Guidelines for the use of statins in secondary prevention of cardiovascular disease and for patients with type 2 diabetes

March 2010
Review date January 2012

© Cheshire & Merseyside Cardiac Network and CHD Collaborative
Guidelines for the use of statins in secondary prevention of cardiovascular disease and for patients with type 2 diabetes

These guidelines represent the views of the Cheshire & Merseyside Cardiac Network (CMCN), which were arrived at after consideration of the available evidence and the development of consensus. They aim to ensure equity and best practice within the context of resources currently available to the NHS locally.

Health professionals are asked to take them into account when exercising their clinical judgement and are encouraged to discuss with colleagues those cases where the assessment of likely benefit from a particular intervention is equivocal.

The guidelines do not override the responsibility of health professionals to make appropriate decisions in the circumstances of the individual patient in consultation with the patient and/or guardian or carer.

This policy refers only to the use of statins for secondary prevention and must not be used for primary prevention or treatment of other hyperlipidaemias.

Introduction

In January 2005, after extensive consultation, CMCN produced its evidence-based guidelines\(^1\) for the use of statins in the secondary prevention of cardiovascular disease (CVD) and for patients with type 2 diabetes mellitus. It was planned to review them in January 2006 but this was delayed due to the initiation of a NICE guideline process. In May 2008, NICE produced its national guideline\(^2\) for cardiovascular risk management including modification of blood lipids in secondary prevention using statins. Compliance with these, as with other NICE guidance, has become a mandatory outcome measure nationwide.

More recently, the Government has also announced a reduction in its allocation of NHS funding in real terms. PCT’s and local Health Economies have been charged with ensuring optimum cost-effectiveness of recommended treatments within the current resource-challenged NHS environment.

However, in the 5 years since the introduction of the CMCN Guidelines, the cardiac and lipid literature has clearly defined that clinical outcomes continue to improve as total cholesterol (TC) and low density lipoprotein cholesterol (LDL) reduce with no identifiable lower limit.

It is on the background of the above that CMCN has produced this updated guideline, being mindful of cost-effectiveness, affordability and opportunity costs.

Recommendations

1. Comprehensive secondary prevention should involve blood tests and clinical assessment including smoking status; alcohol consumption; blood pressure; measures of obesity such as body mass index; lipid measurements including fasting TC, LDL, high density lipoprotein cholesterol (HDL) and triglycerides (if fasting levels are not already available); fasting blood sugar, renal function, liver function including transaminases; and thyroid-stimulation hormone (TSH) if dyslipidaemia is present. However, it is important that lipid modification therapy \textbf{SHOULD NOT BE DELAYED} by management of modifiable risk factors.

2. Statin therapy is recommended as part of the secondary prophylaxis management strategy for:-
   - All adults with evidence of coronary heart disease (CHD), peripheral vascular disease (PVD) or cerebrovascular disease (stroke or TIA)\(^3\)
   - All adults with type 2 diabetes mellitus\(^4\)
3. Based on cost-effectiveness grounds, the 2008 NICE guideline (see algorithm) should be adopted in place of the 2005 CMCN guideline. This recommends for stable patients simvastatin at a dose of 40-80mg (given at night for maximum efficacy) or a drug of similar efficacy and acquisition cost.

4. Patients with acute coronary syndrome (ACS) should be offered a higher intensity statin. For such patients, the current CMCN NSTEACS guideline remains in force and advocates 80mg of atorvastatin for 9-12 months. Some local PCT’s are requiring trusts to limit the treatment period to six months.

5. Apart from ACS, there is no place for the routine use of high acquisition cost statins e.g. atorvastatin, rosuvastatin.

6. Where statin intolerance exists, consider the use of fibrates, nicotinic acid, anion exchange resins or ezetimibe instead.

7. Apart from in the above circumstance, there is no place for the routine use of ezetimibe due to its lack of outcome data and its greater acquisition cost.

**Targets**

Pragmatic targets, as per NICE and QAFF are to lower TC to 5 mol/l and/or LDL to 3mmol/l or less and should replace those in the 2005 CMCN guidelines. However, NICE recognises that these recommendations will result in over half of all patients treated in this way failing to achieve the target levels of TC 4mol/l and LDL 2mmol/l advocated as optimal by National and International academic cardiological societies. CMCN also recognises that this may create a problem for local health care professionals dealing with certain high risk patients whom they may feel will remain sub-optimally treated on simvastatin. In such circumstances, and bearing in mind the over-arching requirement to exercise their clinical judgement, prescribers should undertake a detailed discussion on an individual patient basis taking into account informed preference, co-morbidities, multiple drug therapy, and the benefits and risks of treatment (as recommended by NICE).

**Monitoring**

**Cholesterol:**
Check fasting lipid profile before initiation and random lipid profile three months after initiation or after dose increase until target is achieved, then annually.

**Liver function tests:**
Check before and both at 3 months and 12 months post initiating therapy unless indicated sooner by clinical features suggestive of hepatotoxicity. Treatment with statin therapy should be withdrawn if serum transaminases (AST, ALT) rise to and persist at or above three times the upper limit of normal.

**Creatine Kinase:**
Do not routinely monitor in people without adverse events. Only check if myopathy is suspected, (e.g. patient reports muscle pain, weakness or cramps), or is diagnosed clinically. Stop treatment if symptoms are severe or creatine kinase is elevated to five times or above the upper limit of normal.

**Clinical:**
Advise people to seek medical advice if they develop muscle pain, tenderness or weakness. Stop statins and seek specialist advice if unexplained peripheral neuropathy develops. If drugs that interfere with statin metabolism are introduced for another illness, consider reducing the statin dose or stopping temporarily or permanently.

**Interactions**

- Simvastatin should be avoided and atorvastatin should be used with caution and muscle enzymes monitored in the following drug interactions which increase the risk of myopathy and rhabdomyolysis:
  -
- Grapefruit juice – large quantities raise simvastatin exposure
- Inhibitors of cytochrome P450 (CYP3A4) including:
  - Azole antifungals
  - HIV protease inhibitors
  - Macrolides including erythromycin, clarithromycin, telithromycin.
- Ciclosporin
- Other lipid lowering agents including gemfibrozil, other fibrates and nicotinic acid >1g/day
- Verapamil or amiodarone
- With diltiazem do not exceed 40 mg simvastatin
- Caution when prescribing any statin with warfarin – check INR early and frequently

**Treatment Algorithm**

Offer lipid modification therapy as soon as possible
Offer 40mg simvastatin (or drug of similar efficacy and acquisition cost) to all adults with clinical evidence of CVD
If there are potential drug interactions or if 40mg simvastatin is contraindicated, offer a lower dose of simvastatin or pravastatin

Consider increasing dose to 80mg simvastatin or drug of similar efficacy and cost if the total cholesterol does not fall below 4mmol/l or the LDL cholesterol does not fall below 2mmol/l. Take into account:
- Informed preference
- Co-morbidities
- Other drug therapy
- Benefits and risks

Use an “audit” level of total cholesterol of 5 mmol/l to assess progress in groups with CVD. Recognise that less than half will achieve total cholesterol less than 4 mmol/l or LDL cholesterol less than 2 mmol/l.

Refer to the British National Formulary for further prescribing information.

2. NICE Clinical Guideline 67 – Lipid Modification; Issue date May 2008
4. Overall, the risk of cardiovascular events in patients with type 2 Diabetes equates to that of patients with established cardiovascular disease (CVD). Patients with type 2 diabetes should therefore be managed using these secondary prevention guidelines rather than calculating their individual CVD risk.