SAFETY ALERT

DRAP SAFTEY ALERT NO. 55

Safety Alert of Risk of Drug-Induced Liver Injury (DILI) and Severe Cutaneous Adverse Reactions (SCARs) with Ezetimibe.

Date: 27th of March, 2025.

Target Audience.

- Provincial Health Departments/Provincial PV Centres/Healthcare Commissions;
- Manufacturers and importers of Ezetimibe; and
- Healthcare Professionals.

Background.

Health Canada in March 2024 has updated the product information for ezetimibe (Ezetrol®) to include warnings about serious adverse reactions including drug-induced liver injury (DILI) and severe cutaneous adverse reactions (SCARs) such as Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), and drug reaction with eosinophilic and systemic symptoms (DRESS).

The marketing authorization holder conducted a review of international safety data and the scientific literature and identified 42 post-marketing cases of DILI in patients taking ezetimibe. There was sufficient evidence to suggest a causal association between ezetimibe monotherapy and DILI. Therefore, the current recommendation to consider performing liver function tests at the initiation of, or during treatment with, ezetimibe in combination with a statin or fenofibrate has been expanded to include ezetimibe monotherapy. The review also identified rare cases of SCARs in patients taking Ezetrol. There was sufficient evidence to suggest at least a reasonable possibility of a causal association with some cases of SJS, TEN, and DRESS.

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 should include warnings about serious adverse reactions including drug-induced liver injury (DILI) and severe cutaneous adverse reactions (SCARs) to the prescribing information of Ezetimibe containing medicines (monotherapy or in combination) in the adverse drug reaction and warning and precaution sections.

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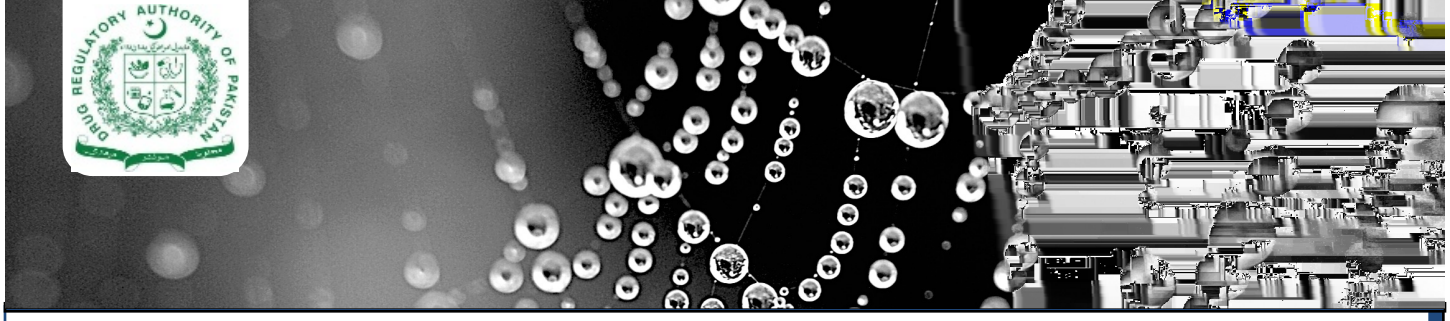


Therapeutic Good Affected.

Name: Ezetimibe is a cholesterol absorption inhibitor and is indicated, as an adjunct to diet and lifestyle changes when the response to these and other non-pharmacological measures alone has been inadequate, for the treatment of primary hypercholesterolemia, homozygous familial hypercholesterolemia and homozygous sitosterolemia (phytosterolemia).

Advice for Healthcare Professionals.

Healthcare professionals are advised to consider performing liver function tests at the initiation of ezetimibe, whether administered as monotherapy or in combination with a statin or fenofibrate and subsequently as required. Instruct patients to immediately contact a healthcare professional if they experience symptoms of liver injury. Liver function should be evaluated if liver injury is suspected. Instruct patients to stop taking ezetimibe and to seek immediate medical help if they experience symptoms of SCARs.

Advice for patients.

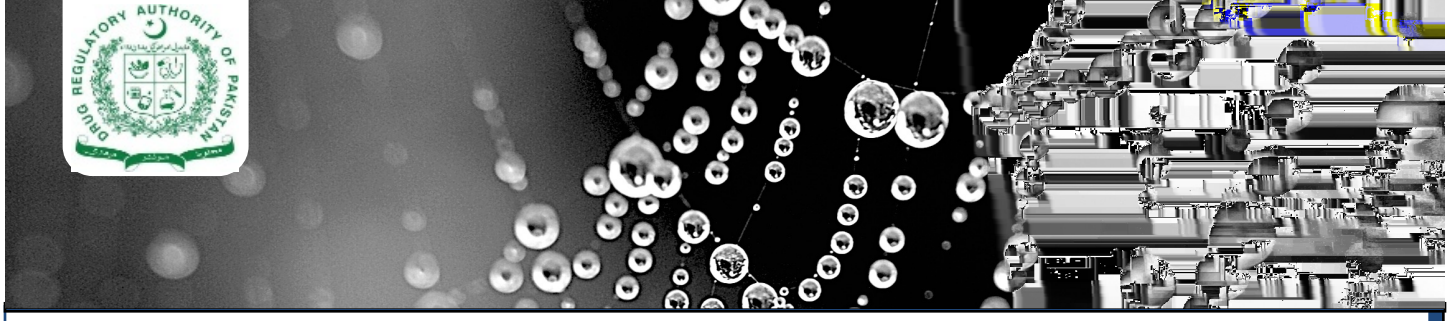
Ezetimibe is used alongside diet and lifestyle changes to lower cholesterol and triglycerides in adults and children (10 years and older) when these measures alone are ineffective. It may be used alone or with statins or fenofibrate, but is not recommended for children under 10. Serious side effects include liver injury and severe skin reactions like Stevens-Johnson syndrome and toxic epidermal necrolysis. Patients may need liver function tests before and during treatment. Immediate medical attention is required for symptoms of liver injury (e.g., severe abdominal pain, dark urine, yellowing skin/eyes) or serious skin reactions (e.g., blistering, swelling, fever, flu-like symptoms). Patients should consult their healthcare professional with any concerns.

Guidelines for reporting Adverse Drug Reactions (ADRs).

Healthcare professionals and patients are requested to report any adverse drug reaction with Ezetimibe and other medicines 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 (PRAEC), DRAP.
- Health Canada's alert on ezetimibe and the Risks of Drug-Induced Liver Injury and Severe Cutaneous Adverse Reaction



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Monday, 07 April, 2025, 1:47:47 PM

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