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Date: 7th of September 2022
Subject: Updated dosage recommendations for EVUSHELD (tixagevimab co-packaged with cilgavimab) for pre-exposure prophylaxis against COVID-19

Dear Healthcare Provider:

AstraZeneca in agreement with the Saudi Food and Drug Authority (SFDA), would like to inform you about the updated in dosage recommendations for EVUSHELD for pre-exposure prophylaxis against COVID-19.

Summary :
The dosage has been increased from 300 mg administered intramuscularly (IM) to 600 mg IM. The previous dosage was 300mg IM of Evusheld (150mg each of tixagevimab and cilgavimab).and guidance on repeat dosing has also been provided1.
The clinical safety of 600 mg EVUSHELD for prophylaxis use is supported by safety data from TACKLE in patients with mild to moderate COVID-19.3

Background on the safety concern:
The updated dosing recommendations are as follows:1

INITIAL DOSING:

- The initial dosage of EVUSHELD is **600 mg (300 mg of tixagevimab and 300 mg of cilgavimab)** administered as two separate, 3.0 mL sequential intramuscular (IM) injections.

DOSING FOR INDIVIDUALS WHO INITIALLY RECEIVED 150 MG OF TIXAGEVIMAB AND 150 MG OF CILGAVIMAB:

- Individuals who initially received 150 mg tixagevimab and 150 mg cilgavimab should receive 300 mg tixagevimab and 300 mg cilgavimab as soon as possible.
- A minimum dosing interval of 3 months should be maintained between administration of the initial (150 mg tixagevimab and 150 mg cilgavimab) dose and second (300 mg tixagevimab and 300 mg cilgavimab) dose.

REPEAT DOSING:

For individuals who require repeat dosing for ongoing prevention of covid-19, subsequent doses of 600 mg of Evusheld (300 mg tixagevimab and 300 mg cilgavimab) should be given once every 6 months.

HEALTHCARE PROVIDER ACTION

Each carton of EVUSHELD contains two vials (one vial of 150 mg/1.5 mL tixagevimab and one vial of 150 mg/1.5 mL cilgavimab); therefore, you will need **2 cartons** of EVUSHELD for a 600 mg dose.

Please note the product preparation of a 600 mg (300 mg tixagevimab and 300 mg cilgavimab) dose as shown in Table 1.[1]

TABLE 1. INITIAL DOSING OF 300 MG OF TIXAGEVIMAB AND 300 MG OF CILGAVIMAB

EVUSHELD Dose* (tixagevimab and cilgavimab) **600 mg** **(2 cartons)**	**Antibody dose**	**Number of vials needed**	**Volume to withdraw from vials**
	tixagevimab 300 mg	2 vials	3 mL * **(1.5 ml from each vial**
	cilgavimab 300 mg	2 vials	3 mL * **(1.5 ml from each**

*Each carton of EVUSHELD contains one vial of tixagevimab 150 mg/1.5 mL and one vial of cilgavimab 150 mg/1.5 mL. The 300 mg of tixagevimab and 300 mg of cilgavimab doses are to be administered as separate, consecutive intramuscular injections. Withdraw the 3 mL of tixagevimab solution and 3 mL of cilgavimab solution into TWO separate syringes. Each vial has overfill to enable withdrawal of 1.5 ml from each vial. **Any leftover product should be discarded.**

This letter has been approved by the SFDA.

Reporting Adverse Events

The prescribing healthcare provider and/or the provider's designee is/are responsible for mandatory reporting of all serious adverse events* and medication errors potentially related to EVUSHELD.

Submit adverse event and medication error reports, using one of the following methods:

- Directly to AstraZeneca patient Safety:
  Email: ksa.ae@astrazeneca.com - Phone: +966 11 2249235
  Portal: https://contactazmedical.astrazeneca.com
- SFDA reporting information:
  Email: npc.drug@sfda.gov.sa -Toll free phone: 19999 - Portal: https: //ade.sfda.gov.sa

Reference(S)

1. FACT SHEET FOR HEALTHCARE PROVIDERS: EMERGENCY USE AUTHORIZATION FOR EVUSHELD™ (tixagevimab co-packaged with cilgavimab)
2. Levin MJ, Ustinaowski A, De Wit S, et al. Intramuscular AZD7442 (tixagevimab/cilgavimab) for prevention of COVID-19 [article and supplementary appendix]. *N Engl J Med*. 2022. https://doi.org/10.1056/NEJMoa2116620.
3. Montgomery H, Hobbs R, Padilla F, et al. Efficacy and Safety of Intramuscular Administration of Tixagevimab-Cilgavimab for Early Outpatient Treatment of COVID-19 (TACKLE): a Phase 3, Randomised, Double-Blind, Placebo-Controlled Trial [article and supplementary appendix]. *Lancet Respir Med*. 2022. https://doi.org/10.1016/ S2213-2600(22)00180-1.

Best Regards,
Malak Alshammari
Saudi QPPV