NHS Lincolnshire

Prescribing and Clinical Effectiveness Bulletin

Volume 4; Number 13 **August 2010**

REVIEW OF LIPID MODIFICATION GUIDELINES

In response to the MHRA and FDA safety reviews of simvastatin 80mg (see *PACE Bulletin* Vol 4 No 11), PACEF have also revised local lipid modification guidelines as follows:

Primary prevention of cardiovascular disease (CVD)

- **Before offering lipid modification therapy for primary prevention, all other modifiable risk factors should be considered and their management optimised.**
- **For primary prevention, statin therapy is recommended first line in adults who have a 20% or greater 10-year risk of developing CVD.**
- **It is important to involve the patient in the decision to commence treatment.**
- **Initiate treatment with simvastatin 40mg. If there are potential drug interactions, or simvastatin 40mg is contraindicated or not tolerated, a lower dose of simvastatin or pravastatin 40mg should be used.**
- **No targets for Total Cholesterol (TC) or Low Density Lipoprotein-Cholesterol (LDL-C) are recommended for primary prevention. For most primary prevention patients started on a statin, repeat lipid measurement is unnecessary.**
- **Practices should ensure that atorvastatin, rosuvastatin, ezetimibe, omega 3 fatty acid supplements (such as Omacor and Maxepa), fibrates, nicotinic acid and anion exchange resins are not used for primary prevention of CVD.**

Secondary prevention of cardiovascular disease

- **For secondary prevention, lipid modification therapy should be offered and should not be delayed by management of modifiable risk factors.**
- **Statin therapy is recommended for adults with clinical evidence of CVD.**
- **Treatment for secondary prevention of CVD should be initiated with simvastatin 40mg. If there are potential drug interactions, or simvastatin 40mg is contraindicated, an alternative low-cost preparation such as pravastatin should be chosen. If simvastatin 40mg is not tolerated, a lower dose or pravastatin should be chosen.**

PACEF Comment:
Prescribers are reminded that pravastatin 40mg represents a viable alternative to simvastatin 40mg in both primary and secondary prevention of CVD. In terms of total cholesterol lowering it performs marginally below simvastatin 40mg, but, due to the advantage of water solubility, it is better tolerated with a lower potential for interactions. A number of key landmark statin trials (most notably WOSCOPS, CARE and LIPID) have established a sound evidence base for the use of pravastatin in both the primary and secondary prevention of CVD.

- **Targets of 4mmol/litre (TC) and 2mmol/litre (LDL-C) as endorsed by NICE are not cost effective unless a low-cost high-intensity statin such as simvastatin 80mg is used; in the absence of a suitable alternative to simvastatin 80mg, local targets have been revised. Prescribers are advised to work to the minimum audit standard and QOF target of 5mmol/l (TC).**
- **If the patient does not reach the target of 5mmol/l (TC) on simvastatin 40mg, initiate atorvastatin 20mg and titrate up as necessary to achieve target. New initiations of simvastatin 80mg are no longer recommended; existing patients can be maintained on simvastatin 80mg subject to MHRA criteria (see *PACE Bulletin* Vol 4 No 11).**
- **Maintain the patient on the dose of statin required to reach the minimum audit standard of 5mmol/l (TC).**
- **Only consider higher-cost, higher-potency agents in those patients that remain above the minimum audit standard of 5mmol/l (TC) despite taking simvastatin 40mg or who are intolerant to simvastatin and pravastatin or have contra-indications or potential interactions.**

PACEF Comment:
Remember that high-cost high-potency statins like atorvastatin and rosuvastatin are effective, but have emerged from NICE cost-effectiveness evaluations as not cost-effective in most patients. £1M spent on simvastatin delivers 854 avoided events; £1M spent on atorvastatin delivers 55 avoided events. Across a population, this level of return is unaffordable. As a result of this, the use of high-cost, high-potency statins for secondary prevention of CVD should be restricted as outlined above.

PACEF Comment:
The atorvastatin (Lipitor) patent is due to expire in November 2011, but may be extended into 2012. In contrast, rosuvastatin (Crestor) remains under patent until 2018. With the atorvastatin patent expiry looming, PACEF have taken the decision to advocate atorvastatin as the high-cost high-potency statin of choice. Atorvastatin 10mg is equipotent to simvastatin 40mg and should not be used unless simvastatin 40mg (or pravastatin 40mg) are not tolerated or are contra-indicated. Where atorvastatin is indicated second line, it should be initiated at the 20mg dose.

- **Fibrates, nicotinic acid and anion exchange resins may be considered for secondary prevention of CVD in people unable to tolerate statins.**
- **Ezetimibe should only be used within licensed indications (i.e. primary hypercholesterolaemia). Prescribers are strongly urged not to prescribe ezetimibe for secondary or primary prevention of CVD; there is no published data to show reduction in mortality or morbidity with ezetimibe. In addition, the product is expensive and shows only modest**

reduction in TC (12 to 13%) and LDL-C (17 to 22%) in comparison with statins. Even a high-cost high-potency branded statin is more cost-effective.

Diabetes

- **For patients with diabetes with or without CVD, treat as for secondary prevention of CVD.**

Acute Coronary Syndrome

- **If a person has acute coronary syndrome, statin treatment should not be delayed until lipid levels are available.**
- **Initiate simvastatin 40mg as the treatment of first choice.**

PACEF Comment:
The NICE review of statins for ACS published as part of Clinical Guideline 67: *Lipid Modification* (May 2008) concluded that: 'there is good evidence that higher intensity statins (specifically simvastatin 80mg and atorvastatin 80mg) are associated with additional cost-effective reductions in CV events for people after recent MI and in ACS'. In view of the emerging safety concerns with simvastatin 80mg, PACEF have been working with ULHT cardiologists to determine a way forward for patients with ACS. We have reviewed the evidence base for atorvastatin 80mg in ACS in comparison to other statins and find it deficient in direct head-to-head comparative trials between simvastatin 40mg/80mg and atorvastatin 80mg. We are in the process of conducting a more detailed review of the cost-effectiveness of atorvastatin 80mg in ACS, but are unable to support its use at present. It has been estimated that to treat all new patients with ACS in Lincolnshire with atorvastatin 80mg would cost over £0.3Mpa (assuming 1,000 new patients pa); this is in contrast with the current cost of simvastatin 80mg of £38,220pa. Treating these patients with simvastatin 40mg as an interim measure will cost £19,630pa. Review of existing patients with ACS on simvastatin 80mg is likely to add to these costs. Patients with ACS should be started on simvastatin 40mg and titrated up as designated for other secondary prevention of CVD patients.

Acknowledgements

Many thanks to: Dr Richard Andrews, Dr David O'Brien and Alun Roebuck from Cardiology at ULHT for their help during the compilation of this *Bulletin.*

Stephen Gibson
Head of Prescribing and Medicines Management August 2010