Medicines & Healthcare products Regulatory Agency

MHRA
Regulating Medicines and Medical Devices

Coronavirus Vaccine - summary of Yellow Card reporting

Data included: 09/12/2020 to 24/01/2021

This information is also available on the gov.uk website

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Summary

At the time of this report, more than 100,000 people across the UK have died within 28 days of a positive test for coronavirus (COVID-19). Rates of COVID-19 infection and hospitalisation remain high.

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.

Two COVID-19 vaccines, Pfizer/BioNTech and AstraZeneca/Oxford vaccines, are currently being used in the UK. Both 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, both vaccines showed very high levels of protection against symptomatic infections with COVID-19. We expect data to be available soon 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.

The 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 (65 years and older) than in younger people.

The AstraZeneca/Oxford vaccine 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 MHRA's role is also to continually monitor 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 most 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 January 2021. At this date, an estimated 5.4 million first doses of the Pfizer/BioNTech vaccine and 1.5 million doses of the AstraZeneca/Oxford vaccine had been administered, and around 0.5 million second doses, mostly the Pfizer/BioNTech vaccine, had been administered.

As of 24 January 2021, for the UK, 16,756 Yellow Cards have been reported for the Pfizer/BioNTech, 6,014 have been reported for the AstraZeneca/Oxford vaccine, and 50 have been reported where the brand of the vaccine was not specified.

For both vaccines the overall reporting rate is around 3 Yellow Cards per 1,000 doses administered.

For both 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.

Severe allergy
On 9 December 2020, the MHRA issued preliminary guidance on severe allergic reactions after the Pfizer/BioNTech vaccine due to early reports of anaphylaxis. Following further detailed review, this advice was amended on 30 December to the current advice. This 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.

Widespread use of the vaccine now suggests that severe allergic reactions to the Pfizer/BioNTech vaccine are very rare (less than 1 in 10,000 people receiving this vaccine) and have been reported at a rate between 1 and 2 cases per 100,000 doses administered. Similar reporting was seen in the United States with the same vaccine. Anaphylaxis can also be a very rare side effect associated with most other vaccines.

Following very substantial exposure across the UK population, no other new safety concerns have been identified from reports received so far.

Conclusion

- The overall safety experience with both vaccines is so far as expected from the clinical trials
- Based on current experience, the expected benefits of both COVID-19 vaccines in preventing COVID-19 and its serious complications far outweigh any known side effects
- As with all vaccines and medicines, the safety of COVID-19 vaccines is being continuously monitored

Further information on the type of suspected adverse reactions (ADRs) reported for the COVID-19 mRNA Pfizer/BioNTech vaccine and the COVID-19 AstraZeneca/Oxford vaccine 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 has played 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 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 they both occurred around the same time. 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 mRNA Pfizer/BioNTech and the COVID-19 AstraZeneca vaccine is 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 coronavirus (COVID-19) vaccines (COVID-19 mRNA Pfizer/BioNTech and COVID-19 AstraZeneca vaccine), and MHRA's analysis of the data, **between 9 December 2020 and 24 January 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 7,164,387 people have received their first vaccination in UK by week ending 24 January 2021, with 474,156 second doses administered. The current priority groups of the immunisation campaign include people over the age of 70 years, care home residents and workers, and frontline health and social care workers.

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 January 2021.

Country	Number of doses
England	6,221,850
Wales	312,305
Northern Ireland	168,140
Scotland	462,092

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 January 2021.

Country	Number of doses
England	444,011
Wales	639
Northern Ireland	22,910
Scotland	6,596

As of 24 January, an estimated 5.4 million first doses of the Pfizer/BioNTech vaccine and 1.5 million doses of the AstraZeneca/Oxford vaccine, had been administered, and around 0.5 million second doses, mostly the Pfizer/BioNTech vaccine, had been administered.

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

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. 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 two vaccines**. All reports are kept under continual review in order to identify possible new risks.

Up to and including 24 January 2021, the MHRA received and analysed 16,756 UK Yellow Cards from people who have received the COVID-19 mRNA Pfizer/BioNTech vaccine. These reports include a total of 49,472 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 January 2021, the MHRA received and analysed a total of 6,014 UK reports of suspected ADRs to the COVID-19 AstraZeneca/Oxford vaccine. These reports include a total of

21,032 suspected reactions (a single report may contain more than one symptom). The first report was received on 4 January 2021. To note, administration of the AstraZeneca/Oxford vaccine only began on 4 January 2021, which accounts for the smaller numbers of reports compared to the Pfizer/BioNTech vaccine so far.

