

Summary of MHRA's regulatory position for specified events reported with COVID-19 Vaccine Pfizer/BioNTech, COVID-19 Vaccine AstraZeneca and COVID-19 Vaccine Moderna

Issue

The MHRA has been requested by the NHS Business Services Authority to provide an update on the current regulatory position regarding COVID-19 vaccination and:

- Bell's Palsy
- Brachial neuritis
- Transverse Myelitis
- Optic neuropathy
- Functional neurological disorder

Summaries of current MHRA position

The following summaries concern the COVID-19 vaccines previously or currently used in the UK vaccination programme (number of doses administered in UK as of 23 August 2022¹):

- Pfizer/BioNTech COVID-19 vaccine (approximately 83 million doses)
- Moderna COVID-19 vaccine (approx. 12.7 million doses)
- AstraZeneca COVID-19 vaccine (approx. 49.2 million doses)

Overall, since December 2020, over 151 million COVID-19 vaccines have been administered to over 93% of the UK population aged over 12 years.

Bell's Palsy

Bell's Palsy (BP) is considered an Adverse Event of Special Interest (AESI) for COVID-19 Vaccine Pfizer/BioNTech, COVID-19 Vaccine AstraZeneca and COVID-19 Vaccine Moderna. Reports of suspected BP following vaccination with these COVID-19 vaccines have been continuously reviewed by the MHRA. Whilst reports of BP following vaccination with the aforementioned COVID-19 vaccines are rare, evidence based on the latest available data shows that there may be an increased risk of BP following vaccination with these COVID-19 Vaccines. To raise awareness of this potential adverse event amongst healthcare professionals and patients, facial paralysis has been included in the product information for COVID-19 Vaccine AstraZeneca (Facial paralysis), COVID-19 Vaccine Pfizer/BioNTech (Acute peripheral facial paralysis) and COVID-19 Vaccine Moderna (Acute peripheral facial paralysis).

Brachial neuritis

Brachial neuritis also known as Parsonage-Turner syndrome is a peripheral neuropathy and would therefore be included under the broad AESI of peripheral neuropathies. Causes of brachial neuritis has been postulated to include a variety of mechanisms including trauma/compression, autoimmune responses, direct viral infection or microvascular ischaemia. Additionally, it has been noted in post-vaccination setting although aetiology and pathophysiology remain unclear. Given the ongoing pandemic, concurrent COVID-19 infection acts as a possible confounder in the event of vaccination.

¹ [Coronavirus vaccine - summary of Yellow Card reporting - GOV.UK \(www.gov.uk\)](https://www.gov.uk/government/news/coronavirus-vaccine-summary-of-yellow-card-reporting)

Brachial neuritis is associated with the Medical Dictionary for Regulatory Activities (MedDRA) terms, neuralgic amyotrophy and radiculitis brachial.

COVID-19 Vaccine Pfizer/BioNTech

Brachial neuritis is currently not recognised as an undesirable effect of COVID-19 vaccine Pfizer/BioNTech. Up to and including 24th August 2022, 19 suspected ADR reports of the term radiculitis brachial have been received following Pfizer vaccination, and 13 reports of neuralgic amyotrophy. Brachial neuritis and similar terms, including more overarching peripheral neuropathies, have not been reviewed previously by the MHRA. Due to the low numbers of spontaneous reports, no further assessment or regulatory action has been considered.

COVID-19 Vaccine AstraZeneca

Brachial neuritis is not currently recognised as an undesirable effect for COVID-19 Vaccine AstraZeneca. The MHRA has received 33 suspected ADR reports of radiculitis brachial and 11 reports of neuralgic amyotrophy with COVID-19 Vaccine AstraZeneca. Peripheral neuropathies including brachial neuritis have not been reviewed by the MHRA. Due to low spontaneous report numbers of brachial neuritis and neuralgic amyotrophy, no further assessment or regulatory action has been considered.

COVID-19 Vaccine Moderna

Brachial neuritis is not currently recognised as an undesirable effect for COVID-19 Vaccine Moderna. The MHRA has received four reports of radiculitis brachial and four reports of neuralgic amyotrophy with COVID-19 Vaccine Moderna. Peripheral neuropathies including brachial neuritis have not been reviewed by the MHRA for COVID-19 Vaccine Moderna. Due to low spontaneous report numbers of brachial neuritis and neuralgic amyotrophy, no further assessment or regulatory action has been considered.

