ROYAL COLLEGE OF PHYSICIANS OF IRELAND

National Immunisation Advisory Committee

RECOMMENDATIONS FOR THE USE OF COVID-19 VACCINE ASTRAZENECA®

NIAC | 19.03.2021

Request for National Immunisation Advisory Committee advice

On 14 March 2021, the National Immunisation Advisory Committee (NIAC) recommended the temporary deferral of the administration of COVID-19 Vaccine AstraZeneca®. This document presents updated evidence relating to the safe use of COVID-19 vaccine AstraZeneca® and provides advice in respect of the use of this vaccine in Ireland.

Background

The decision to temporarily defer administration of COVID-19 Vaccine AstraZeneca® followed notification by the Health Products Regulatory Authority (HPRA) of a new safety alert from the Norwegian Medicines Agency on Saturday 13 March 2021. The alert related to four reports of serious, rare thromboembolic (clotting) events, including some complicated by thrombocytopenia (low platelet count) in adults under 65 years of age after vaccination with COVID-19 Vaccine AstraZeneca®.

NIAC, after discussion with representatives from the HPRA, Health Service Executive (HSE) and Department of Health (DOH), reviewed this new information in light of an ongoing investigation by the European Medicines Agency (EMA) into earlier reports from Austria and Denmark of serious, complicated thromboembolic events following vaccination with COVID-19 Vaccine AstraZeneca®.

On 11 March 2021 the EMA stated that "there is currently no indication that vaccination has caused these conditions" and that "the vaccine's benefits continue to outweigh its risks and the vaccine can continue to be administered while investigation of cases of thromboembolic events is ongoing".

On 14 March 2021 the NIAC recommended temporary deferral of the administration of COVID-19 Vaccine AstraZeneca® based on the additional events from Norway reported after the initiation of the EMA review, pending receipt of further evidence and the conclusion of the EMA review.

To date, no reports of serious clotting events associated with low platelets have been notified to the HPRA. Over 129,000 doses of COVID-19 Vaccine AstraZeneca® have been given in Ireland.

Discussion

The EMA Pharmacovigilance Risk Assessment Committee (PRAC) conducted a rigorous investigation following reports of blood clots following COVID-19 Vaccine AstraZeneca®. To date, 20 million doses of the COVID-19 vaccine Astra Zeneca® have been administered within the UK and EEA and there is no concern that the vaccine is associated with any overall increased risk of blood clotting events.

On 18 March 2021 the EMA concluded their preliminary review and confirmed that

- The benefits of the vaccine in combating the still widespread threat of COVID-19 (which itself results in clotting problems and may be fatal) continue to outweigh the risk of side effects
- The vaccine is not associated with an increase in the overall risk of thromboembolic events in those who receive it
- There is no evidence of a problem related to specific batches of the vaccine or to particular manufacturing sites
- However, the vaccine may be associated with very rare thromboembolic events associated with thrombocytopenia with or without bleeding, including cases of cerebral venous sinus thrombosis (CVST).

These are very rare events. Around 20 million people in the UK and EEA had received the vaccine by 16 March 2021. The EMA had received reports of only 7 cases of disseminated intravascular coagulation (DIC) and 18 cases of CVST, mostly in women under 55 years of age. A causal link with the vaccine is not proven and the preponderance of young women may simply reflect the targeting of healthcare workers for vaccination. However, because of the rarity of these events a possible association with the vaccine cannot be excluded and deserves further analysis.

The PRAC review involved experts in haematological disorders and other health authorities including the UK's Medicines and Healthcare products Regulatory Agency (MHRA). Overall, the number of thromboembolic events reported after vaccination, both in studies before licensing and in reports after rollout of vaccination campaigns (469 reports, 191 of them from the EEA), was lower than that expected in the general population. The PRAC confirmed that there is no increase in overall risk of thromboembolic events.

The PRAC stated that the vaccine's proven efficacy in preventing hospitalisation and death from COVID-19 outweighs the extremely small possibility of developing DIC or CVST. However, in light of its findings, patients should be aware of the remote possibility of such syndromes, and if symptoms suggestive of clotting problems occur patients should seek immediate medical attention and inform healthcare professionals of their recent vaccination. The EMA is updating the product information to include more information on these risks.

The PRAC is undertaking additional review of these risks, including looking at the risks with other COVID-19 vaccines, although no signal has been identified from monitoring so far. Close safety monitoring will continue and further studies are being instituted.

