

New Restrictions, Contraindications and Dose Limitations for Simvastatin-containing Medications (Zocor®, Vytorin®) Due to Dose-related Risk of Muscle Injury

Based on the FDA's review of the Study of the Effectiveness of Additional Reductions in Cholesterol and Homocysteine (SEARCH), new changes to the drug labels for simvastatin-containing medications were made. In this trial, 52 patients in the 80 mg group developed myopathy compared to one patient in the 20 mg group. Twenty-two patients in the 80 mg group developed rhabdomyolysis compared to non-patients in the 20 mg group.

Label changes include:

- Simvastatin 80 mg should not be started in new patients.
- Patients may continue simvastatin 80 mg only if they have been taking this dose for 12 or more months without evidence of muscle injury.
- Use alternative LDL cholesterol-lowering treatment if patients do not meet their LDL cholesterol goal on simvastatin 40 mg
- Follow recommendations in the drug labeling (contraindications and dose limitations) regarding interacting drugs that may increase levels of simvastatin. Consider switching patients who need to be initiated on a drug that interacts with simvastatin to an alternative statin with less potential for the drug-drug interaction.

Simvastatin Dose Limitations (new labeling highlighted in red)

Drugs contraindicated with simvastatin:	Do not exceed 10 mg simvastatin daily with:
<ul style="list-style-type: none">• Itraconazole• Ketoconazole• Posaconazole• Erythromycin• Clarithromycin• Telithromycin• HIV protease inhibitors• Nefazodone• Gemfibrozil• Cyclosporine• Danazol	<ul style="list-style-type: none">• Amiodarone• Verapamil• Diltiazem
	Do not exceed 20 mg simvastatin daily with:
	<ul style="list-style-type: none">• Amlodipine• Ranolazine

Relative LDL-lowering Efficacy of Statin and Statin-based Therapies

Atorva	Fluva	Pitava	Lova	Prava	Rosuva	Simva	Ezet/Simva	%↓ LDL-C
-----	40 mg	1 mg	20 mg	20 mg	-----	10 mg	-----	30%
10 mg	80 mg	2 mg	40 or 80 mg	40 mg	-----	20 mg	-----	38%
20 mg	-----	4 mg	80 mg	80 mg	5 mg	40 mg	10/10 mg	41%
40 mg	-----	-----	-----	-----	10 mg	80 mg	10/20 mg	47%
80 mg	-----	-----	-----	-----	20 mg	-----	10/40 mg	55%
-----	-----	-----	-----	-----	40 mg	-----	10/80 mg	63%

Atorva=Atorvastatin; Fluva=Fluvastatin; Pitava=Pitavastatin; Lova=Lovastatin;
Prava=Pravastatin; Rosuva=Rosuvastatin; Simva=Simvastatin;
Ezet/Simva=Ezetimibe/Simvastatin.

References

1. Food and Drug Administration. [FDA drug safety communication: New restrictions, contraindications, and dose limitations for Zocor \(simvastatin\) to reduce the risk of muscle injury](#). June 8, 2011.
2. Merck. [Health Care Professional Letter for restricted dosing of simvastatin 80-mg dose and updated drug interaction information due to dose-related risk of myopathy/rhabdomyolysis](#). [Health Care Letter]. June 8, 2011.