calculated*	Not applicable**	Not applicable**	Not applicable**	Not applicable**
18-29	21	22	50	70	8	14
30-39	18	20	39	51	10	9
40-49	16	16	38	22	11	7
50-59	5	13	31	34	7	6
60-69	4	10	Not applicable**	Not applicable**	6	5
70+	3	4	Not applicable**	Not applicable**	4	4

\*There is currently insufficient data to calculate a reliable estimate of the reporting rate post-dose 2 in under 18-year-olds in the UK due to, as yet, relatively limited exposure of dose 2 in these individuals. This estimate will be included once sufficient exposure has accumulated.

\*\*There have been no reports of suspected heart inflammation events received for individuals in these age groups

**Table 9: Number of UK ADR reports associated with suspected myocarditis, pericarditis and other related terms received for the COVID-19 Vaccine AstraZeneca, COVID-19 Pfizer/BioNTech Vaccine and COVID-19 Vaccine Moderna by patient age up to and including 24 November 2021.**

Age range (years)	Number of reports		
	COVID-19 Pfizer/BioNTech Vaccine	COVID-19 Vaccine Moderna	COVID-19 Vaccine AstraZeneca
Under 18	34	0	0
18-29	249	74	26
30-39	199	46	36
40-49	77	14	90
50-59	47	2	83
60+	86	2	85
Unknown	84	20	37
<b>Total</b>	<b>776</b>	<b>158</b>	<b>357</b>

**Table 10: Number of UK ADR reports associated with suspected myocarditis, pericarditis and other related terms received for the COVID-19 Vaccine AstraZeneca, COVID-19 Pfizer/BioNTech Vaccine and COVID-19 Vaccine Moderna by patient sex up to and including 24 November 2021.**

Sex	Number of reports		
	COVID-19 Pfizer/BioNTech Vaccine	COVID-19 Vaccine Moderna	COVID-19 Vaccine AstraZeneca
Female	308	43	163
Male	442	109	185

Unknown	26	6	9
<b>Total</b>	<b>776</b>	<b>158</b>	<b>357</b>

Myocarditis and pericarditis happen very rarely in the general population, and it is estimated that in the UK there are about 60 new cases of myocarditis diagnosed per million patients per year and about 100 new cases of pericarditis diagnosed per million patients per year.

The MHRA will continue to closely monitor reports of suspected myocarditis and pericarditis with all of the currently authorised COVID-19 vaccines.

### **Delayed hypersensitivity reactions**

The MHRA has been reviewing reports of skin reactions occurring around the vaccination site that appear a little while after vaccination. These reactions are suggestive of a delayed hypersensitivity reaction that occurs 4-11 days after vaccination. The reactions are characterized by a rash, swelling and tenderness that can cover the whole upper arm and may be itchy and/or painful and warm to the touch. The majority of the reports received have been with the COVID-19 Vaccine Moderna and the product information for this vaccine has been updated to highlight the possibility of delayed injection site reactions

The reactions are usually self-limiting and resolve within a day or two, although in some patients it can take slightly longer to disappear. Individuals who experience this reaction after their first dose may experience a similar reaction in shorter timeframe following the second dose, however, none of the reports received have been serious and people should still take their second dose when invited. Those who experience delayed skin reactions after their COVID-19 vaccination which do not resolve within a few days should seek medical advice.

### **Guillain-Barré Syndrome**

Guillain-Barré Syndrome is a very rare condition which causes inflammation of the nerves and can lead to numbness, weakness and pain, usually in the feet, hands and limbs and can spread to the chest and face. Guillain-Barré Syndrome tends to affect both sides of the body at once. This condition is known to be associated with certain infectious diseases.

Up to and including the 24 November 2021, the MHRA has received 463 reports of suspected Guillain-Barré Syndrome with the COVID-19 Vaccine AstraZeneca and 26 reports of a related disease called Miller Fisher syndrome. Up to the same date, the MHRA has received 68 reports of Guillain-Barre Syndrome following use of the COVID-19 Pfizer/BioNTech Vaccine and 1 report of Miller Fisher syndrome and for the COVID-19 Vaccine Moderna there have been seven reports of Guillain-Barré Syndrome.

