SAFETY ALERT

DRAP SAFTEY ALERT NO. 20

Risk of Anaphylactic Reaction /Anaphylactic Shock with Diclofenac Sodium Injection.

Update from Pharmacovigilance Risk Assessment Expert Committee of Pakistan.

Date: 10th of November, 2022.

Target Audience:

- Manufacturers and importers of Diclofenac Sodium;
- 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) through the Provincial Pharmacovigilance Centre (PPC), Directorate of Drugs Control Punjab received two serious cases of anaphylactic reactions upon STAT dose administration of injection Diclofenac Sodium 75mg/3ml intramuscular (IM). The cases were reported by Clinical Pharmacy and Pharmacovigilance Officers (CPPOs) of two public sector hospitals in the Punjab province. The diclofenac injection was used in these cases for the wound pain in the left leg and backache. One of the patients has a history of asthma. The symptoms noted were pruritus, erythema, sweating, apprehension and fainting due to a sudden drop in blood pressure, severe shortness of breath, wheezy chest, hypoxia and hypotension. The adverse drug reactions were assessed for causality using the WHO Causality Assessment Criteria and were categorized as “Possible” and “Probable” based on plausible time to onset (same day immediately after administration), positive dechallenge (recovered on withdrawing) and unable to explain from other drugs/ disease.

The two cases of Diclofenac Sodium injection-associated anaphylactic reactions were discussed in the 10th meeting of the Provincial Pharmacovigilance Centre of the Punjab’s Adverse Drug Reaction Scrutiny Committee (ADRSC) held on 25-03-2022. The ADRSC recommended reporting the cases to the Drug Regulatory Authority of Pakistan (DRAP) for detailed investigation and if necessary for an update in prescribing information/ label of Diclofenac Sodium with warning signs of anaphylactic reactions (anaphylactic shock).

NPC, DRAP, Islamabad | +92 51 910 7413 | npc@dra.gov.pk

Further assessment was carried out at National Pharmacovigilance Centre (NPC), Drug Regulatory Authority of Pakistan (DRAP), where the signal was confirmed from the approved label of United States Food and Drugs Administration (US-FDA) and Summary of Product Characteristics (SmPC) of Medicine and Health Products Agency and from the published research articles about rare cases of severe anaphylactic reactions/ hypersensitivity/ anaphylaxis with diclofenac sodium. There was also significant disproportionality and potential association of diclofenac with anaphylactic reaction/shock as per statistical tool of available in VigiLyze of the Uppsala Monitoring Centre.

The case were, therefore, discussed in the 1st meeting of the Pharmacovigilance Risk Assessment Expert Committee (PRAEC) of the NPC, DRAP which after detailed deliberation and discussion decided to update the warning, precaution & contraindication sections of the prescribing information/ safety specification/ label of Diclofenac Sodium injection about the occurrence of anaphylactic reaction/ anaphylactic shock and its contraindication in a patient with a history of asthma, urticaria, or allergic-type reactions after taking aspirin or other NSAIDs.

Therapeutic Goods Affected.

Generic Name: **Diclofenac Sodium injection**

Diclofenac Sodium through the intra-muscular route is effective in acute forms of pain, including renal colic, exacerbations of osteo- and rheumatoid arthritis, acute back pain, acute gout, acute trauma and fractures, and postoperative pain. Diclofenac sodium is an NSAID that exhibits anti-inflammatory, analgesic and antipyretic effects. The mechanism of action may involve the inhibition of prostaglandin synthesis by inhibiting the cyclooxygenase (COX-1 and COX-2) pathways.

Advice for patients.

Patients are informed that there are rare chances of the development of anaphylactic reaction/ anaphylactic shock with an injection of diclofenac sodium. Talk to your doctor if you have a history of asthma or urticaria, or if you had previously experienced an anaphylactic reaction/ allergic-type reaction with diclofenac sodium or after taking aspirin or other NSAIDs.

Advice for healthcare professionals.

Healthcare professionals are informed that Pharmacovigilance Risk Assessment Expert Committee of the DRAP has recommended to update the warning, precaution & contraindication sections of the prescribing information/ safety specification/ label of Diclofenac Sodium injection about the occurrence of anaphylactic reaction/ anaphylactic shock and its contraindication in a

patient with a history of asthma, urticaria, or allergic-type reactions after taking aspirin or other NSAIDs. Therefore, healthcare professionals should know that are rare chances that anaphylactic reactions may occur with diclofenac sodium injection in patients with the aspirin triad or in patients without prior exposure to diclofenac. Immediately discontinue the diclofenac injection if an anaphylactic reaction occurs. Likewise, Diclofenac is contraindicated in patients with a history of asthma, urticaria, or allergic-type reactions after taking aspirin or other NSAIDs.

Guidelines for reporting of Adverse Drug Reactions (ADRs):

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

Similarly, ADRs can also be reported through MedSafety App that 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.