Transverse myelitis

Transverse myelitis (TM) is an inflammation of both sides or one section of the spinal cord. This is known to be associated with a number of viruses, such as the herpes and influenza virus and is an AESI for all COVID-19 vaccines. The MHRA has continually monitored reports of suspected transverse myelitis following COVID-19 vaccination since the start of the vaccination programme.

COVID-19 Vaccine AstraZeneca

The risk of TM was assessed in October 2021 with COVID-19 Vaccine AstraZeneca. The totality of the evidence available at the time of this review suggested a possible causal association with this COVID-19 vaccine. Due to the serious nature of this adverse event and as a precaution, the product information has been updated to raise healthcare professionals' and patients' awareness of the signs and symptoms associated with TM which may include muscle weakness, localised or radiating back pain, bladder and bowel symptoms and changes in sensation.

Up to and including 24 August 2022, the MHRA has received 128 reports of TM following COVID-19 Vaccine AstraZeneca. There were no reports received with a fatal outcome following suspected TM. Whilst the incidence rate of this adverse event with any of the COVID-19 vaccines used in the UK remains extremely rare (less than 1 report per 100,000 doses of each vaccine), the available evidence reviewed by the MHRA suggests an association between TM and COVID-19 Vaccine AstraZeneca is possible.

COVID-19 Vaccine Pfizer/BioNTech

TM is not currently recognised as an undesirable effect for COVID-19 Vaccine Pfizer/BioNTech. A review of TM was undertaken by the MHRA in October 2021 and presented to the COVID-19 vaccine Expert Working Group (EWG) for consideration. The EWG agreed with the Agency's assessment and conclusions of the data presented for COVID-19 Vaccine Pfizer/BioNTech that at the current time, no regulatory action was needed but should continue to be closely monitored. At the time of this review, the Agency was in receipt of 27 suspected ADR reports where a notable proportion were considered as potentially confounded by factors including prior COVID infection, concurrent medication conditions including cancer, rheumatoid arthritis or spinal conditions. It was noted that reports of TM were not represented in the Pfizer/BioNTech clinical trials. Similarly, review of the Pfizer assessment of TM did not indicate a clear causal association noting background expected levels of new incidence was greater than what was being observed as possible new cases.

Up to and including the data lock point 24th August 2022, the Agency was in receipt of 40 suspected reports of TM following vaccination with COVID-19 Vaccine Pfizer BioNTech and the MHRA continues to keep this event under review. No clear mechanism has been proposed for TM however it is considered that vaccinations in the past have been associated with TM onset in addition to the conservative approach to include TM for COVID-19 Vaccine AstraZeneca, however, the totality of the evidence for COVID-19 Vaccine Pfizer/BioNTech is considered weak and no regulatory action has been implemented.

COVID-19 Vaccine Moderna

The risk of transverse myelitis was assessed in October 2021 with this COVID-19 vaccine and the current evidence does not suggest a causative link with COVID-19 Vaccine Moderna. At the time of this review, the MHRA had received one ADR report concerning transverse myelitis with COVID-19 Vaccine Moderna. Up to and including 24 August 2022, the MHRA has received seven reports of transverse myelitis with COVID-19 Vaccine Moderna and continues to keep this event under close review. As of the data lock point 25 November 2020, there were no cases of transverse myelitis reported in clinical trials with the Moderna vaccine.

Optic neuropathy

Optic neuropathy is damage to the optic nerve and is suspected to be often caused by concurrent infection, both bacterial and viral, noting it as a likely rare complication of COVID-19 infection itself. Optic neuritis refers to inflammation of the optic nerve and is an AESI for COVID-19 vaccines

COVID-19 Vaccine Pfizer/BioNTech

Optic neuropathy is not currently recognised as an undesirable effect for COVID-19 vaccine Pfizer/BioNTech. Optic nerve neuropathy was included as an event considered for analysis when reviewing COVID-19 Vaccine Pfizer/BioNTech and optic neuritis and taken for advice to the EWG in October 2021, however no reports with optic neuropathy as the specified term have been received. Following consideration of the evidence presented by the MHRA, including Yellow Card data, clinical trial data and data presented by the MAH, no regulatory action was recommended by the EWG, although continued close monitoring was advised. Up to and including 24th August 2022, the Agency has yet to receive reports detailing this specific term. Similar terms reported include optic neuritis which returned 46 reports and 2 reports for neuromyelitis optica spectrum disorder. Optic conditions of this nature are under review by the Agency however the current evidence does not suggest a causative link between optic neuritis and COVID-19 Vaccine Pfizer/BioNTech.