The MHRA has been closely monitoring and assessing reports of suspected Guillain-Barré Syndrome (GBS) received following administration of the COVID-19 vaccine. Following the most recent review of the available data the evidence of a possible association has strengthened. Therefore, following advice from the government's independent advisory body, the Commission on Human Medicines (CHM) and its COVID-19 Vaccines Benefit Risk Expert Working Group, the product information for the COVID-19 Vaccine AstraZeneca was further updated to include GBS in the tabulated list of adverse reactions associated with the COVID-19 Vaccine AstraZeneca and to encourage healthcare professionals and the public to look out for signs of GBS.

The MHRA will continue to review reports of Guillain-Barré Syndrome received following vaccination with COVID-19 vaccines to further assess a possible association between Guillain-

Barré Syndrome and COVID-19 vaccines, with independent advice from its Vaccine Benefit-Risk Working Group.

### **Swelling of the vaccinated limb**

There have been rare reports of extensive swelling of the vaccinated limb after receiving the COVID-19 Pfizer/BioNTech Vaccine. The product information has been updated to include “extensive swelling of the vaccinated limb” as a side effect of the vaccine. This type of swelling is also recognised to occur with other (non-COVID-19) vaccines.

### **Facial swelling in those with a history of facial dermal fillers**

Rare reports of facial swelling occurring 1-2 days after vaccination in vaccine recipients with a history of injection of facial dermal fillers were observed in the clinical trials for the COVID-19 Vaccine Moderna. Information about this possible side effect has been included in the product information for the COVID-19 Vaccine Moderna since it was first authorised for use.

The MHRA has also received Yellow Card reports of facial swelling in those with a history of injection of facial dermal fillers for the COVID-19 Pfizer/BioNTech Vaccine. A recent review of the world-wide ADR data for the COVID-19 Pfizer/BioNTech Vaccine found that, in most instances, the facial swelling was mild, transient and was localised to the site of the dermal filler. The product information for the COVID-19 Pfizer/BioNTech Vaccine has been updated to include facial swelling in those with a history of injection of facial dermatological fillers as a side effect of the vaccine.

### **Events with a fatal outcome**

Vaccination and surveillance of large populations means that, by chance, some people will experience and report a new illness or events in the days and weeks after vaccination. A high proportion of people vaccinated early in the vaccination campaign were very elderly, and/or had pre-existing medical conditions. Older age and chronic underlying illnesses make it more likely that coincidental adverse events will occur, especially given the millions of people vaccinated. It is therefore important that we carefully review these reports to distinguish possible side effects from illness that would have occurred irrespective of vaccination.

Part of our continuous analysis includes an evaluation of natural death rates over time, to determine if any specific trends or patterns are occurring that might indicate a vaccine safety concern. Based on age-stratified all-cause mortality in England and Wales taken from the [Office for National Statistics death registrations](#), several thousand deaths are expected to have occurred, naturally, within 7 days of the many millions of doses of vaccines administered so far, mostly in the elderly.

The MHRA has received 628 UK reports of suspected ADRs to the COVID-19 Pfizer/BioNTech Vaccine in which the patient died shortly after vaccination, 1,136 reports for the COVID-19 Vaccine AstraZeneca, 18 for the COVID-19 Vaccine Moderna and 32 where the brand of vaccine was unspecified. The majority of these reports were in elderly people or people with underlying illness. Usage of the vaccines has increased over the course of the campaigns and as such, so has reporting of fatal events with a temporal association with vaccination. However, this does not mean that there is a link between vaccination and the fatalities reported. Review of specific fatal reports is provided in the summaries above. The pattern of reporting for all other fatal reports does not suggest the vaccines played a role in these deaths.

A range of other isolated events or series of reports of non-fatal, serious suspected ADRs have been reported. These all remain under continual review, including thorough analysis of expected rates in the absence of vaccine. There are currently no indications of specific patterns or rates of reporting that would suggest the vaccine has played a role.



## 4 Conclusion

At the time of this report, over 144,432 people across the UK have died within 28 days of a positive test for coronavirus.

Vaccination is the single most effective way to reduce deaths and severe illness from COVID-19. A national immunisation campaign has been underway since early December 2020.

