SPINE SAFETY CAUTIONARY NOTICE:

Information for Healthcare Professionals:
Zocor (simvastatin) tablets:
Labeling Changes

According to MedWatch, FDA notified healthcare professionals of labeling changes for Zocor (simvastatin) tablets. The following has been added to the labeling:

CONTRAINDICATIONS

- Concomitant administration of strong CYP3A4 inhibitors (e.g., itraconazole, ketoconazole, posaconazole, HIV protease inhibitors, erythromycin, clarithromycin, telithromycin and nefazodone).
- Concomitant administration of gemfibrozil, cyclosporine, or danazol.

WARNINGS AND PRECAUTIONS

Myopathy/Rhabdomyolysis

- ...the incidence of myopathy (defined as unexplained muscle weakness or pain with a serum creatine kinase [CK] >10 times upper limit of normal [ULN]) in patients on 80 mg/day was approximately 0.9% compared with 0.02% for patients on 20 mg/day. The incidence of rhabdomyolysis (defined as myopathy with a CK >40 times ULN) in patients on 80 mg/day was approximately 0.4% compared with 0% for patients on 20 mg/day.
- The risk of myopathy, including rhabdomyolysis, is greater in patients on simvastatin 80 mg compared with other statin therapies with similar or greater LDL-C-lowering efficacy and compared with lower doses of simvastatin. Therefore, the 80-mg dose of ZOCOR should be used only in patients who have been taking simvastatin 80 mg chronically (e.g., for 12 months or more) without evidence of muscle toxicity. If, however, a patient who is currently tolerating the 80-mg dose of ZOCOR needs to be initiated on an interacting drug that is contraindicated or is associated with a dose cap for simvastatin, that patient should be switched to an alternative statin with less potential for the drug-drug interaction. Patients should be advised of the increased risk of myopathy, including rhabdomyolysis, and to report promptly any unexplained muscle pain, tenderness or weakness. If symptoms occur, treatment should be discontinued immediately
- Therefore, the 80-mg dose of Zocor should be used only in patients who have been taking simvastatin 80 mg chronically (e.g., for 12 months or more) without evidence of muscle toxicity.
- In vitro studies have demonstrated a potential for voriconazole to inhibit the metabolism of simvastatin. Adjustment of the simvastatin dose may be needed to reduce the risk of myopathy, including rhabdomyolysis, if voriconazole must be used concomitantly with simvastatin.
- The combined use of simvastatin with gemfibrozil, cyclosporine, or danazol is contraindicated.

- Caution should be used when prescribing other fibrates with simvastatin, as these agents can cause myopathy when given alone and the risk is increased when they are co-administered.
- Cases of myopathy, including rhabdomyolysis, have been reported with simvastatin coadministered with colchicine, and caution should be exercised when prescribing simvastatin with colchicine.
- Caution should be used when treating Chinese patients with simvastatin in doses exceeding 20 mg/day coadministered with lipidmodifying doses of niacin-containing products.
- Note that ALT may emanate from muscle, therefore ALT rising with CK may indicate myopathy.

ADVERSE REACTIONS

Clinical Trials Experience

- In a clinical trial in which 12,064 patients with a history of myocardial infarction were treated with Zocor (mean follow-up 6.7 years), the incidence of myopathy (defined as unexplained muscle weakness or pain with a serum creatine kinase [CK] >10 times upper limit of normal [ULN]) in patients on 80 mg/day was approximately 0.9% compared with 0.02% for patients on 20 mg/day. The incidence of rhabdomyolysis (defined as myopathy with a CK >40 times ULN) in patients on 80 mg/day was approximately 0.4% compared with 0% for patients on 20 mg/day. The incidence of myopathy, including rhabdomyolysis, was highest during the first year and then notably decreased during the subsequent years of treatment. In this trial, patients were carefully monitored and some interacting medicinal products were excluded.
- ...the incidence of myopathy (defined as unexplained muscle weakness or pain with a serum creatine kinase [CK] >10 times upper limit of normal [ULN]) in patients on 80 mg/day was approximately 0.9% compared with 0.02% for patients on 20 mg/day. The incidence of rhabdomyolysis (defined as myopathy with a CK >40 times ULN) in patients on 80 mg/day was approximately 0.4% compared with 0% for patients on 20 mg/day. The incidence of myopathy, including rhabdomyolysis, was highest during the first year and then notably decreased during the subsequent years of treatment. In this trial, patients were carefully monitored and some interacting medicinal products were excluded.

DRUG INTERACTIONS

- Concomitant use of drugs labeled as having a strong inhibitory effect on CYP3A4 is contraindicated [see Contraindications (4)]. If treatment with itraconazole, ketoconazole, posaconazole, erythromycin, clarithromycin or telithromycin is unavoidable, therapy with simvastatin must be suspended during the course of treatment.
- Although not studied clinically, voriconazole has been shown to inhibit lovastatin metabolism in vitro (human liver microsomes). Therefore, voriconazole is likely to increase the plasma concentration of simvastatin. It is recommended that dose

adjustment of simvastatin be considered during concomitant use of voriconazole and simvastatin to reduce the risk of myopathy, including rhabdomyolysis.

- Cyclosporine or Danazol: The risk of myopathy, including rhabdomyolysis is increased by concomitant administration of cyclosporine or danazol. Therefore, concomitant use of these drugs is contraindicated.

Colchicine

- Cases of myopathy, including rhabdomyolysis, have been reported with simvastatin coadministered with colchicine, and caution should be exercised when prescribing simvastatin with colchicine.

USE IN SPECIFIC POPULATIONS

Geriatric Use

- Because advanced age (≥65 years) is a predisposing factor for myopathy, including rhabdomyolysis, Zocor should be prescribed with caution in the elderly. In a clinical trial of patients treated with simvastatin 80 mg/day, patients ≥65 years of age had an increased risk of myopathy, including rhabdomyolysis, compared to patients <65 years of age.

The North American Spine Society is committed to quality patient care through promotion of patient safety and prevention of medical errors. NASS monitors a variety of government and other resources for patient safety related notices that may be useful to our members. Information from these notices is also archived on the NASS website at http://www.spine.org/Pages/PracticePolicy/ClinicalCare/SpineSafetyAlerts/Default.aspx. This information is provided as a service for information and education only.