SAFETY ALERT

DRAP SAFTEY ALERT NO. 30

Safety Alert of Risk of Hypersensitivity Reactions with Pegaspargase (Peg L Asparaginase).

Date: 10th of April, 2023.

Target Audience:

- Manufacturers and importers of Peg L Asparaginase;
- Healthcare Professionals; and
- Patients, consumers or caregivers.

Problem or Issue:

The National Pharmacovigilance Centre (NPC), Division of Pharmacy Services, Drug Regulatory Authority of Pakistan (DRAP) received six cases of hypersensitivity reactions from Indus Hospital Karachi with Pegaspargase (Peg L Asparaginase) with different batches having the same importer i.e. M/S Lab Diagnostic System and same manufacture i.e. Jiangsu Hengrui Medicine Co Ltd, China. The drug was prescribed for Acute Lymphoid Leukemia/ Leukemia with a dose of 2500 IU/m2 in children. The events of hypersensitivity reactions including swelling of lips, nausea, rash, vomiting, swelling of the tongue, itching all over the body, shivering, red eyes and abdominal pain were noted in the six cases after administration of Pegaspargase (Peg L Asparaginase) 3750IU. The time to onset of reactions was one day. The Pegaspargase was withdrawn in all cases except one case where the status is unknown and the patients recovered in all those cases. The causality assessment of all six cases was performed by the Causality Assessment Group of the National Pharmacovigilance Centre (NPC) and classified all six cases to have a possible relationship with drug intake.

Further assessment was carried out at the National Pharmacovigilance Centre (NPC), Drug Regulatory Authority of Pakistan (DRAP), where the signal was confirmed from the approved label of Peg L Asparaginase of United States Food and Drugs Administration (US-FDA) and Summary of Product Characteristics (SmPC) of Medicine and Health Products Agency (MHRA) and from the published research articles of hypersensitivity reactions with the drug. There was also significant disproportionality and potential association of hypersensitivity with Pegaspargase as per statistical tool available in VigiLyze of the Uppsala Monitoring Centre, Sweden.

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The case was therefore discussed in the 2nd meeting of the Pharmacovigilance Risk Assessment Expert Committee (PRAEC) of the NPC, DRAP which after detailed deliberation, decided to update the prescribing information/ safety specification/ label of Pegaspargase injection with the inclusion of information related to hypersensitivity reactions and its monitoring in the warning and precaution section and information on treatment modification as per the grade of hypersensitivity reactions in dosage and administration sections. Registration holder was also directed to introduce an educational training programme for healthcare professionals on proper preparation, administration and monitoring of Pegaspargase and to ensure that resuscitation equipment are available at the treatment sites.

Therapeutic Goods Affected.

Name: **Pegaspargase (Peg L Asparaginase)**

Pegaspargase is indicated as a component of a multi-agent chemotherapeutic regimen for the treatment of pediatric and adult patients with Acute Lymphoid Leukaemia (ALL) and hypersensitivity to native forms of L-asparaginase.

Advice for patients.

Patients are informed that hypersensitivity reactions with Pegaspargase injection can occur during chemotherapy of Acute Lymphoid Leukaemia (ALL). Talk to your doctor if you have a history of hypersensitivity with conventional asparaginase formulations.

Advice for healthcare professionals.

Healthcare professionals are informed that hypersensitivity reactions to Pegaspargase, including life-threatening anaphylaxis, can occur during therapy, including in patients with known hypersensitivity to *E. coli*-derived asparaginase formulations. Other hypersensitivity reactions can include angioedema, lip swelling, eye-swelling, erythema, decreased blood pressure, bronchospasm, dyspnoea, pruritus and rash. Premedicate patients 30-60 minutes before administration of pegaspargase. As a routine precautionary measure, the patient should be monitored for an hour after administration and resuscitation equipment and other appropriate means for the treatment of anaphylaxis such as epinephrine, oxygen, intravenous steroids, etc should be available at the treatment sites. Pegaspargase should be discontinued in patients with serious hypersensitivity reactions. Monitoring of patients and modification of treatment is recommended as per the following schedule: reduce the infusion rate by 50% in case of Grade 1 hypersensitivity reaction; interrupt the infusion, treat the symptoms, when symptoms resolved, resume the infusion and reduce the infusion rate by 50% in case of Grade 2 hypersensitivity reaction; and for Grade 3 to 4 hypersensitivity reactions permanently discontinue the pegaspargase.

Guidelines for reporting Adverse Drug Reactions (ADRs):

Both healthcare professionals and patients are requested to report any suspected adverse drug reaction (ADRs) with Pegaspargase (Peg L Asparaginase) to the National Pharmacovigilance Centre, Drug Regulatory Authority of Pakistan through the Med Vigilance E-Reporting system available on DRAP website.

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

References:

1. Minutes of 2nd meeting of Pharmacovigilance Risk Assessment Expert Committee.

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