HPRA
An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

2nd HPRA Safety Update

COVID-19 Vaccines, Overview of National Reporting Experience

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Highlights from the 2nd HPRA safety update

- Up to 28 January, a total of 740 reports of suspected side effects were notified to the HPRA.
- Up to 27 January, the cumulative total doses of COVID 19 vaccines administered was reported as 147,700 (dose 1) and 13,800 (dose 2).[1]
- Of the reports notified to the HPRA, the most commonly reported suspected side effects 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 any risks.
- The European Medicines Agency (EMA) published its first safety update on the COVID-19 vaccine, Comirnaty®, on 29 January.[3] This update concluded that the safety data collected for Comirnaty® to date is consistent with the known safety profile of the vaccine and there were no changes to the recommended use of the vaccine.

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. Reporting of all suspected side effects to COVID-19 vaccines (www.hpra.ie/report) is encouraged. Any reports received by the HPRA from the companies concerned (i.e. the licence holder, to date, BioNtech, Moderna and 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] https://www.hpra.ie/homepage/medicines/covid-19-updates/covid-19-vaccines-product-information

[3] https://www.ema.europa.eu/en/news/first-covid-19-vaccine-safety-update-published

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. *Note; this vaccine was not used in Ireland at the time of this update.*

Overview of suspected side effect reports

Up to 28 January, the HPRA received 740 reports in association with approved COVID-19 vaccines.[4]

Overall, the national reporting experience to date supports the favourable benefit/risk profile.

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

- Dizziness, headache
- Numbness, tingling/pins and needles, sensitive skin
- Weakness, tiredness, feeling unwell, chills, fever
- Itchiness, rash, hives
- Nausea, diarrhoea, vomiting
- Joint pain, muscle pain, pain in limb
- Injection site pain, injection site redness
- Enlarged lymph nodes

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

Further points of interest are described below.

Reports following the 2nd dose of vaccine

- The HPRA has started to receive reports following the 2nd dose of vaccination, with a small number including comment on the impact of otherwise mild and moderate reactions on normal daily activities.
- These effects are not unexpected and are in line with the known safety profile for Comirnaty® with systemic events (such as fatigue, headache, muscle pain, chills, joint pain and fever) observed to occur at an increased frequency and/or intensity after the 2nd dose, in particular in younger age groups.[5]

Reports of Allergic type reactions

- Reports describing signs and symptoms of allergic type reactions have been received. As described in the first HPRA safety update, these reactions include itchy rash, throat tightness and/or swelling of the face or tongue.
- In some cases, medical treatment and/or clinical observation of the individual for a period of time was needed. Based on the available information, the HPRA has classified a small number of these reports as anaphylaxis, which is a serious allergic reaction. In all cases, the individuals concerned recovered.
- The EMA's safety committee continues to monitor reports of anaphylaxis, however, no new aspects were identified from the most recent review for Comirnaty®[3]. It was noted that anaphylaxis is a known side effect, with information on managing the risk already available in product information. A recent analysis in the US which estimated a frequency of anaphylaxis of approximately 11 cases per million doses of Comirnaty® was noted.[6] A frequency estimate appropriate for the EU product information remains under review.
- As for all vaccines, COVID-19 vaccines should be administered under close supervision with appropriate medical treatment available in case of such a reaction.

Reports of facial paralysis/facial palsy cases

- Since the 1st HPRA safety update, monitoring and follow up is ongoing on the small number of reports received, however, no further relevant information is available at this time.

Reports of deaths following vaccination

- Given concerns which arose from Norway about deaths reported in frail elderly individuals after vaccination with Comirnaty®, the EMA's Safety Committee reviewed available reports of suspected side effects with fatal outcome in individuals of any age. This review did not suggest a safety concern.[3]
- In many reports, the individuals involved were above 65 years of age, and progression of (multiple) pre-existing diseases seemed to be a plausible explanation for death. In some individuals, palliative care had already been initiated before vaccination.
- Similarly, the HPRA has also received a small number of reports of elderly patients, who had underlying conditions and passed away following vaccination. These reports have been carefully reviewed and based on the information provided, have not raised any concern regarding the safe use of Comirnaty® in this population.
- 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 it was caused by the vaccine. As can be seen from the EMA review, in which the HPRA participated, all such reports are carefully evaluated as part of the close safety monitoring performed by regulatory authorities, and the outcome of this thorough review did not suggest a safety concern.

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[4] Of these, two reports were made for which the brand of vaccine was unknown. 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.

[5] European Public Assessment Report (EPAR) for Comirnaty® available from the EMA website https://www.ema.europa.eu/en/medicines/human/EPAR/comirnaty

[6] Centres for Disease Control and Prevention (CDC) COVID-19 Response Team, Food and Drug Administration: Allergic Reactions Including Anaphylaxis After Receipt of the First Dose of PfizerBioNTech COVID-19 Vaccine: United States, December 14–23, 2020. MMWR. 2021; 70 (2): 46-52 (epub 6 Jan 2021).

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 global safety reporting 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.