SAFETY ALERT

DRAP SAFTEY ALERT NO. 29

Risk of Kidney Injury and Death due to Hydroxyethyl-Starch Solutions for Infusion

Date: 29th of November, 2022.

Target Audience:

- Manufacturers and importers of hydroxyethyl-starch solutions for infusion.
- Healthcare Professionals; and
- Patients, consumers or caregivers.

Background:

The Pharmacovigilance Risk Assessment Committee (PRAC) of the European Medicine Agency (EMA) on 11th February, 2022 recommended that the market authorization of hydroxyethyl-starch (HES) solutions for infusion should be suspended across the European Union. These solutions for infusion products are indicated as an addition to other treatments for plasma volume replacement following acute (sudden) blood loss.

The safety of these solutions for infusion was reviewed in 2013, and a number of restrictions and measures to minimise the risk of kidney injury and death in certain patients (those critically ill, with burn injuries or with sepsis, a bacterial infection in the blood) were put in place at that time.

Likewise, as a result of a third review conducted in 2018, the use of HES solutions for infusion was further restricted to only accredited hospitals, and healthcare professionals prescribing or administering the medicines had to be trained in their appropriate use. In addition, further warnings were introduced to remind healthcare professionals that these medicines must not be used in patients with sepsis or kidney impairment or in other vulnerable patients such as the critically ill in order to ensure these solutions for infusion were not used in patients who were at

increased risk of harm. Market authorization holders of HES solutions for infusion were also requested to conduct a drug utilization study to check that the restrictions were adhered to in clinical practice.

The PRAC of the EMA accordingly reviewed the results of the study, which show that HES solutions for infusion are still being used outside the recommendations included in the product information and concluded that the further restrictions introduced in 2018 have not sufficiently ensured that the medicines are used safely and that HES solutions were continually used in certain groups of patients in whom serious harm has been demonstrated. In view of the serious risks that certain patient populations were still exposed to, the PRAC recommended the suspension of the marketing authorisations for HES solutions for infusion in the European Union. Accordingly, the European Commission on 24th May, 2022 issued a legal decision confirming the suspension of the market authorization of HES solution for infusion.

Action in Pakistan:

Accordingly, the case of the risk of kidney injury and death due to hydroxyethyl-starch solutions for infusion was discussed in the 1st meeting of the Pharmacovigilance Risk Assessment Expert Committee (PRAEC) of the National Pharmacovigilance Centre (NPC), Division of Pharmacy Services, Drug Regulatory Authority of Pakistan (DRAP). The PRAEC-DRAP after detailed deliberation and discussion and as per Rule 10 (1) (h) (v) of Pharmacovigilance Rules, 2022 (reliance mechanism) decided to recommend to the Registration Board of the DRAP to suspend the registration of Hydroxyethyl-Starch (HES) solutions in Pakistan subject to the availability of alternative treatment options.

Therapeutic Goods Affected:

Name: **Hydroxyethyl-Starch solutions for infusion.**

These solutions for infusion products are indicated as an addition to other treatments for plasma volume replacement following acute (sudden) blood loss.

Advice for patients:

Patients are informed that the National Pharmacovigilance Centre, DRAP is working with the Registration Board and manufacturers/importers of hydroxyethyl-starch solutions for infusion to suspend the registration of these solutions in Pakistan. Therefore, talk with your doctor before initiation of treatment with those solutions as alternative treatment options are available in the market.

Advice for healthcare professionals:

Healthcare professionals are informed that the National Pharmacovigilance Centre, DRAP is working with the Registration Board and manufacturers/importers of hydroxyethyl-starch solutions for infusion to suspend the registration of these solutions in Pakistan. Therefore, healthcare professionals are reminded that there are alternative solutions for infusion available in the Pakistani market for the treatment of plasma volume replacement following acute (sudden) blood loss and the same must be considered as the treatement in these conditions.

Guidelines for reporting of Adverse Drug Reactions (ADRs):

Both healthcare professionals and patients are requested to report any suspected adverse drug reaction (ADRs) with hydroxyethyl-starch solutions for infusion they have experienced to the National Pharmacovigilance Centre**,** Drug Regulatory Authority of Pakistan through Med Vigilance E-Reporting system available on the DRAP website.

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Similarly, ADRs can also be reported through Med Safety App which is available for download from App Store (for iOS devices) and Google Play (for Android devices).

References:

1. Minutes of 1st meeting of Pharmacovigilance Risk Assessment Expert Committee of the DRAP.
2. European Medicine Agency update regarding hydroxyethyl-starch solutions for infusion recommended for suspension from the market.