HPRA
An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

HPRA Safety Update

COVID-19 Vaccines, Overview of National Reporting Experience

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Highlights from this HPRA safety update

- Up to 11 February, a total of 2103 reports of suspected side effects were notified to the HPRA.
- The cumulative total doses of COVID 19 vaccines administered as of that date was reported as 171,239 (dose 1) and 89,834 (dose 2),[1] with administration of COVID-19 Vaccine AstraZeneca® commencing 8 February.
- For all COVID-19 vaccines, the most commonly reported suspected side effects notified to the HPRA are in line with those typically associated with vaccination, including the types of side effects described in COVID-19 vaccine product information.[2]
- National reporting experience to date continues to support the favourable assessment that the benefits of COVID-19 vaccines outweigh the risks.
- The European Medicines Agency (EMA) commenced publication of safety updates for the vaccines in January, with the first safety update for COVID-19 Vaccine Moderna® published on 5 February. No changes to the recommended use of the vaccine were made following this review.[2]

Understanding the data presented within this safety update

This update includes an overview of reports of ***suspected side effects*** notified to the HPRA safety monitoring system and is provided as an enhanced transparency measure for members of the public and healthcare professionals.

Reports included in the overview are those notified to the HPRA on a voluntary basis by healthcare professionals and members of the public, with reporting of suspected side effects to COVID-19 vaccines (www.hpra.ie/report) encouraged. Reports received by the HPRA from the company (i.e. the licence holder, to date, BioNtech, Moderna, Astra Zeneca) responsible for the vaccine are also included within this update. This overview provides an up-to-date summary of national reporting experience.

[1] https://covid19ireland-geohive.hub.arcgis.com/
[2] COVID-19 vaccine safety update for Covid-19 vaccine Moderna: February 2021 (europa.eu)

However, it is important to understand that conclusions on the safety of a vaccine cannot be drawn based on the information provided, given well-established and known limitations in interpreting such data in isolation, examples of which are described below.

Causation

- The HPRA receives reports based on ***suspicion*** that an adverse experience may be associated with vaccination. This does not mean the vaccine ***caused*** the adverse experience**.** As such, these are referred to as ***"suspected"*** side effects.
- Reports may describe coincidental events, which have occurred post-vaccination, but would have occurred even if vaccination had not taken place (e.g. they may be due to an underlying medical condition, or be signs and symptoms of another illness).
- Each individual report is carefully reviewed, however, the totality of data from all sources (e.g. clinical and epidemiological studies and literature) must be considered as part of ongoing safety monitoring to ensure ***evidenced based conclusions*** are drawn.

Number/volume

- As the HPRA system is based on voluntary reporting, ***not all*** suspected side effects will be reported. As such, the number and types of reports notified can vary for a variety of reasons.
- An increased number of reports is expected for COVID-19 vaccines, given public interest as well as HPRA calls encouraging reporting. This is known as ***stimulated reporting***.
- A single report may describe more than one suspected side effect in an individual (e.g. headache and nausea reported together), therefore, the number of side effects may exceed the total number of reports received.

Comparisons

- The type and number of reports received for different COVID-19 vaccines are ***not directly comparable*** as, for example, the vaccines have not been used in the vaccination programme for the same length of time, and will have been administered to different numbers of people, with different underlying medical conditions and across different settings.
- Each vaccine is authorised on the basis that its benefits-risk profile has and continues to be favourable.

Changes to data over time

- The description of suspected side effects in this update reflects available information known at the time by the HPRA. These data may undergo changes as more information about individual reports becomes available through follow-up, and as more data are reported and evaluated.

For these reasons, the information in this report is not sufficient in isolation to draw conclusions on the safety profile of a vaccine. Like all vaccines, some side effects are to be expected, with the vast majority mild or moderate in intensity and resolving within a few days. Vaccines are approved for use on the basis of robust scientific evidence that demonstrates their benefits outweigh any risks.

Always refer to the product information for information on the established safety profile, including known side effects of a COVID-19 vaccine.

This includes the Package Leaflet (for members of the public) and Summary of Product Characteristics (for healthcare professionals)

Product information is accessible from
www.hpra.ie/homepage/medicines/covid-19-updates

Authorised COVID-19 vaccines

COVID-19 vaccines currently authorised for use in the European Union by the European Medicines Agency include:

- Comirnaty® (licence holder: BioNTech), granted conditional marketing authorisation on 21 December 2020. For further information on this vaccine click here.
- COVID-19 Vaccine Moderna® (licence holder: Moderna), granted conditional marketing authorisation on 6 January 2021. For further information on this vaccine click here.
- COVID-19 Vaccine AstraZeneca® (licence holder: Astra Zeneca), granted conditional marketing authorisation on 29 January 2021. For further information on this vaccine click here.

Overview of suspected side effect reports

Up to 11 February, the HPRA received 2103 reports[3] in association with COVID-19 vaccines, as follows:

Comirnaty® and COVID-19 Vaccine Moderna® (mRNA vaccines)	2021
COVID-19 Vaccine AstraZeneca®	66
Brand unknown/not specified	16

Commonly reported suspected side effects (reported as 1% or more of all suspected side effects) are as follows:

mRNA vaccines (Comirnaty® and COVID-19 Vaccine Moderna®)
▪ Dizziness, headache, insomnia ▪ Enlarged lymph nodes ▪ Injection site pain ▪ Joint pain, muscle pain, pain in limbs, general pain ▪ Nausea, vomiting ▪ Numbness, tingling/pins and needles ▪ Weakness, tiredness, feeling unwell, chills, fever/feeling hot, sweating

[3] A single report may contain more than one suspected side effect for an individual (e.g. rash and hives reported together). Therefore, the total number of suspected side effects will exceed the total number of reports.