In [clinical trials](#), the COVID-19 Pfizer/BioNTech Vaccine, COVID-19 Vaccine AstraZeneca and COVID-19 Vaccine Moderna have demonstrated very high levels of protection against symptomatic infection. [Data](#) are available on the impact of the vaccination campaign in reducing infections and illness in the UK.

All vaccines and medicines have some side effects. These side effects need to be continuously balanced against the expected benefits in preventing illness.

Following widespread use of these vaccines across the UK, the vast majority of suspected adverse reaction reports confirm the safety profile seen in clinical trials. Most reports relate to injection-site reactions (sore arm for example) and generalised symptoms such as a 'flu-like' illness, headache, chills, fatigue, nausea, fever, dizziness, weakness, aching muscles, and rapid heartbeat. Generally, these reactions are not associated with more serious illness and likely reflect an expected, normal immune response to the vaccines.

The expected benefits of the vaccines in preventing COVID-19 and serious complications associated with COVID-19 far outweigh any currently known side effects. As with all vaccines and medicines, the safety of COVID-19 vaccines is continuously monitored and benefits and possible risks remain under review.

We take every report of a suspected ADR seriously and encourage everyone to report through the Yellow Card scheme.

# Annex 1 Vaccine Analysis Print

The attached Vaccine Analysis Prints contain a complete listing of all suspected adverse reactions that have been reported to the MHRA via the Yellow Card scheme for the COVID-19 Pfizer/BioNTech Vaccine, the COVID-19 Vaccine AstraZeneca, the COVID-19 Vaccine Moderna and where the brand of the vaccine was not specified. This includes all reports received from healthcare professionals, members of the public, and pharmaceutical companies.

This information does not represent an overview of the potential side effects associated with the vaccines. A list of the recognised adverse effects of COVID-19 vaccines is provided in the information for healthcare professionals and the recipient information [here](#). These can also be found on the [Coronavirus Yellow Card](#) reporting site. Conclusions on the safety and risks of the vaccines cannot be made on the data shown in the Print alone.

When viewing the vaccine analysis print you should remember that:

- Reporters are asked to submit Yellow Card reports even if they only have a suspicion that the medicine or vaccine may have caused the adverse reaction. The existence of an adverse reaction report in the print does not necessarily mean that the vaccine has caused the suspected reaction.
- It may be difficult to tell the difference between something that has occurred naturally and a suspected adverse reaction. Sometimes these events can be part of the condition being treated rather than being caused by the vaccine.
- Many factors have to be considered when assessing whether the vaccine has caused a reported adverse reaction. When monitoring the safety of vaccines and medicines, MHRA staff carry out careful analysis of these factors.

For a medicine or vaccine to be considered safe, the expected benefits will be greater than the risk of having harmful reactions. It is important to note that most people take medicines and vaccines without having any serious side effects.

Vaccine Analysis Print – COVID-19 Pfizer/BioNTech Vaccine

Vaccine Analysis Print - COVID-19 Vaccine AstraZeneca

Vaccine Analysis Print – COVID-19 Vaccine Moderna

Vaccine Analysis Print - Brand unspecified

# Annex 2 Glossary

## **Anaphylaxis or anaphylactoid reactions**

Anaphylaxis is a severe and potentially life-threatening allergic reaction. These reactions can occur after an exposure to a trigger, such as a certain ingredient in foods or medicines or an insect sting. Anaphylaxis and anaphylactoid reactions can be treated with adrenaline.

## **Bell's palsy**

Bell's palsy is a condition that causes temporary weakness or paralysis (lack of movement) of the muscles in one side of the face. It is the most common cause of facial paralysis. For most people, the facial paralysis is temporary. Viral infections such as those with herpes viruses have been linked to Bell's palsy.

## **Booster dose/vaccination**

A COVID-19 booster vaccine dose helps improve the protection obtained from the first two doses of the vaccine. It helps give longer-term protection against getting seriously ill from COVID-19.

**Capillary Leak Syndrome (CLS)** Capillary Leak Syndrome (CLS) occurs when fluid leaks from the small blood vessels into the body.

