REPUBLIC OF CYPRUS
MINISTRY OF HEALTH

Press release

COVID-19 Vaccine AstraZeneca: benefits still outweigh the risks despite possible link to rare blood clots with low blood platelets

EMA's safety committee, PRAC, concluded its preliminary review of a signal of blood clots in people vaccinated with COVID-19 Vaccine AstraZeneca at its extraordinary meeting of 18 March 2021. The Committee 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 blood clots (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 cases of blood clots associated with thrombocytopenia, i.e. low levels of blood platelets (elements in the blood that help it to clot) with or without bleeding, including rare cases of clots in the vessels draining blood from the brain (CVST).

These are rare cases – around 20 million people in the UK and EEA had received the vaccine as of March 16 and EMA had reviewed only 7 cases of blood clots in multiple blood vessels (disseminated intravascular coagulation, DIC) and 18 cases of CVST. A causal link with the vaccine is not proven, but is possible and deserves further analysis.

The PRAC involved experts in blood disorders in its review, and worked closely with other health authorities including the UK's MHRA which has experience with administration of this vaccine to around 11 million people. 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. This allows the PRAC to confirm that there is no increase in overall risk of blood clots. However, in younger patients there remain some concerns, related in particular to these rare cases.

The Committee's experts looked in extreme detail at records of DIC and CVST reported from Member States, 9 of which resulted in death. Most of these occurred in people under 55 and the majority were women. Because these events are rare, and COVID-19 itself often causes blood clotting disorders in patients, it is difficult to estimate a background rate for these events in people who have not had the vaccine. However, based on pre-COVID figures it was calculated that less than 1 reported case of DIC might have been expected by 16 March among people under 50 within 14 days of receiving the vaccine, whereas 5 cases had been reported. Similarly, on average 1.35 cases of CVST might have been expected among this age group whereas by the same cut-off date there had been 12. A similar imbalance was not visible in the older population given the vaccine.

The Committee was of the opinion that the vaccine's proven efficacy in preventing hospitalisation and death from COVID-19 outweighs the extremely small likelihood of developing DIC or CVST. However, in the 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. Steps are already being taken to update the product information for the vaccine to include more information on these risks.

The PRAC will undertake additional review of these risks, including looking at the risks with other types of COVID-19 vaccines (although no signal has been identified from monitoring so far). Close safety monitoring of reports of blood

clotting disorders will continue, and further studies are being instituted to provide more laboratory data as well as real-world evidence. EMA will communicate further as appropriate.

Information for patients

- 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.
- Because COVID-19 can be so serious and is so widespread, the benefits of the vaccine in preventing it outweigh the risks of side effects.
- However, 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,

please seek prompt medical assistance and mention your recent vaccination.

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, although some of this may reflect greater exposure of such individuals due to targeting of particular populations for vaccine campaigns in different Member States.

- The number of reported events exceeds those expected, and causality although not confirmed, cannot therefore be 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 considers that the benefit-risk balance of the medicine remains positive, and there is no association with thromboembolic disorders overall. However, steps will be taken to update the SmPC and package leaflet with information on cases of DIC and CVST that have occurred.
- 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.

A direct healthcare professional communication (DHPC) will be sent to healthcare professionals prescribing, dispensing or administering the medicine. The DHPC will also be published on a dedicated page on the EMA website.

More about the medicine

COVID-19 Vaccine AstraZeneca is a vaccine for preventing coronavirus disease 2019 (COVID-19) in people aged 18 years and older. COVID-19 is caused by SARS-CoV-2 virus. COVID-19 Vaccine AstraZeneca is made up of another virus (of the adenovirus family) that has been modified to contain the gene for making a protein from SARS-CoV-2. COVID-19 Vaccine AstraZeneca does not contain the virus itself and cannot cause COVID-19.

The most common side effects with COVID-19 Vaccine AstraZeneca are usually mild or moderate and improve within a few days after vaccination.

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More about the procedure

The review of thromboembolic events with COVID-19 Vaccine AstraZeneca was carried out in the context of a safety signal, under an accelerated timetable. A safety signal is information on a new or incompletely documented adverse event that is potentially caused by a medicine such as a vaccine and that warrants further investigation.

The review was carried out by EMA's Pharmacovigilance Risk Assessment Committee (PRAC), the Committee responsible for the evaluation of safety issues for human medicines. EMA's human medicine committee, CHMP, will now rapidly assess any necessary changes to the product information.

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Ministry of Health
18 March 2021