ADVISORY

Reports of serious adverse reactions with Ceftriaxone injection due to unintentional mixing during reconstitution.

Date: 17th of March, 2025.

Target Audience.

- Provincial Health Departments/Healthcare Commissions;
- Provincial Pharmacovigilance Centres;
- Public and private sector hospitals; and
- Healthcare Professionals.

Background.

The Provincial Pharmacovigilance Centre (PPC), the Directorate of Drugs Control, Punjab received cases of Therapeutic Goods Related Problem Reports (TGRP) regarding the death of three children following the administration of Ceftriaxone injection at District Headquarters Hospital Khanewal in June, 2024. After administration of Ceftriaxone, the patients became unconscious and pulseless with fixed dilated pupils and absent Cardiac activity.

Action in Pakistan.

The investigation team constituted by the Directorate of Drugs Control, Punjab was sent to the respective facility for a complete investigation of the said matter. Upon investigation, it was transpired that the incident might have occurred due to the un-intentional mixing of any High Alert Medications (HAMs) such as Lidocaine, Potassium Chloride, and Amiodarone etc. during the reconstitution of the said injection at the nursing station.

The investigation report was presented in the 14th meeting of the Provincial Pharmacovigilance Committee (PVPC), Directorate of Drugs Control of Punjab, held on 29th of October, 2024, which after due deliberation and discussion, recommended the following proposal for consideration of the DRAP to avoid such incidences in the future:

a. Injection Potassium Chloride should be available in ready-to-use hydration form/pre-diluted solution instead of currently available concentrated injection.

b. Distant and standardized branding strategies, including unique colour schemes and labelling should be applied for the critical injectables such as Inj. Dextrose 25%, Sodium Bio-carbonate, and Potassium Chloride etc.

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Subsequently, the case was discussed in the 5th meeting of the Pharmacovigilance Risk Assessment Expert Committee (PRAEC), DRAP held on 2nd of January, 2025, after detailed discussion and deliberation the committee agreed with the proposal of the Provincial Pharmacovigilance Committee (PVPC), Punjab Pharmacovigilance Centre, that "*Injection Potassium Chloride should be available in ready-to-use hydration form/pre-diluted solution instead of currently available concentrated injection*". As per Rule 10 (1) (e) of the Pharmacovigilance Rules, 2022, the PRAEC recommended that the Registration Board may take necessary measures with respect to the availability of ready-to-use hydration form/pre-diluted solution of injection Potassium Chloride instead of the currently available concentrated injection. The PRAEC also advised the National Pharmacovigilance Centre to prepare a proposal for distinct and standardized branding strategies, including unique colour schemes and labelling for concentrated electrolytes such as Dextrose 25%, Sodium Bio-carbonate and Potassium Chloride etc.

Advice for Healthcare Professionals and Hospitals

Healthcare providers should inform patients about the signs and symptoms of anaphylactic reactions associated with Ceftriaxone use and if occur should discontinue the drug and take appropriate measures. A history of drug allergy may be taken and test doses of Injection Ceftriaxone should be given before the administration. At the hospital level, measures should be taken to optimise storage practices for concentrated electrolyte injections with round-the-clock monitoring. Likewise, measures should be taken by removing Potassium Chloride from the floor or ward stock/patient bedside and issuance should be through the Pharmacy on a patient-need basis with proper labelling, as it will reduce the chances of medication error.

References.

- Minutes of the 5th meeting of Pharmacovigilance Risk Assessment Expert Committee.