SAFETY ALERT

DRAP SAFTEY ALERT NO. 52

Safety Alert risk of severe chemical irritation and damage to tissues with Promethazine hydrochloride injection.

Date: 27th of March, 2025.

Target Audience.

- Provincial Health Departments/Provincial Pharmacovigilance Centres/Healthcare Commissions;
- Manufacturers and importers of Promethazine hydrochloride injection; and
- Healthcare Professionals.

Background.

The United States Food and Drug Administration (US-FDA) in December 2023 alerted healthcare professionals of labelling updates intended to further reduce the risk of severe chemical irritation and damage to tissues from intravenous administration of promethazine hydrochloride injection.

The FDA inform that if intramuscular injection is not possible, promethazine hydrochloride injection:

- Can be administered intravenously only after dilution, as recommended, and infused through an intravenous catheter inserted in a large vein and preferably through a central venous catheter. Do not administer using intravenous catheters placed into veins in the hand or wrist.
- Should not be mixed with other drugs or diluted with solutions other than 0.9% sodium chloride injection.
- Is contraindicated for intravenous injection at concentrations greater than 1 mg/mL.

When diluting and administering promethazine hydrochloride injection by intravenous infusion, infuse over 20 to 40 minutes and follow the below preparation and infusion instructions in adult and pediatric patients (see the first and second tables below, respectively):

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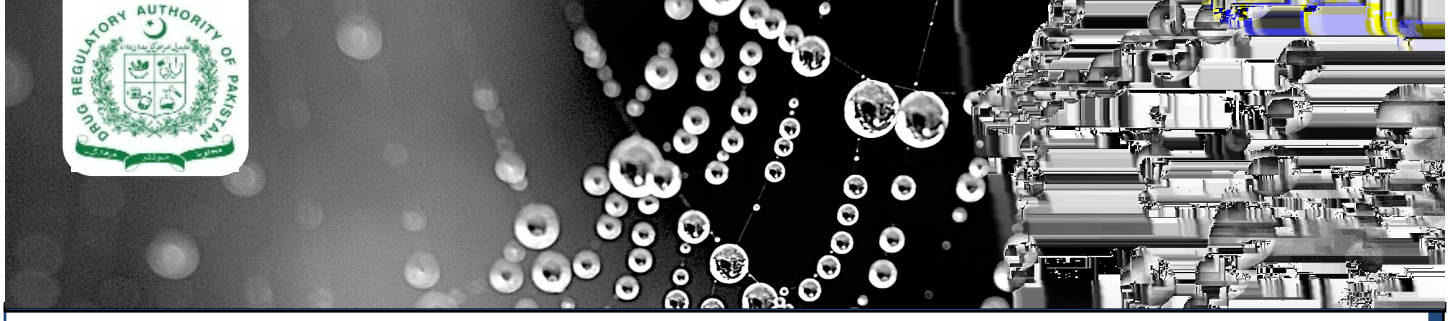

Table 1: Preparation and Infusion Information by Adult Dose of Promethazine Hydrochloride Injection

Dose of Promethazine Hydrochloride Injection	Volume of 0.9% Sodium Chloride Injection for Dilution	Maximum Concentration of the Diluted Promethazine Hydrochloride Injection Solution	Maximum Rate of Infusion
12.5 mg	50 mL	1 mg/mL	2.5 mL/minute
25 mg	50 mL		2.5 mL/minute
50 mg	50 mL		2.5 mL/minute
75 mg	100 mL		5 mL/minute

Table 2: Preparation and Infusion Information by Pediatric Dose of Promethazine Hydrochloride Injection

Dose of Promethazine Hydrochloride Injection	Volume of 0.9% Sodium Chloride Injection for Dilution	Maximum Concentration of the Diluted Promethazine Hydrochloride Injection Solution	Maximum Rate of Infusion
Up to 25 mg	25 mL	1 mg/mL	1.25 mL/minute
25 mg to 50 mg	50 mL		

Action in Pakistan.

The case was discussed in the 5th meeting of the Pharmacovigilance Risk Assessment Expert Committee (PRAEC) of the DRAP held on 2nd of Janauary, 2025 which decided as per Rule 10 (1) (h) (iv) of Pharmacovigilance Rules, 2022 that registration holders of Promethazine hydrochloride injection should include information related to the risk of severe chemical irritation and damage to tissues when administered through intravenous route as per US-FDA label.

Therapeutic Good.

Name: Promethazine hydrochloride injection is indicated to help manage certain allergic reactions, motion sickness, postoperative nausea and vomiting, and as a sedative or adjunct to analgesics.

Advice for Healthcare Professionals.

Healthcare professionals are advised to administer promethazine hydrochloride injection by deep intramuscular administration instead of intravenous administration. If promethazine hydrochloride injection must be administered intravenously, healthcare professionals should

review and follow the updated information in the labelling to dilute promethazine hydrochloride injection and administer it by intravenous infusion to reduce the risk of severe tissue injury. The DRAP has required that manufacturers update their prescribing information for promethazine hydrochloride injection to include new safety information and update the labelling with the corresponding information.

Guidelines for reporting Adverse Drug Reactions (ADRs).

Both healthcare professionals and patients are requested to report any adverse drug reaction with Promethazine hydrochloride injection to the National Pharmacovigilance Centre (NPC), Drug Regulatory Authority of Pakistan (DRAP) through the Med Vigilance E-Reporting System (E-forms) available on the DRAP website. Similarly, ADRs can also be reported through the VigiMobile App, which can be downloaded by scanning the barcode available on the DRAP website.

References.

- Minutes of the 5th meeting of the Pharmacovigilance Risk Assessment Expert Committee.
- FDA labeling for promethazine hydrochloride injection products.