Clinic Medication Summary
Simvastatin - Safe Prescribing

- Use simvastatin 80 mg or ezetimibe 10 mg/simvastatin 80 mg only in patients who have been taking this dose for \(\geq 12\) months without evidence of muscle injury (myopathy).
- Do not start new patients or titrate up current patients to simvastatin 80 mg or ezetimibe 10 mg/simvastatin 80 mg. Use alternative agents as needed to achieve LDL goal or to avoid drug-drug interactions.
- Simvastatin in combination with gemfibrozil is now contraindicated.
- Do not exceed simvastatin 10mg in combination with amiodarone, verapamil or diltiazem.
- Do not exceed simvastatin 20mg in combination with amlodipine.
- Atorvastatin 40mg and 80mg are available as brand-preferred on Group Health's formulary (July 2011).

<table>
<thead>
<tr>
<th>Contraindicated with Simvastatin</th>
<th>Do Not Exceed Simvastatin 10 mg daily with:</th>
<th>Do Not Exceed Simvastatin 20 mg daily with:</th>
<th>Grapefruit Juice</th>
</tr>
</thead>
<tbody>
<tr>
<td>Itraconazole</td>
<td>HIV protease inhibitors</td>
<td>Amiodarone (revised)</td>
<td>Avoid large quantities (&gt;1 quart daily)</td>
</tr>
<tr>
<td>Ketoconazole</td>
<td>Nefazodone</td>
<td>Verapamil (revised)</td>
<td></td>
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<tr>
<td>Posaconazole (new)</td>
<td>Gemfibrozil (revised)</td>
<td>Diltiazem (revised)</td>
<td></td>
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<tr>
<td>Erythromycin</td>
<td>Cyclosporine (revised)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>Danazol (revised)</td>
<td></td>
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<tr>
<td>Telithromycin</td>
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</tbody>
</table>

What are the risk factors for developing simvastatin-related myopathy?
- Risk is dose-related (highest risk with simvastatin 80mg)
- Less than 1 year on simvastatin 80mg
- On interacting medications
- Female
- Age \(\geq 65\) years
- Uncontrolled hypothyroidism
- Renal impairment
- Co-administration of fibrates or niacin \(\geq 1\) g/day
- Patients of Chinese descent on simvastatin >20mg/day and niacin \(\geq 1\) g/day

<table>
<thead>
<tr>
<th>CLINICAL SCENARIOS</th>
<th>RECOMMENDATIONS FOR MANAGEMENT OF SIMVASTATIN REVISED LABEL CHANGES PER GH ASCVD GUIDELINE TEAM</th>
</tr>
</thead>
<tbody>
<tr>
<td>SIMVASTATIN DOSE 80MG/DAY</td>
<td></td>
</tr>
<tr>
<td>On simvastatin 80 mg daily for (\geq 12) months without evidence of myopathy and not taking interacting meds At LDL goal</td>
<td>Maintain on current treatment</td>
</tr>
<tr>
<td>On simvastatin 80 mg daily &lt; 12 months At LDL goal</td>
<td>Switch to atorvastatin 40 mg daily</td>
</tr>
<tr>
<td>On simvastatin 80 mg daily Not at LDL goal</td>
<td>Switch to atorvastatin 80 mg daily</td>
</tr>
<tr>
<td>SIMVASTATIN DOSE &lt;80MG/DAY</td>
<td></td>
</tr>
<tr>
<td>On simvastatin &lt;80 mg daily without evidence of myopathy and not taking interacting meds At LDL goal</td>
<td>Maintain on current treatment</td>
</tr>
<tr>
<td>On simvastatin 40 mg daily Not at LDL goal, despite compliance</td>
<td>Switch to atorvastatin 40 mg daily</td>
</tr>
</tbody>
</table>
SIMVASTATIN AND CONTRAINDICATED DRUGS

- Simvastatin AND gemfibrozil
- Evaluate whether combination therapy is needed.
- Statin monotherapy (GH preferred 1st option) may lower TG levels sufficiently without addition of a fibrate. Statin % TG lowering is dependent on the baseline TG and dose of the statin. The greater the baseline TG the greater the % TG lowering:
  - Baseline TG <300mg/dL: atorvastatin 40mg decreases TG by 24.9%
  - Baseline TG > 600mg/dL: atorvastatin 40mg decreases TG by 45%
- There is no evidence on the effectiveness of dual therapy for primary prevention in ASCVD.
- If combination therapy is needed in a patient with ASCVD and TG ≥500 mg/dL, consider the following guidance from the GH ASCVD guideline:
  - Add fish oil (2nd)
  - Statin and fenofibrate (3rd)
  - Statin and niacin IR/niacin SR (Slo-Niacin) (4th)

- Simvastatin AND one of these anti-infectives:
  - Itraconazole
  - Ketoconazole
  - Posaconazole
  - Erythromycin
  - Clarithromycin
  - Telithromycin
- If anti-infective course of therapy is of short duration, hold simvastatin doses until anti-infective course is completed, then resume simvastatin.
- If need to be on anti-infective long-term, switch to equipotent dose of pravastatin or atorvastatin.
- Note that per manufacturer, itraconazole may double pravastatin levels, and that caution should be used if on atorvastatin >20 mg daily with clarithromycin or itraconazole.

SIMVASTATIN AND INTERACTING DRUGS – SIMVASTATIN DOSE LIMITS

- Simvastatin >10 mg daily AND amiodarone
  - Switch to equipotent dose of pravastatin or atorvastatin
- Simvastatin >10 mg daily AND diltiazem OR verapamil
  - Switch to equipotent dose of pravastatin or atorvastatin (however, be aware that diltiazem can increase atorvastatin levels by ~50%)
- Simvastatin >20 mg daily AND amlodipine
  - Switch amlodipine to felodipine. Dosing conversion is usually 1:1 (i.e., amlodipine 10 mg daily → felodipine 10 mg daily)
  - Switch simvastatin to equipotent dose of pravastatin or atorvastatin

Relative LDL-Lowering Efficacy of Statins

<table>
<thead>
<tr>
<th>Statin</th>
<th>10 mg</th>
<th>20 mg</th>
<th>40 mg</th>
<th>80 mg</th>
<th>10/20 mg</th>
<th>10/40 mg</th>
<th>10/80 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atorvastatin</td>
<td>-</td>
<td>20 mg</td>
<td>20 mg</td>
<td>-</td>
<td>-</td>
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<td>-</td>
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<tr>
<td>Lovastatin</td>
<td>10 mg</td>
<td>-</td>
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<td>-</td>
<td>-</td>
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<td>-</td>
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<tr>
<td>Pravastatin</td>
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<td>Ezetimibe</td>
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<tr>
<td>Simvastatin</td>
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<td>-</td>
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<td>-</td>
</tr>
<tr>
<td>%LDL Reduction</td>
<td>30%</td>
<td>38%</td>
<td>41%</td>
<td>47%</td>
<td>55%</td>
<td>63%</td>
<td></td>
</tr>
</tbody>
</table>

References

- FDA drug safety communication: new restrictions, contraindications, and dose limitations for Zocor (simvastatin) to reduce the risk of muscle injury, June 8, 2011 (accessed June 24, 2011).