Additionally, up to and including 24 January 2021, the MHRA received 50 Yellow Card reports where the brand of vaccine was not specified by the reporter.

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 Yellow Cards per 1,000 doses administered for both vaccines. It is known from the clinical trials that the more common side effects for both 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 MHRA's main roles is to continually monitor 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 vaccine 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 national epidemic, and because most of the millions of people offered the vaccine in this early phase of a vaccination campaign are elderly and/or have 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. 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, and this is discussed below.

We also take into account the international experience based on data from other countries using the same vaccines.

Overall safety

As with any vaccine, the COVID-19 vaccines will cause side effects in some people. The total number and the nature of Yellow Cards reported 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 both 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 both 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.

Comments on specific reports

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

Anaphylaxis (Severe allergic reactions)

The MHRA has received 101 UK spontaneous adverse reactions associated with anaphylaxis or anaphylactoid reactions with the Pfizer/BioNTech vaccination. All patients have recovered from the anaphylaxis episode. Thirteen reports of anaphylaxis have been received for the COVID-19 AstraZeneca/Oxford vaccine.

On 9 December 2020, following receipt of two reports, the MHRA took immediate precautionary action and issued advice that people with a history of anaphylaxis to any medicine, vaccine or food should not receive the Pfizer/BioNTech vaccine. However, following review of further data by the Commission on Human Medicines (CHM), updated guidance was issued on 30 December 2020 stating that only those with a previous history of allergic reactions to the ingredients of the vaccine should not receive it. This advice was added to the information for healthcare professionals and UK recipients about the Pfizer/BioNTech vaccine. Widespread use of the vaccine now suggests that severe allergic reactions to the Pfizer/BioNTech vaccine are very rare, reported at a rate between 1 and 2 cases per 100,000 doses administered. Similar reporting was seen in the United States with the same vaccine. Anaphylaxis can also be a very rare side effect to most other vaccines.

Bell's Palsy

Up to the 24 January 2021 the MHRA have received 69 reports of facial paralysis or paresis with Pfizer/BioNTech vaccine. This is currently listed as a possible side effect in the Pfizer/BioNTech vaccine based on a small number of reports in the trials, but because this can also occur naturally an association with the vaccine is not yet confirmed. Six reports of facial paralysis have been received for the COVID-19 AstraZeneca/Oxford vaccine.

As well as individual clinical review of such reports, we are analysing these against the number of reports we would expect to occur in the absence of vaccination (the 'natural rate'). Based on this review, 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.

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 event in the days and weeks after vaccination. A high proportion of people vaccinated in the vaccination campaign so far are very elderly, many of whom will also have 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 107 UK reports of suspected ADRs to the Pfizer/BioNTech vaccine in which the patient died shortly after vaccination, 34 reports for the AstraZeneca/Oxford vaccine and 2 where the brand of vaccine was unspecified. The majority of these reports were in elderly people or people with underlying illness. Review of individual reports and patterns of reporting does not suggest the vaccine played a role in the death.

A range of other isolated or series of reports of non-fatal, serious suspected ADRs have been reported. These all remain under continual review, including through 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, more than 100,000 people across the UK have died within 28 days of a positive test for coronavirus. Rates of COVID-19 infection and hospitalisation remain high.

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 Pfizer/BioNTech and AstraZeneca/Oxford COVID-19 vaccines have demonstrated very high levels of protection against symptomatic infection. We expect data to be available soon on the impact of the vaccination campaign in reducing infections and illness with COVID-19 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 so far 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.

Following very substantial exposure across the UK population, no other new safety concerns have been identified from reports received to date, and for the cases of other medical conditions reported in temporal association with vaccination, the available evidence does not currently suggest that the vaccine caused the event.

The overall safety experience with both vaccines is so far as expected from the clinical trials. 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 a 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 Profile contains a complete listing of all suspected adverse reactions or that have been reported to the MHRA via the Yellow Card scheme for the COVID-19 mRNA Pfizer/BioNTech vaccine. 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 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.

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.

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.

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.

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.

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

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.