SAFETY ALERT

DRAP SAFTEY ALERT NO. 44

Safety Alert of Risk of Rare and Serious Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) reaction with Levetiracetam and Clobazam.

Date: 24th of April, 2024.

Target Audience.

- Manufacturers and importers of Levetiracetam and Clobazam;
- Healthcare professionals; and
- Patients, consumers or caregivers.

Background.

The United States Food and Drug Administration (US-FDA) in November 2023 through a drug safety communication warned that the antiseizure medicines levetiracetam and clobazam can cause a rare but serious reaction that can be life-threatening if not diagnosed and treated quickly. This reaction is called Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) which may start as a rash but can quickly progress, resulting in injury to internal organs, the need for hospitalisation, and even death. This hypersensitivity reaction to these medicines is serious but rare. DRESS can include fever, rash, swollen lymph nodes, or injury to organs including the liver, kidneys, lungs, heart, or pancreas. The US FDA accordingly decided to add new warnings about DRESS to the prescribing information and the medication guide of levetiracetam and clobazam for patients and caregivers. It was informed that the warnings for both levetiracetam and clobazam medicines would include information that "early symptoms of DRESS such as fever or swollen lymph nodes can be present even when a rash cannot be seen. This is different from other serious skin-related reactions that can happen with these medicines and where a rash is present early on, including Stevens-Johnson Syndrome (SJS) and toxic epidermal necrolysis (TEN)."

Action in Pakistan.

The case was discussed in the 4th meeting of the Pharmacovigilance Risk Assessment Expert Committee (PRAEC) of the DRAP held on 26th of February, 2024 which decided as per Rule 10 (1) (h) (iv) of Pharmacovigilance Rules, 2022 that registration holders should include information about rare and serious DRESS reactions in warning and precaution sections of the prescribing information/label of medicines containing levetiracetam and clobazam.

Therapeutic Goods.

Name: **Levetiracetam** is an antiseizure medicine indicated for use alone or together with other medicines to control certain types of seizures in adults and children such as partial seizures, myoclonic seizures, or tonic-clonic seizures.

Clobazam is a benzodiazepine indicated for use in combination with other medicines to control seizures in adults and children 2 years and older who have a specific severe form of epilepsy called Lennox-Gastaut syndrome).

Advice for Healthcare Professionals.

Healthcare professionals are informed that levetiracetam and clobazam have been linked to a rare, potentially life-threatening reaction called Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS), occurring 2-8 weeks post-treatment. This may lead to severe inflammation and organ damage, requiring prompt medical attention. Prescribers should inform patients, explain DRESS signs, and advise seeking immediate care. DRESS involves cutaneous reactions, eosinophilia, fever, and systemic complications. Early recognition, discontinuation, and supportive care are crucial.

Advice for Patients.

Patents are informed that levetiracetam and clobazam, prescribed for seizures, can trigger a rare but severe reaction called Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS). This immune system response may cause widespread inflammation and organ damage, leading to hospitalisation or death if untreated. Patients are advised not to stop the medication abruptly and; to consult their healthcare professionals if necessary. DRESS symptoms, such as fever, rash, and organ-related issues, may occur 2 to 8 weeks after starting treatment. Seek immediate medical attention for concerning symptoms.

Guidelines for reporting Adverse Drug Reactions (ADRs).

Both healthcare professionals and patients are requested to report any suspected adverse drug reaction (ADRs) with medicine containing Levetiracetam and Clobazam to the National Pharmacovigilance Centre (NPC), Drug Regulatory Authority of Pakistan (DRAP) through the Med Vigilance E-Reporting System available on the DRAP website. Similarly, ADRs can also be reported through Med Safety App which is available for download from the App Store (for iOS devices) and Google Play (for Android devices).

References.

- Minutes of 4th meeting of Pharmacovigilance Risk Assessment Expert Committee, DRAP.
- US-FDA Drug Safety Communication regarding Levetiracetam and Clobazam.

NPC, DRAP, PM Health Complex, Chak Shahzad Islamabad +92 51 9255981 npc@dra.gov.pk