# EZETROL®

## Backgrounder

Ezetrol® (ezetimibe), the first and only cholesterol absorption inhibitor in Canada, helps lower total and low-density lipoprotein (LDL) cholesterol by inhibiting the absorption of both dietary cholesterol (from food) and biliary cholesterol (manufactured by the liver) across the wall of the small intestine. This mechanism of action is distinct from other lipid-lowering agents, such as statins, bile acid sequestrants/resins and fibrates. Ezetimibe is taken as a 10 mg tablet once daily, with or without food.

### Mechanism of action

There are two important cholesterol pathways: intestinal absorption and liver synthesis. Since ezetimibe inhibits cholesterol absorption from both dietary and biliary sources across the wall of the small intestine and statins inhibit cholesterol synthesis in the liver, adding ezetimibe to statin therapy inhibits both sources of cholesterol. In treating high-risk patients and getting them to goal, inhibiting both cholesterol absorption and production is a proven and effective strategy.

### Indications

Ezetimibe, alone or in combination with a statin, is indicated as adjunctive therapy to diet for:

- The reduction of elevated total cholesterol, LDL-cholesterol, Apo-B, and triglycerides;
- The increase of HDL-cholesterol in patients with primary high blood cholesterol.

### Efficacy

Ezetimibe provides additional cholesterol reduction when added to any on-going statin therapy. In the Canadian Ezetrol® Add-On study:[1]

- Statistically significant mean reductions were observed in LDL-cholesterol (30%), total cholesterol (21%), triglycerides (10%), Apo-B (20%) and TC/HDL-C (20%)

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]

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Ezetimibe can also be administered alone. In studies where ezetimibe was tested as monotherapy, there was an average 18% LDL-cholesterol reduction.[4]

Studies have also shown that ezetimibe can be used for two rare genetic disorders: homozygous familial hypercholesterolemia and homozygous sitosterolemia.

**Tolerability**

Ezetimibe has been evaluated for tolerability in more than 5,000 patients in clinical trials. These trials demonstrated that when administered alone, ezetimibe has a tolerability profile that is similar to placebo. When administered with any statin, ezetimibe has a tolerability profile similar to the statin alone, except for liver enzyme ≥ 3 x ULN (1.3% compared to 0.4% in patients on a 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 to placebo. Ezetimibe has been used to treat more than 7.5 million patients around the world.

**Dosage**

- 10 mg tablet taken once daily, with or without food



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[1] Bissonnette, S et al. Efficacy and Tolerability of Ezetimibe 10mg/Day Co-Administered With Statins In Patients with Primary Hypercholesterolemia Not Achieving Target LDL-C While On Statin Monotherapy: A Canadian, Multi-Center, Prospective Study. The Ezetrol Add-On Study, *Canadian Journal of Cardiology*, 2006;22 (12), 1035-1044.
[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 Co-Administered with Simvastatin in Patients with Primary Hypercholesterolemia. *Journal of the American College of Cardiology* 2002;40:2125-34
[4] Ezetrol Product Monograph, p. 18, Table 3.