If a patient wants to take a statin, and offering it is in line with national guidance, which one should be recommended?

By Chris Corfield

Three clinical guidelines from the National Institute for Health and Clinical Excellence (NICE) cover statin use in some detail: there are guidelines on lipid modification,1 type 2 diabetes2 and on familial hypercholesterolaemia.3

The guidelines recommend a specific first-choice statin and dose for some indications — such as primary prevention in the absence of familial hypercholesterolaemia — but not for others, such as acute coronary syndrome, where the recommendation is to offer a higher intensity statin, with higher intensity statin defined as one used in doses that produce greater cholesterol lowering than simvastatin 40mg. For some indications the guidelines include ezetimibe among options to be considered.

The choice of statin is important, in part because of the large difference in the price of low-cost generic statins compared with statins protected by patent or supplementary protection certificate (See Panel 1).

This paper highlights three relevant questions, suggests responses to them and then suggests first- or second-line statin choices informed by the responses. Panel 2 shows the percentage reduction in LDL cholesterol achieved by simvastatin and the more potent statins atorvastatin and rosuvastatin.

Questions and suggested responses

Question 1
In some circumstances the guidelines issued by NICE suggest considering increasing the dose of simvastatin to 80mg daily. These guidelines were published before the recent warning from the Medicines and Healthcare products Regulatory Agency about increased risk of myopathy associated with 80mg simvastatin4 and the finding by the Cholesterol Treatment Trials’ Collaboration that all the observed excess of rhabdomyolysis with more intensive statin therapy occurred in trials of simvastatin 80mg versus 20mg daily.5 Given this, is it still reasonable to increase a patient’s simvastatin dose to 80mg daily rather than using a more potent statin?

Suggested response

It is best to avoid new prescriptions for simvastatin 80mg daily. If greater LDL cholesterol reduction than is achievable with simvastatin 40mg daily is indicated, it is preferable to use a more potent statin.

Question 2
If the prescriber decides not to write new prescriptions for simvastatin 80mg daily, which of the newer, more potent statins should be used instead?

Suggested response

Factors to take into account include:
• The Cholesterol Treatment Trials’ Collaboration finding that each 1.0mmol/L reduction in LDL cholesterol reduces the annual rate of major vascular events by just over a fifth
• The patient’s baseline LDL cholesterol and the mean percentage reductions achieved by the various doses of atorvastatin and rosuvastatin (for example, Panel 2 shows that the mean reduction with rosuvastatin 20mg is around 3.3 to 5 per cent greater than the reduction with atorvastatin 40mg daily, so for a patient with baseline LDL cholesterol of 5.0mmol/L using rosuvastatin 20mg rather than atorvastatin 40mg might reduce LDL cholesterol by around 0.25mmol/L more)
• The British National Formulary statement that the dose of rosuvastatin should only be increased to 40mg daily under specialist supervision
• Current prices
• The November 2011 expiry of the UK Supplementary Protection Certificate for atorvastatin (cheaper generics should then appear, although it is not possible to say how rapidly the Drug Tariff price would fall)
• How likely it is that the patient could and would be switched from rosuvastatin to atorvastatin when the Drug Tariff price of atorvastatin falls significantly

Question 3
How does ezetimibe, another LDL cholesterol lowering drug, fit in?

Suggested response


A recent systematic review compared the benefits and harms of high-dose statin monotherapy with those of combination therapy (statin plus lipid modifying drugs other than statins) in adults at high risk of coronary disease.7 No trials compared the effect of combination therapy versus high-dose statin monotherapy on the incidence of myocardial infarction, stroke, or revascularisation procedures.

The Drug and Therapeutics Bulletin recently questioned whether adding ezetimibe to statin

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<th>ABSTRACT</th>
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This paper, the second of two, aims to provide information to help pharmacists discuss economically important choices about which statin to use with prescribers. NICE guidelines recommend a specific first-choice statin and a dose for some indications, but not for others.

Design |
The paper highlights three relevant questions, suggests responses to them and suggests first- or second-line statin choices informed by those responses.

Content |
Included are Panels showing the cost of the various statins and the mean percentage reduction in LDL cholesterol achieved by simvastatin, atorvastatin and rosuvastatin. The paper outlines three questions that are relevant to choices when greater LDL cholesterol reduction than is achievable with simvastatin 40mg daily is indicated, and provides suggested responses to those questions and a Table of suggested statin choices informed by those responses.

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About the author
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treatment is a cost-effective or outcome-based intervention. There are no published trials to show it reduces mortality or morbidity. The DTB said: “Since it is proving increasingly expensive for the NHS, prescribers should ask why they are using [ezetimibe].”

