CAREMARK TrendsRx® Clinical Alert

What's new...What's next...What to do now October 2004

DRUG APPROVAL

Vytorin™ (ezetimibe/simvastatin)

Vytorin™ (ezetimibe/simvastatin, Merck/Schering-Plough Pharmaceuticals) was approved in July 2004 by the U.S. Food and Drug Administration (FDA) for the treatment of primary hypercholesterolemia and homozygous familial hypercholesterolemia (HoFH). Vytorin is a combination of the cholesterol-absorption inhibitor, ezetimibe (Zetia™), and the HMG Co-A reductase inhibitor, simvastatin (Zocor®). By targeting two different mechanisms that contribute to increased cholesterol, Vytorin has been shown to reduce LDL levels by up to 60 percent. The most commonly reported side effects seen in clinical trials were headache, respiratory tract infection and muscle pain. Vytorin is available in four different dosing combinations utilizing the 10 mg strength of ezetimibe and the 10, 20, 40 or 80 mg strength of simvastatin. The annual cost of therapy, based on average wholesale price, is 46 percent to 61 percent less than the cost of Vytorin's individual components.

BACKGROUND

Hypercholesterolemia is a risk factor for heart disease and studies have shown that elevated LDL cholesterol is a major contributor. The primary objective of lipid-lowering therapy is to reduce LDL levels to a recommended goal. Risk factors for developing heart disease include cigarette smoking, hypertension (>140/90 mmHg), low HDL cholesterol (<40 mg/dL), family history of early heart disease, and age (men 45 years or older; women 55 years or older). The number of risk factors a person has will determine their LDL goal. The National Cholesterol Education Program* released an update to the clinical practice guidelines on cholesterol management in the July 13, 2004, issue of *Circulation: Journal of the American Heart Association*. The update advises physicians to consider more intensive treatment for persons at high- and moderately high-risk for a heart attack. The table below shows the LDL goal in different risk categories based on the updated guidelines.

Risk Category	LDL-C Goal
High-Risk	< 100 mg/dL (< 70 mg/dL optional goal in very high-risk)
Moderately High-Risk	< 130 mg/dL (< 100 mg/dL optional goal)
Moderate-Risk	< 130 mg/dL
Lower-Risk	< 160 mg/dL

*Grundy SM, Cleeman JI, Bairey Merz CN, Brewer HB, Clark LT, Hunninghake DB, Pasternak RC, Smith SC, Stone NJ; for the Coordinating Committee of the National Cholesterol Education Program. Implications of Recent Clinical Trials for the National Cholesterol Education Program Adult Treatment Panel III Guidelines. Circulation. 2004; 110:227-239.

The guidelines suggest initiating therapy that will reduce LDL levels by at least 30 percent to 40 percent in persons at high- and moderately-high risk.

DOSAGE AND ADMINISTRATION

Primary Hypercholesterolemia
The usual starting dose is 10/20 mg daily with therapeutic lifestyle changes. Persons requiring a larger reduction in LDL levels (greater than 55 percent) may be started at 10/40 mg daily.

Homozygous Familial Hypercholesterolemia (HoFH)
The recommended dosage for HoFH is 10/40 mg/day or 10/80 mg/day in the evening.

MONITORING

- Myopathy / Rhabdomyolysis
  - Increased risk with concomitant use of potent CYP3A4 inhibitors (e.g. itraconazole, erythromycin, clarithromycin, etc), gemfibrozil, and other lipid-lowering drugs
  - Concomitant use of these agents with Vytorin should be avoided
  - Risk is dose-related for simvastatin
- Elevated Liver Enzymes
  - Liver function tests (LFTs) to be performed prior to initiation of therapy and thereafter as clinically appropriate
  - Persons on the 10/80 mg dose should have LFTs done prior to initiation, three months after, and semi-annually for the first year of treatment

PREFERRED PROVIDER INFORMATION

Based on currently available data, Caremark suggests considering coverage of Vytorin under your prescription benefit. Vytorin is available through both mail service and retail channels.

For clients with CustomCare Retail, Caremark will include Vytorin in the current intervention for cholesterol-lowering drugs focusing on optimal drug utilization based on cardiovascular risk factors. Caremark will continue to monitor the utilization of Vytorin to determine if any additional clinical programs are needed.

CONTACT

For more information, call your Caremark account representative.

Please Note: This document provides a brief overview of the subject. Please refer to the manufacturer's full prescribing information for a complete discussion of the product. This review is provided as a reference only, and is based in part on information derived from third parties.

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