## **Cerebral venous sinus thrombosis (CVST)**

Cerebral venous sinus thrombosis occurs when the brain's venous sinuses or the smaller veins draining into them are partially or completely blocked by a blood clot. This prevents blood from draining out of the brain. As a result, the oxygen supply to nerve cells may be impaired and blood cells can leak into the brain tissue causing damage to the brain (haemorrhagic infarction).

## **Clinical Practice Research Datalink (CPRD)**

[Clinical Practice Research Datalink \(CPRD\)](#) is a real-world research service to support public health and clinical studies. CPRD is jointly sponsored by the Medicines and Healthcare products Regulatory Agency and the National Institute for Health Research (NIHR), as part of the Department of Health and Social Care. CPRD collects anonymised patient data from a network of GP practices across the UK.

## **Commission on Human Medicines (CHM)**

The [Commission on Human Medicines \(CHM\)](#) advises ministers on the safety, efficacy and quality of medicinal products. For COVID-19 vaccines, the CHM has a COVID-19 Vaccines Safety Surveillance Methodologies Expert Working Group and a COVID-19 Vaccines Benefit Risk Expert Working Group.

## **Endocarditis**

Endocarditis is inflammation of the inner lining of the heart (endocardium).

## **Epidemiology studies**

Epidemiological studies include large numbers of people and are designed to compare the risk of a particular event in an exposed population, in this case those who have received a vaccine, to those who have not. They attempt to account for differences in the different groups to help us understand if any difference in risk is caused by the exposure. Epidemiological studies measure the risk of illness or death in an exposed population compared to that risk in an identical, unexposed population.

## **Guillain-Barré Syndrome**

Guillain-Barré Syndrome is inflammation of the nerves and can lead to numbness, weakness and pain, usually in the feet, hands and limbs and can spread to the chest and face. This syndrome has been associated with viral infections such as the flu.

### **Miller-Fisher Syndrome**

Miller-Fisher syndrome is a variation of Guillain-Barré Syndrome that affects the nervous system and can cause weakness in the face and a lack of balance and co-ordination. Similar to Guillain-Barré Syndrome, this syndrome has been associated with viral infections such as the flu.

### **Miscarriage**

The loss of a pregnancy during the first 23 weeks.

### **Myocarditis**

Myocarditis is the inflammation of the heart muscle (myocardium).

### **Non-clinical studies**

Non-clinical studies refer to studies that are not performed on the human body. These are largely done before clinical trials in humans and can include animal safety and efficacy studies, human tissue sample studies or toxicology.

### **Pericarditis**

Pericarditis is inflammation of the pericardium, the protective sac that surrounds your heart.

### **Regulation 174 authorisation**

Temporary authorisation for supply of a medicine or vaccine by the UK Department of Health and Social Care and the Medicines and Healthcare products Regulatory Agency. This temporary authorisation grants permission for a medicine (vaccine) to be used for active immunisation to prevent COVID-19 disease caused by SARS-CoV-2 virus. Authorisation is subject to a number of conditions. These are available for each vaccine on the MHRA website.

### **Suspected adverse reactions**

Also known as side effects. All medicines or vaccines can cause adverse reactions in some people. Adverse drug reactions reported to the MHRA are looked at and used to assess the balance of risks and benefits of medicines and vaccines.

### **Stillbirth**

A stillbirth is when a baby is born dead after 24 completed weeks of pregnancy. If the baby dies before 24 completed weeks, it's known as a miscarriage.

### **Temporal Association**

Events occurring following vaccination but may or may not be caused by the vaccine.

### **Third dose/vaccination**

A COVID-19 third vaccine is being offered to those who had a weakened immune system when they had the first two doses of the COVID-19 vaccination. The third dose may help to improve immune response and give better protection.

### **Thrombocytopenia**

Thrombocytopenia is where the blood contains a lower than normal number of platelets. Platelets are the smallest of the blood cells and are involved in the clotting process.

### **Yellow Card scheme**

The MHRA's scheme for healthcare professionals and members of the public to report suspected adverse reactions for a medicine or vaccine, as well as medical devices and other products. The

[dedicated Coronavirus Yellow Card reporting site](#) was launched in May 2020 specifically for medicines and medical devices used in COVID-19, as well as COVID-19 vaccines when authorised.