Ezetimibe 10mg/day costs £342 a year. The ezetimibe 10mg plus simvastatin 40mg combination product costs £507 a year.

The suggestions in Panel 3 below assume:

- The prescriber agrees that it is best to avoid new prescriptions for simvastatin 80mg daily
- Atorvastatin is favoured over rosuvastatin because prices of the former are likely to fall sooner
- It is generally best to use a statin alone, when not contraindicated and when tolerated, rather than adding ezetimibe
- The suggested drug is tolerated

Choosing which statin to use remains economically important. The financial challenge currently facing the NHS makes it particularly important not to use higher priced statins for indications for which NICE’s guidance recommends low cost simvastatin or pravastatin.

References
### PANEL 3: SUGGESTED STATIN CHOICES INFORMED BY RECENT EVIDENCE*

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<tr>
<th>Drug</th>
<th>Dose</th>
<th>Suggested role and why</th>
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<tr>
<td>Simvastatin</td>
<td>40mg</td>
<td>First choice statin for primary prevention of CVD if the patient’s CVD risk is above the threshold for offering a statin recommended by NICE, and if the patient chooses to try a statin after discussion of factors such as the potential risk reduction or number needed to treat, potential adverse effects and the numbers needed to harm where known (see part 1 of this update). First choice statin for secondary prevention of CVD, except after an acute coronary syndrome (see atorvastatin below). First choice statin in NICE’s clinical guideline on type 2 diabetes.</td>
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<td></td>
<td></td>
<td>Only for patients currently taking and tolerating it.</td>
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<td></td>
<td>80mg</td>
<td></td>
</tr>
<tr>
<td>Atorvastatin</td>
<td>10/20mg</td>
<td>No role, except when up-titrating the dose to &gt;20mg/day for one of the indications listed below, or when other first and second line options are not tolerated. Simvastatin 40mg reduces LDL cholesterol by a similar percentage and costs much less.</td>
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<tr>
<td></td>
<td>&gt;20mg</td>
<td>First choice for use after an acute coronary syndrome. Some cardiologists initiate atorvastatin at 40mg/day but see SPC for the manufacturer’s starting dose recommendations. In people taking simvastatin 40mg/day for secondary prevention, consider increasing to atorvastatin &gt;20mg/day if total cholesterol of less than 4mmol/L or an LDL cholesterol of less than 2mmol/L is not attained (if either figure is below that level, increasing the intensity of treatment is not recommended — National Prescribing Centre). Any decision to offer a higher intensity statin, such as atorvastatin, should take into account informed preference, comorbidities, other drug therapy, and the benefit and risks of treatment.</td>
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<td></td>
<td></td>
<td>In type 2 diabetes: see NICE clinical guideline on type 2 diabetes for when simvastatin 40mg is indicated. Increase from simvastatin 40mg/day to atorvastatin &gt;20mg/day (see SPC for starting dose) unless total cholesterol level is below 4.0mmol/L or LDL cholesterol level is below 2.0mmol/L.</td>
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<tr>
<td></td>
<td></td>
<td>In type 2 diabetes: see NICE clinical guideline on type 2 diabetes for when simvastatin 40mg is indicated. Consider intensifying cholesterol-lowering therapy to atorvastatin &gt;20mg/day (see SPC for starting dose) if there is existing or newly diagnosed cardiovascular disease, or if there is an increased albumin excretion rate, to achieve a total cholesterol level below 4.0mmol/L (HDL cholesterol not exceeding 1.4mmol/L) or an LDL cholesterol level below 2.0mmol/L. Consider for adults with familial hypercholesterolaemia (except when an adult who does not have CHD is diagnosed with familial hypercholesterolaemia after the age of 60 years, when NICE’s guideline recommends offering a statin with a low acquisition cost, e.g. simvastatin).</td>
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<tr>
<td>Rosuvastatin</td>
<td></td>
<td>Adults with familial hypercholesterolaemia, only if the maximum tolerated dose of atorvastatin (check the patient is taking it) fails to achieve the recommended reduction of LDL cholesterol of &gt;50 per cent from the baseline concentration before treatment. The Supplementary Protection Certificate for rosuvastatin does not expire until 2017. The price of atorvastatin will fall much sooner.</td>
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<tr>
<td>Pravastatin</td>
<td></td>
<td>If simvastatin is not tolerated for primary or secondary prevention. If a likely drug interaction makes it a better choice than a statin suggested above.</td>
</tr>
<tr>
<td>Fluvastatin</td>
<td></td>
<td>Probably not a first- or second-line statin for any indication.</td>
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* For cautions, contraindications and drug interactions, see the BNF