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Bureau for Medical Services

DUR Capsules

News and Information for West Virginia Providers from the West Virginia Bureau for Medical Services (WVBMS)

New Prescribing Recommendations for Simvastatin
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Issue

Simvastatin (Zocor®) is one of several available HMG CoA Reductase Inhibitors (commonly known as "statins") and is considered a first-line therapy for treating hyperlipidemia. However, muscle related adverse events continue to plague this class of medications, including the highest approved dose of simvastatin. As of June 8, 2011, the manufacturer and Food and Drug Administration (FDA) have placed new restrictions on simvastatin 80 mg due to an increased risk of muscle injury (myopathy/rhabdomyolysis).[1-4] This newsletter highlights the new recommendations for simvastatin as they apply to the single entity agent and the combinations of ezetimibe/simvastatin (Vytorin®) and niacin/simvastatin (Simcor®).

New Recommendations

An increased risk of adverse drug events has been documented with simvastatin 80 mg compared with other statin therapies with similar LDL-C lowering efficacy and with lower doses of simvastatin. This risk is highest during the first year of treatment. Therefore, updated prescribing information recommends use of the 80 mg dose of simvastatin only for patients who have been taking that dose chronically (e.g., for 12 months or more) without evidence of muscle toxicity.[1,2,4] Patients who have not received simvastatin 80 mg therapy previously should not be started on it. If higher LDL-C lowering is required, an alternative statin or statin-based regimen should be prescribed.[1,2,4] Alternative statin therapy with equivalent LDL-C lowering should also be considered in patients who have been on simvastatin 80 mg for less than 12 months.[1,2,4]

Additionally, simvastatin drug-interactions have been updated to reflect new contraindications and dose restrictions when administered with certain medications. Concomitant use of the medications listed in Table 1 with any available dose of simvastatin or a simvastatin-based combination regimen is now contraindicated.

Table 1. Simvastatin Drug-Drug Contraindications[4,5-7]

Interacting drugs	Updated label
Strong CYP3A4 inhibitors (e.g., itraconazole, ketoconzaole, **posaconazole (new medication added to label)**, HIV Protease Inhibitors, erythromycin, clarithromycin, telithromycin, and nefazodone)	Contraindicated
Gemfibrozil, cyclosporine, and danazol	Contraindicated

Concomitant use of the medications listed in Table 2 with certain doses of simvastatin leads to an increased risk of myopathy due to drug interactions that increase the blood levels of simvastatin. Patients taking a drug that has an interaction with simvastatin should be switched to an alternative statin or alternative LDL-C lowering treatment with less potential for the drug interaction.

Table 2. Simvastatin Drug-Interactions with Dose Restrictions[4,5-7]

Interacting drugs	Updated label
Amiodarone, verapamil, and diltiazem	Do not exceed simvastatin 10 mg daily
Amlodipine and ranolazine	Do not exceed simvastatin 20 mg daily

Clinical Evidence Supporting the Updated Label Information

The updated drug labels for simvastatin and simvastatin-containing medications are based on the FDA's review of the SEARCH (the Study of the Effectiveness of Additional Reductions in Cholesterol and Homocysteine) trial.[2] It was a seven-year, randomized, double-blind clinical trial comparing the efficacy and safety of simvastatin 80 mg to simvastatin 20 mg daily. The incidence of myopathy (defined as unexplained muscle weakness or pain with a serum creatine kinase [CK] > 10 times upper limit of normal [ULN]) was higher with simvastatin 80 mg/day (0.9%) compared to simvastatin 20 mg/day (0.02%). The incidence of rhabdomyolysis (defined as myopathy with a CK > 40 times ULN) was also higher with simvastatin 80 mg/day (0.4%) compared to simvastatin 20 mg/day (0%). The risk of myopathy and rhabdomylysis with simvastatin 80 mg was highest in the first 12 months of treatment, and then decreased during the subsequent years of treatment. The SEARCH trial results, along with analyses of the FDA Adverse Event Reporting System (AERS) database and other clinical trial data, provide the clinical evidence supporting the changes in the new simvastatin recommendations.

Alternative Therapy

There are alternative treatment options available within the statin class that are equally efficacious in reducing the LDL-C level compared to simvastatin 80 mg that are not associated with an increased risk of myopathy. These alternatives include atorvastatin (Lipitor®) 40 mg, rosuvastatin (Crestor®) 10 mg, and ezetimibe/simvastatin (Vytorin®) 10/20 mg. Additional information comparing the relative LDL-C lowering efficacy of statin and statin-based therapies can be found in Table 3.

Table 3. Statin LDL Lowering Efficacy[2,3,5-7]

Atorvastatin (Lipitor®)	Fluvastatin (Lescol®)	Lovastatin (Mevacor®)	Pravastatin (Pravachol®)	Rosuvastatin (Crestor®)	Vytorin®	Simvastatin (Zocor®)	% ↓ LDL
-----	40 mg	20 mg	20 mg	-----	-----	10 mg	30%
10 mg	80 mg	40 or 80 mg	40 mg	-----	-----	20 mg	38%
20 mg	-----	80 mg	80 mg	5 mg	10/10 mg	40 mg	41%
40 mg	-----	-----	-----	10 mg	10/20 mg	80 mg	47%
80 mg	-----	-----	-----	20 mg	10/40 mg	-----	55%
-----	-----	-----	-----	40 mg	10/80 mg	-----	63%

Summary of the Updated Label Information: What you need to know

- Simvastatin 80 mg and Vytorin® 10/80 mg significantly increases the risk of muscle toxicity.
- The updated label recommends use of the 80 mg dose of simvastatin and Vytorin® 10/80 only in patients who have been taking that dose chronically (e.g., for 12 months or more) without evidence of muscle toxicity (e.g., muscle pain, tenderness or weakness, dark or red colored urine, or unexplained tiredness).
- Patients taking a drug that has an interaction with simvastatin should be switched to an alternative statin or alternative LDL-C lowering treatment with less potential for the drug interaction.
- Patients unable to achieve their LDL-C goal with simvastatin 40 mg or Vytorin® 10/40 mg should consider alternative LDL-C lowering treatments instead of titrating to simvastatin 80 mg or Vytorin® 10/80mg.

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