<xx June 2021>

VAXZEVRIA/COVID-19 Vaccine AstraZeneca: contraindication in individuals with previous capillary leak syndrome

Dear Healthcare Professional,

Please also refer to previous Direct Healthcare Professional Communications (DHPCs), <XX> March, <XX> April and <ZZ> May, 2021.

AstraZeneca AB in agreement with the European Medicines Agency and the <National Competent Authority> would like to inform you of the following:

Summary

- **Very rare cases of capillary leak syndrome (CLS) have been reported in the first days after vaccination with Vaxzevria. A history of CLS was apparent in some of the cases. A fatal outcome has been reported.**

- **Vaxzevria is now contraindicated in individuals who have previously experienced episodes of CLS.**

- **CLS is characterised by acute episodes of oedema mainly affecting the limbs, hypotension, haemoconcentration and hypoalbuminaemia. Patients with an acute episode of CLS following vaccination require prompt recognition and treatment. Intensive supportive therapy is usually warranted.**

The Vaxzevria Summary of Product Characteristics (SmPC) will be updated accordingly with this information.

Background on the safety concern

COVID-19 Vaccine AstraZeneca is indicated for active immunisation to prevent COVID-19 caused by SARS-CoV-2 in individuals 18 years of age and older.

Very rare cases of capillary leak syndrome (CLS) have been reported following vaccination with Vaxzevria, with an estimated reporting rate of one case for more than 5 million doses. A history of CLS was noted in some of the cases.

CLS is a rare disorder characterised by dysfunctional inflammatory response, endothelial dysfunction, and extravasation of fluid from the vascular space to the interstitial space leading to shock, haemoconcentration, hypoalbuminaemia and potentially consequent organ failure. Patients may present with a rapid swelling of the arms and legs, sudden weight gain and feel faint due to low blood pressure.

Some cases of systemic CLS reported in the literature have been triggered by COVID-19 infection. CLS occurs rarely in the general population with fewer than 500 cases described worldwide in the literature (National Organisation for Rare Disorders), however, it is likely that estimates are lower than the true event rates.

The European Medicines Agency has recommended an update to the product information of the Vaxzevria suspension for injection to reflect the current knowledge of the safety topic.

Call for reporting

Healthcare professionals should report any suspected adverse reactions associated with the use of Vaxzevria in accordance with the national spontaneous reporting system *<include the details (e.g. name, postal address, fax number, website address) on how to access the national spontaneous reporting system>*.

Please note the importance of reporting the vaccine product name and batch details.

Company contact point

<Contact point details for access to further information, including relevant website address(es), telephone numbers and a postal address (company contact point in the concerned EU MS should be included, respectively)>

Yours Faithfully

Medical Director of AstraZeneca AB

Communication Plan for Direct Healthcare Professional Communication

DHPC COMMUNICATION PLAN	
Medicinal product(s)/active substance(s)	VAXZEVRIA/COVID-19 Vaccine AstraZeneca suspension for injection (ChAdOx1-S [recombinant])
Marketing authorisation holder(s)	AstraZeneca AB
Safety concern and purpose of the communication	Capillary leak syndrome: To communicate addition of a contraindication, and information on the condition, including the need for prompt diagnosis and treatment.
DHPC recipients	General practitioners, specialists in internal medicine, haematology, emergency medicine, intensive care and vaccination centres. The target group should be further defined at national level, in agreement with the respective national competent authority.
Member States where the DHPC will be distributed	All EU member states where VAXZEVRIA/COVID-19 Vaccine AstraZeneca is marketed.

Timetable	Date
DHPC and communication plan (in English) agreed by PRAC	10 June 2021
DHPC and communication plan (in English) agreed by CHMP	14 June 2021
Submission of translated DHPCs to the national competent authorities for review	16 June 2021
Agreement of translations by national competent authorities	18 June 2021
Dissemination of DHPC	23 June 2021