COVID-19 Vaccine AstraZeneca

Similarly, optic neuropathy is not currently recognised as an undesirable effect for COVID-19 vaccine AstraZeneca. In the review conducted in October 2021, similar conclusions of no regulatory action were endorsed by the EWG. It was noted that there was not strong evidence of causal association presented by the low numbers of reports pertaining to optic neuropathy, and these reports were sparse and lacking in diagnostic detail. This conclusion was similarly drawn across the associated PTs of optic neuritis, optic nerve disorder and optic nerve injury. Data concerning optic neuritis, and subsequently optic neuropathy, was recommended to be continued to be closely monitored going forward including following up for clinical detail surrounding presence of aquaporin-4- and MOG-antibodies to help with diagnostic certainty. Up to and including 24th August 2022, the Agency is in receipt of 11 reports of optic neuropathy and 67 reports of optic neuritis. Optic conditions of this nature are under review by the Agency however the current evidence does not suggest a causative link between optic neuritis/optic neuropathy and COVID-19 Vaccine AstraZeneca.

COVID-19 Vaccine Moderna

Up to and including 24 August 2022, the MHRA has received five reports of optic neuritis with COVID-19 Vaccine Moderna. Optic neuritis with COVID-19 Vaccine Moderna was reviewed in October 2021, at this time there was no evidence of a possible increased risk of optic neuritis following vaccination. At the time of this review, the MHRA had received two ADR reports of optic neuritis. Up to the DLP of 25 November 2020, no clinical trial reports of optic neuritis have been reported with Moderna vaccine. The current evidence does not suggest a causative link between optic neuritis and COVID-19 Vaccine Moderna.

Functional neurological disorder

Functional neurological disorder (FND, also referred to as ‘conversion disorder’) is a condition which relates to function disorder rather than structural disorders, differentiating it from multiple sclerosis and stroke. As it can present as a wide range of neurological symptoms, there is an expected element of possible under-reporting. Historically, FND has often been a diagnosis of exclusion but more recent considerations mean a diagnosis can be more confidently made in an inclusionary manner by identifying neurological signs that are specific to FNDs without reliance on presence or absence of psychological stressors or suggestive historical clues².

FND is not currently recognised as an AESI or undesirable effect of any of the COVID-19 vaccines. Assessment of the available evidence concerning COVID-19 vaccines and FND in July 2021 concluded there was no association between the COVID-19 vaccines and FND.

COVID-19 Vaccine Pfizer/BioNTech

FND has previously been reviewed and taken for advice to the EWG in July 2021 following an increase in concern following COVID-19 vaccination identified via social media. At the time of the review, 7 reports of suspected FND were received, but as noted above, the wide range of presenting neurological symptoms may lend itself to under-reporting and differential diagnoses. The EWG concluded that reporting rate was low compared to background rate in the general population. Consideration was given to the difficulties in accurately diagnosing FND due to the various tests required to diagnose FND and exclude other causes. Similarly, it was discussed that FND was poorly understood so establishing causality would be difficult. Up to and including 24th August 2022, the Agency is in receipt of 36 reports of the term ‘Conversion disorder’ following vaccination with

² <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7293766/>

COVID-19 vaccine Pfizer/BioNTech, 32 of which were reported by members of the public, so medical confirmation cannot be assumed. As such, no immediate regulatory action was proposed.

COVID-19 Vaccine AstraZeneca

A total of 47 suspected reports having been received following COVID-19 vaccine AstraZeneca up to the same data lock point. Similarly, the majority of reports are received by members of the public (44 out of 47). It is suspected that there is an element of stimulated reporting regarding the receipt of these cases.

COVID-19 Vaccine Moderna

A total of five reports have been received following COVID-19 Vaccine Moderna by the Agency up to the same data lock point, all of which were reported by members of the public.

Conclusion

Of the five events for which a summary of the UK regulatory position was requested, only Bell's palsy (for all 3 COVID-19 vaccines used in the UK) and transverse myelitis (for COVID-19 vaccine AstraZeneca) have been included as undesirable effects in the respective product information on the basis of available evidence suggesting a possible link. For optic neuropathy, brachial neuritis and functional neurological disorder, links have not been established with any of the COVID-19 vaccines used in the UK to date.

MHRA

12 September 2022

Review of regulatory summary

There has been no change to the regulatory position on these conditions.

MHRA

12 August 2024