

EZETROL™

Backgrounder

- EZETROL™ (ezetimibe) is the first in a new class of cholesterol lowering drugs, called cholesterol absorption inhibitors, since the introduction of statins to the Canadian market over 15 years ago.
- Ezetimibe, alone or in combination with a statin, is indicated as adjunctive therapy to diet for:
 - The reduction of elevated total cholesterol, LDL-cholesterol, apolipoprotein B, and triglycerides
 - The increase of HDL-cholesterol in patients with primary high blood cholesterol
- Ezetimibe comes in a 10 mg dose tablet, to be taken once a day, with or without food.
- There are two important cholesterol pathways – liver synthesis and intestinal absorption. In treating patients and getting them to goal, it is critical to inhibit both pathways.
- Ezetimibe has a unique, highly specific, mechanism of action which is distinct from other lipid-lowering agents (statins, bile acid sequestrants/resins and fibrates) and is complementary to that of statins:
 - Ezetimibe lowers LDL, or “bad”, cholesterol by selectively inhibiting the absorption of both dietary (cholesterol from food) and biliary (cholesterol manufactured by the liver) across the wall of the small intestine.
 - Statins work on the liver, inhibiting cholesterol synthesis.
- The unique mechanism of action of ezetimibe provided additional LDL-cholesterol reduction when added to any on-going statin therapy. The Add-On study showed:¹
 - An additional LDL-cholesterol reduction of 25 per cent compared with four per cent for the addition of placebo
 - 72 per cent of patients who were not at their LDL-cholesterol goal while being treated with a statin, reached their cholesterol goal when ezetimibe 10 mg was added (vs. 19 per cent with statin plus placebo).
 - A significant lowering of triglyceride levels and an increase in HDL, or “good”, cholesterol.

- In studies where ezetimibe and statin treatments were initiated at the same time, the incremental effect on LDL-cholesterol reduction was independent of the dose or specific statin used. When ezetimibe was co-administered with the lowest dose of any statin, the LDL-cholesterol reduction was similar to that achieved with the highest dose of the corresponding statin alone.^{2,3}
- Ezetimibe can also be administered alone. In studies where ezetimibe 10 mg was tested as monotherapy, there was an 18 per cent LDL-cholesterol reduction (vs. a one per cent increase with placebo).⁴
- Studies have also shown that ezetimibe can be used for two rare genetic disorders: homozygous familial hypercholesterolemia and homozygous sitosterolemia.
- Ezetimibe has been evaluated for tolerability in more than 4,700 patients in clinical trials. These trials demonstrated that when administered alone, ezetimibe has an excellent tolerability profile similar to placebo. When administered with a statin, ezetimibe has a tolerability profile similar to the statin alone. Adding ezetimibe to any statin provides additional LDL-cholesterol reduction, without compromising tolerability.
- In these trials, the overall incidence of adverse events reported with ezetimibe was similar to that reported with placebo, and the discontinuation rate due to adverse events was also similar for ezetimibe and placebo.
- Ezetimibe costs \$1.58 excluding pharmacists' dispensing fees.

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FOR MORE INFORMATION:

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¹ Gagné C, Bays HE, Weiss SR, Mata P et al. Efficacy and Safety of Ezetimibe Added to Ongoing Statin Therapy for Treatment of Patients with Primary Hypercholesterolemia *Am J Cardiol* 2002;90:1084-1091.

² Ballantyne, C., et al., EZETROL Co-Administered With Atorvastatin in 628 Patients With Primary Hypercholesterolemia, presented at the American College of Cardiology, March 2002.

³ Davidson MF, McGarry T, Bettis R et al. Ezetimibe Coadministered with Simvastatin in Patients with Primary Hypercholesterolemia. *Journal of the American College of Cardiology* 2002;40: 2125-34

⁴ Dujovne CA, Ettinger MP, McNeer JF et al. Efficacy and Safety of a Potent New Selective Cholesterol Absorption Inhibitor, Ezetimibe, in Patients with Primary Hypercholesterolemia *Am J Cardiol* 2002;90:1092-1097.