Prescribing tips for Simvastatin

Simvastatin is available in tablet form in doses ranging from 10 mg to 40 mg. An up-to-date listing of all available preparations is freely accessible on the Irish Medicines Board website www.imb.ie.

Therapeutic Indications

- Hypercholesterolaemia, including homozygous familial hypercholesterolaemia
- Prevention of cardiovascular events

Dosing & Administration

The dose range is 10 mg to 40 mg* given as a single oral dose in the evening. Simvastatin may be taken with or without food.

<table>
<thead>
<tr>
<th>Indication</th>
<th>Starting Dose</th>
<th>Comment</th>
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</thead>
<tbody>
<tr>
<td>Hypercholesterolaemia</td>
<td>10 - 20 mg daily</td>
<td>Those requiring a large reduction in low density lipoprotein (LDL) cholesterol (&gt;45%) may commence on 20-40 mg daily.</td>
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<tr>
<td>Homozygous familial hypercholesterolaemia</td>
<td>40 mg daily</td>
<td>Used as an adjunct to other lipid-lowering treatments</td>
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<tr>
<td>Prevention of cardiovascular events</td>
<td>20 - 40 mg daily</td>
<td></td>
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</tbody>
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* Simvastatin 80 mg is recommended only in patients with severe hypercholesterolaemia at high risk of cardiovascular events and should preferably be initiated and managed under specialist supervision.

Dose Adjustments

Dose adjustments may be made at intervals of at least 4 weeks. Liver function tests are recommended following dose increases.

Important prescribing Information

Muscle Effects Cases of myopathy, myositis & rhabdomyolysis associated with statin use are rare. Muscle toxicity can occur with all statins, however, the likelihood increases with higher doses and in certain patients, e.g. the elderly (>65 years), women, patients with renal impairment or uncontrolled hypothyroidism, patients with heavy alcohol consumption, and those with a personal or family history of muscle problems during statin therapy. Concomitant drug therapy may also increase the risk of statin-related muscle toxicity.

Drug Interactions Simvastatin is metabolised via the cytochrome P450 3A4 (CYP3A4) enzyme system. Consequently, concomitant use with CYP3A4 inhibitors may increase the risk of statin-related toxicity including myopathy and/or rhabdomyolysis.

- **Contraindicated combinations:** Potent CYP3A4 inhibitors, e.g. itraconazole, ketoconazole, posaconazole, HIV protease inhibitors (e.g. ritonavir), boceprevir, telaprevir, erythromycin, clarithromycin, telithromycin & nefazodone. Concomitant administration of gemfibrozil, ciclosporin, danazol or grapefruit juice is also contraindicated.

- **Maximum recommended dose** for simvastatin in conjunction with amlodipine, diltiazem, verapamil and amiodarone is 20 mg daily.

- **Fusidic acid:** temporary suspension of simvastatin treatment may be considered.

For additional information please consult the relevant Summary of Product characteristics (SmPC).