In determining the recommendations below, the NIAC met on a number of occasions, attended EU meetings and consulted a relevant expert on coagulation disorders from the National Coagulation Centre.

Recommendations

Recommendation 1
The administration of the COVID-19 Vaccine AstraZeneca® should be recommenced for use in all those aged 18 and over

Recommendation 2
Healthcare professionals and vaccine recipients should be informed that very rare, complicated thromboembolic events have been reported in a small number of people who have recently received COVID-19 Vaccine AstraZeneca®.

Recommendation 3
Healthcare professionals should be alert to the signs and symptoms of thromboembolism and/or thrombocytopenia and report any suspected adverse reactions to the Health Products Regulatory Authority.

Recommendation 4
Recipients of COVID-19 Vaccine AstraZeneca® should be advised to seek immediate medical attention if they develop symptoms such as shortness of breath, chest pain, leg swelling and/or persistent abdominal pain within weeks of vaccination. Additionally, anyone with neurological symptoms including severe or persistent headaches (particularly 3 or more days after vaccination) or blurred vision, or who develop petechiae or ecchymoses beyond the site of vaccination, should seek prompt medical attention. These rare events have usually occurred within 14 days of the COVID-19 Vaccine AstraZeneca®.

Recommendation 5
Healthcare professionals should seek early expert advice from the National Coagulation Centre about the specialised testing and treatment options for patients presenting with thromboembolic events that are associated with thrombocytopenia, (including Disseminated Intravascular Coagulation (DIC) or Cerebral venous sinus thrombosis (CVST)) occurring within weeks following vaccination with COVID-19 Vaccine AstraZeneca®.

These recommendations are based on current data and are subject to ongoing review.

DOH will be informed of any changes.

References

AstraZeneca statement. Published 14 March 2021. Update on the safety of COVID-19 Vaccine AstraZeneca https://www.astrazeneca.com/media-centre/press-releases/2021/update-on-the-safety-of-covid-19-vaccine-astrazeneca.html

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Appendix

Information for vaccine recipients

- COVID-19 Vaccine AstraZeneca is not associated with an increased overall risk of blood clotting disorders.
- There have been very rare cases of unusual blood clots accompanied by low levels of blood platelets (components that help blood to clot) after vaccination. The reported cases were almost all in women under 55 years of age. This may be due to vaccination of healthcare workers in this age group.
- Because COVID-19 can be so serious and is so widespread, the benefits of the vaccine far outweigh the risks of these very rare events.
- Seek prompt medical assistance and mention your recent vaccination if you get any of the following after receiving the COVID-19 Vaccine AstraZeneca:
    - breathlessness,
    - pain in the chest or stomach,
    - swelling or coldness in an arm or leg,
    - severe or worsening headache or blurred vision after vaccination,
    - persistent bleeding,
    - multiple small bruises, reddish or purplish spots, or blood blisters under the skin
- Remember, some people will experience mild flu-like symptoms including headache, chills, fever and/or muscle aches. These are common side effects of any COVID-19 vaccine. These usually appear within a few hours and resolve within one or two days.

Information for healthcare professionals

- Cases of thrombosis and thrombocytopenia, some presenting as mesenteric vein or cerebral vein/cerebral venous sinus thrombosis, have been reported in persons who had recently received COVID-19 Vaccine AstraZeneca, mostly occurring within 14 days after vaccination. The majority of reports involved women under 55 years of age, although this may reflect higher vaccination rates due to a large number of healthcare workers in this group.
- The number of reported complicated events exceeds those expected, and causality cannot be confirmed or excluded. However, given the rarity of the events, and the difficulty of establishing baseline incidence since COVID-19 itself is resulting in hospitalisations with thromboembolic complications, the strength of any association is uncertain.
- EMA concluded that the benefit-risk balance of the vaccine strongly favours continuing vaccination.
- Healthcare professionals are urged to be alert for possible cases of thromboembolism, DIC or CVST occurring in vaccinated individuals.
- Recipients should be warned to seek immediate medical attention for symptoms of thromboembolism, and especially signs of thrombocytopenia and cerebral blood clots such as easy bruising or bleeding, and persistent or severe headache, particularly beyond 3 days after vaccination.
- Healthcare professionals should seek early expert advice from the National Coagulation Centre about specialised testing and treatment options for any patients presenting with thromboembolism, Disseminated Intravascular Coagulation (DIC) or Cerebral venous sinus thrombosis (CVST) within weeks of vaccination with COVID-19 Vaccine AstraZeneca®.