COVID-19 Vaccine AstraZeneca®
▪ Dizziness, headache ▪ Injection site pain ▪ Joint pain, muscle pain, pain in limbs, back pain ▪ Nausea, vomiting ▪ Weakness, tiredness, feeling unwell, chills, fever/feeling hot, sweating

These reports are consistent with the types of events typically observed following vaccination, including those described in the vaccine package leaflet. The majority were mild to moderate in nature and had resolved/were resolving at the time of reporting.

Further points of interest regarding the reports received are described below.

Reports of Allergic type reactions

- The HPRA continues to closely review reports of allergic type reactions, however, no new information on this known side effect has been revealed since the last safety update.
- In relation to mRNA vaccines, and based on currently available information, a small number of reports (less than 5) have been classified by the HPRA as anaphylaxis, which is a serious allergic reaction. In all cases, the individuals concerned were reported to have recovered.
- Anaphylaxis is a known side effect, with information on managing this risk described in the product information. As for all vaccines, COVID-19 vaccines should be administered under close supervision with appropriate medical treatment available in case of such a reaction.
- The most recent review of this matter by EMA's safety committee was for the COVID-19 Vaccine Moderna, and followed a number of reports of suspected allergic reactions from a single vaccination site in the United States. The outcome of this review was published 5 February and no changes to the recommended use of the vaccine were made.[2]
- As reported in the 2nd HPRA safety update,[4] a frequency estimate appropriate for the vaccine product information in the EU remains under review by EMA's safety committee.

Reports of facial paralysis/facial palsy

- Temporary facial paralysis is described in the product information for mRNA vaccines as a rare possible side effect.
- The HPRA has received 13 reports associated with mRNA vaccine, describing signs and symptoms of facial paralysis, including suspected cases of Bell's Palsy (a temporary weakness/paralysis of one side of the face).
- Of these, a number had resolved or were ongoing for approximately one week at the time of reporting. Further follow up for outstanding information is ongoing for incomplete reports.
- The overall number of these reports is relatively small, as would be expected for a rare possible side effect.
- The EMA Safety Committee continue to monitor reports of facial paralysis and any relevant updates arising from these reviews will be provided.

[4] safety-update-covid-19-vaccines-overview-of-national-reporting-experience-(04022021).pdf (hpra.ie)

Reports of deaths following vaccination

- The second HPRA safety update included an overview of national reports as well as the outcome of a review by the EMAs Safety Committee for Comirnaty® and suspected side effects with a fatal outcome in individuals of any age. This review concluded that the data did not show a link to vaccination with Comirnaty® and therefore did not raise a safety concern.[4]
- Since that update, the HPRA has received a small number of additional national reports. In total, 12 reports have been received describing elderly patients who passed away following vaccination. In all cases, the patients had underlying conditions and/or concurrent illness, with a small number having tested positive for COVID-19.
- All reports have been carefully reviewed and based on the information provided it is not considered that the vaccine played a contributory role in these events. It can be expected that fatalities due to progression of underlying disease or natural causes will continue to occur, including following vaccination, however, this does not mean that the deaths were caused by the vaccine.

Reports of systemic events

- In a small number of cases received, reporters have commented on an impact on normal daily activities within the day(s) following vaccination, due to expected systemic events, such as fatigue, headache, muscle pain, chills, joint pain and fever.
- Systemic events post vaccination are common, in particular in younger populations, with the vast majority mild to moderate in nature and usually resolve within a few days of vaccination.
- Systemic events may occur after either dose, with some differences in intensity and frequency observed after the first and second dose in clinical trials. Refer to the specific vaccine product information for further details.

All reports received, including those not specifically described within this update, are subject to ongoing close monitoring as described in the next section.

Background information on the evaluation of suspected side effect reports

As for all medicines and vaccines, suspected side effect reports in association with COVID-19 vaccines submitted to the HPRA are recorded and stored on the HPRA's national adverse reactions database. They are subsequently submitted (with any personal identifiers and contact details removed) to the EudraVigilance database operated and managed by the European Medicines Agency (EMA). EudraVigilance provides for the transfer of reports from national regulatory agencies such as the HPRA and marketing authorisation holders to the EMA, and supports early detection and monitoring of possible safety signals in relation to reported side effects.

The EMA also make available anonymised information on all reports, based on global safety experience, publically available through the following link www.adrreports.eu and regularly publish recommendations made by the EMA Safety Committee (www.ema.europa.eu).

Information from side effect reports, together with additional safety data (e.g. from the scientific literature, cumulative safety data analysis, epidemiological studies etc.) are assessed on an on-going basis, in conjunction with our EU counterparts to consider their impact on the known safety profile of the COVID-19 vaccines and any need for regulatory changes to support safe and appropriate use.

Partially anonymised details of reports are also shared with other bodies also involved in safety monitoring of medicines, in accordance with the legislative provisions, including GDPR (please see

the HPRA privacy statement here). These bodies include the World Health Organisation (WHO) and as appropriate, the company(ies) that hold the licence(s) for the medicine(s) concerned (i.e. marketing authorisation holders or 'MAHs'). Sharing of this information ensures that the information is available to all parties responsible for the ongoing safety monitoring of medicines.

Further information to support interpretation of the data provided in this update is available here