HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use VYTORIN safely and effectively. See full prescribing information for VYTORIN.

VYTORIN® (ezetimibe and simvastatin) Tablets
Initial U.S. Approval: 2004

----------INDICATIONS AND USAGE ----------
VYTORIN, which contains a cholesterol absorption inhibitor and an HMG-CoA reductase inhibitor (statin), is indicated as adjunctive therapy to diet to:
- reduce elevated total-C, LDL-C, Apo B, TG, and non-HDL-C, and to increase HDL-C in patients with primary (heterozygous familial and non-familial) hyperlipidemia or mixed hyperlipidemia. (1.1)
- reduce elevated total-C and LDL-C in patients with homozygous familial hypercholesterolemia (HoFH), as an adjunct to other lipid-lowering treatments. (1.2)

Limitations of Use (1.3)
- No incremental benefit of VYTORIN on cardiovascular morbidity and mortality over and above that demonstrated for simvastatin has been established.
- VYTORIN has not been studied in Fredrickson Type I, III, IV, and V dyslipidemias.

---------- DOSAGE AND ADMINISTRATION----------
- Dose range is 10/10 mg/day to 10/40 mg/day. (2.1)
- Recommended usual starting dose is 10/10 or 10/20 mg/day. (2.1)
- Due to the increased risk of myopathy, including rhabdomyolysis, use of the 10/80-mg dose of VYTORIN should be restricted to patients who have been taking VYTORIN 10/80 mg chronically (e.g., for 12 months or more) without evidence of muscle toxicity. (2.2)
- Patients who are currently tolerating the 10/80-mg dose of VYTORIN who need to be initiated on an interacting drug that is contraindicated or is associated with a dose cap for simvastatin should be switched to an alternative statin or statin-based regimen with less potential for the drug-drug interaction. (2.2)
- Due to the increased risk of myopathy, including rhabdomyolysis, associated with the 10/80-mg dose of VYTORIN, patients unable to achieve their LDL-C goal utilizing the 10/40-mg dose of VYTORIN should not be titrated to the 10/80-mg dose, but should be placed on alternative LDL-C-lowering treatment(s) that provides greater LDL-C lowering. (2.2)
- Dosing of VYTORIN should occur either ≥2 hours before or ≥4 hours after administration of a bile acid sequestrant. (2.3, 7.5)

---------- DOSAGE FORMS AND STRENGTHS ----------
- Tablets (ezetimibe mg/simvastatin mg): 10/10, 10/20, 10/40, 10/80 (3)

----------CONTRAINDICATIONS ----------
- Concomitant administration of strong CYP3A4 inhibitors. (4, 5.1)
- Concomitant administration of gemfibrozil, cyclosporine, or danazol. (4, 5.1)
- Hypersensitivity to any component of this medication (4, 6.2)
- Active liver disease or unexplained persistent elevations of hepatic transaminase levels (4, 5.2)
- Women who are pregnant or may become pregnant (4, 8.1)
- Nursing mothers (4, 8.3)

----------WARNINGS AND PRECAUTIONS----------
- **Patients should be advised of the increased risk of myopathy, including rhabdomyolysis, with the 10/80-mg dose. (5.1)**
- Patients should be advised to report promptly any unexplained and/or persistent muscle pain, tenderness, or weakness. VYTORIN should be discontinued immediately if myopathy is diagnosed or suspected. (5.1)
- Skeletal muscle effects (e.g., myopathy and rhabdomyolysis): Risks increase with higher doses and concomitant use of certain medicines. Predisposing factors include advanced age (≥65), female gender, uncontrolled hypothyroidism, and renal impairment. Rare cases of rhabdomyolysis with acute renal failure secondary to myoglobinuria have been reported. (4, 5.1, 8.5, 8.6)
- Liver enzyme abnormalities: Persistent elevations in hepatic transaminases can occur. Check liver enzyme tests before initiating therapy and as clinically indicated thereafter. (5.2)

---------- ADVERSE REACTIONS----------
- Common (incidence ≥2% and greater than placebo) adverse reactions in clinical trials: headache, increased ALT, myalgia, upper respiratory tract infection, and diarrhea. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., at 1-877-888-4231 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

----------DRUG INTERACTIONS ----------
Drug Interactions Associated with Increased Risk of Myopathy/Rhabdomyolysis (2.3, 2.4, 4, 5.1, 7.1, 7.2, 7.3, 7.8, 12.3)

Interacting Agents	Prescribing Recommendations
Strong CYP3A4 Inhibitors, (e.g., itraconazole, ketoconazole, posaconazole, voriconazole, erythromycin, clarithromycin, telithromycin, HIV protease inhibitors, boceprevir, telaprevir, nefazodone, cobicistat-containing products), gemfibrozil, cyclosporine, danazol	Contraindicated with VYTORIN
Verapamil, diltiazem, dronedarone	Do not exceed 10/10 mg VYTORIN daily
Amiodarone, amlodipine, ranolazine	Do not exceed 10/20 mg VYTORIN daily
Lomitapide	For patients with HoFH, do not exceed 10/20 mg VYTORIN daily*
Grapefruit juice	Avoid grapefruit juice

* For patients with HoFH who have been taking 80 mg simvastatin chronically (e.g., for 12 months or more) without evidence of muscle toxicity, do not exceed 10/40 mg VYTORIN when taking lomitapide.

- Coumarin anticoagulants: simvastatin prolongs INR. Achieve stable INR prior to starting VYTORIN. Monitor INR frequently until stable upon initiation or alteration of VYTORIN therapy. (7.8)
- Cholestyramine: Combination decreases exposure of ezetimibe. (2.3, 7.5)
- Other Lipid-lowering Medications: Use with fenofibrates or lipid-modifying doses (≥1 g/day) of niacin increases the risk of adverse skeletal muscle effects. Caution should be used when prescribing with VYTORIN. (5.1, 7.2, 7.4)
- Fenofibrates: Combination increases exposure of ezetimibe. If cholelithiasis is suspected in a patient receiving ezetimibe and a fenofibrate, gallbladder studies are indicated and alternative lipid-lowering therapy should be considered. (7.2, 7.7, 12.3)

---------- USE IN SPECIFIC POPULATIONS ----------
- Moderate to severe renal impairment: Doses exceeding 10/20 mg/day should be used with caution and close monitoring (2.5, 8.6).

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 03/2015

FULL PRESCRIBING INFORMATION: CONTENTS*