Important Safety Information on EZETROL (ezetimibe) and the Risks of Drug-Induced Liver Injury and Severe Cutaneous Adverse Reactions

ORGANON

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Audience
Healthcare professionals including general practitioners, family physicians, cardiologists, dermatologists, pediatricians, emergency physicians, gastroenterologists, internists, endocrinologists, nurse practitioners, and pharmacists.

Key messages

- **EZETROL (ezetimibe) may cause 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).**

- **Healthcare professionals are advised to:**
  - **Consider performing liver function tests at the initiation of EZETROL monotherapy, 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 EZETROL and to seek immediate medical help if they experience symptoms of SCARs.**

- **The Canadian Product Monograph (CPM) for EZETROL has been updated to include warnings about these serious adverse reactions. Health Canada will work with the manufacturers of generic versions of ezetimibe to update their respective CPMs.**

What is the issue?
EZETROL (ezetimibe) may cause 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).

Products affected
EZETROL (ezetimibe) 10 mg tablets (DIN 02247521).

Other products affected by this risk information include all generic ezetimibe 10 mg tablets.

Background information
EZETROL is indicated for adults and children 10 years of age and older as an adjunct to diet and lifestyle changes when the response to these and other non-pharmacological measures alone has been inadequate. Specifically, EZETROL is indicated for use in primary hypercholesterolemia (administered alone, with an HMG-CoA reductase inhibitor (statin) or in combination with fenofibrate, depending on the clinical objective), homozygous familial hypercholesterolemia (administered with a statin) and homozygous sitosterolemia (phytosterolemia). Treatment with EZETROL in children less than 10 years of age is not recommended.

A recent review of international safety data and the scientific literature, conducted by the Market Authorization Holder, identified several post-marketing cases of DILI in patients taking EZETROL, including a Canadian case of liver injury associated with ezetimibe monotherapy. There was sufficient evidence to suggest a causal association between ezetimibe monotherapy and DILI.

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.

Information for consumers
EZETROL is used along with a change in diet and lifestyle to lower the level of cholesterol and other fats (such as triglycerides) in the blood of children (10 years of age and older) and adults. In these children and adults, diet and other lifestyle changes alone were not effective in lowering their cholesterol. The use of EZETROL in children less than 10 years of age is not recommended.

EZETROL can cause serious side effects including drug-induced liver injury, and serious skin reactions such as Stevens-Johnson syndrome, toxic epidermal necrolysis, and drug reaction with eosinophilic and systemic symptoms.

Patients taking EZETROL alone or with a statin or fenofibrate may need to have blood tests done before and during treatment to check and monitor the health of their liver.

Patients should contact their healthcare professional immediately if they experience symptoms of liver injury such as severe abdominal pain (especially if felt on the upper right side below the ribs), dark urine, general itchiness, severe nausea or vomiting, pale stools, or yellowing of the skin or eyes.

Patients should stop taking EZETROL and seek immediate medical help if they experience symptoms of serious skin reactions, including serious illness with severe peeling and swelling of the skin, blistering on the skin, mouth, eyes, or genitals,

and fever; skin rash with pink-red blotches, particularly on the palms of the hands or soles of the feet, which may blister; accompanying flu-like symptoms such as fever, chills, or aching muscles.

Patients should discuss any questions or concerns about this information with their healthcare professional.

Information for health care professionals
Healthcare professionals are advised to:

- Consult the safety information in the EZETROL Canadian Product Monograph (CPM). Consider the benefits and risks for patients prior to initiating or continuing treatment with EZETROL.
- Consider performing liver function tests at the initiation of EZETROL monotherapy, and subsequently as required. This practice aligns with the existing recommendation to consider performing liver function tests when initiating EZETROL in patients who are already taking 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 EZETROL and to seek immediate medical help if they experience symptoms of SCARs.

Action taken by Health Canada
Health Canada, in collaboration with Organon Canada Inc., updated the CPM for EZETROL. Health Canada will work with manufacturers of generic versions of ezetimibe to update their respective CPMs.

Health Canada is communicating this important safety information to healthcare professionals and Canadians via the Recalls and Safety Alerts Database on the Healthy Canadians Web Site. This communication will be further distributed through the MedEffect™ e-Notice email notification system.

Report health or safety concerns
Managing marketed health product-related side effects depends on health care professionals and consumers reporting them. Any case of DILI or SCARs including SJS, TEN, and DRESS, or other serious or unexpected side effects, in patients receiving EZETROL should be reported to Organon Canada Inc., to the respective generic ezetimibe manufacturer, or Health Canada.

Organon Canada Inc.
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Kirkland, QC Canada
H9H 4M7
Email: medinfocanada@organon.com
Telephone: 1-844-820-5468
Fax: 1-844-820-5470

You can report any suspected adverse reactions associated with the use of health products to Health Canada by:

- Calling toll-free at 1-866-234-2345; or

- Visiting MedEffect Canada's Web page on Adverse Reaction Reporting (http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/index-eng.php) for information on how to report online, by mail or by fax.

For other health product inquiries related to this communication, contact Health Canada at:

Marketed Health Products Directorate
Email: hc.mhpd-dpsc.sc@canada.ca
Telephone: 1-613-954-6522
Fax: 1-613-952-7738

Original signed by

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