Lincolnshire NHS

Prescribing and Clinical Effectiveness Bulletin

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CONTENTS

DRAFT NICE CLINICAL GUIDELINE ON LIPID MODIFICATION FOR THE PRIMARY AND SECONDARY PREVENTION OF CARDIOVASCULAR DISEASE

Key Points

- It is the purpose of this bulletin to summarize **key proposals from the draft NICE Clinical Guideline on lipid modification**. Prescribers are advised that this is a draft for consultation and does not yet constitute NHS policy. The final version of the guideline is due for publication early in 2008.
- For **primary prevention**, statin therapy is recommended first line as part of the management strategy for the primary prevention of CVD in adults who have a 20% or greater 10-year risk of developing CVD. Simvastatin 40mg or pravastatin 40mg are advocated first line. In the absence of an evidence base for targets in primary prevention, no targets are advocated and target chasing is not recommended. Atorvastatin, rosuvastatin, fibrates, nicotinic acid, ezetimibe, omega 3 fatty acid supplements (such as Omacor) and anion exchange resins are not recommended for routine use in primary prevention.
- For **secondary prevention**, statin therapy is recommended for adults with clinical evidence of cardiovascular disease. Simvastatin 40mg is the first line agent of choice. Recommendations within the draft on secondary prevention targets are confused and will require clarification in the final version. At different points within the draft, the options for no targets, 4mmol/l (TC) and 2mmol/l (LDL-C) and a minimum audit standard of 5mmol/l (TC) are all covered. **Prescribers are reminded that current NHS policy endorses targets of 5mmol/l (TC) and 3 mmol/l (LDL-C) and that the DoH has given assurance in writing that this will remain the case until April 2008 at the earliest.** Atorvastatin, rosuvastatin, fibrates, nicotinic acid, ezetimibe, and anion exchange resins should be confined to those insufficiently responsive to first line simvastatin 40mg or where issues relating to intolerance, interaction or contra-indication arise. This draft reinforces the view that omega 3 fatty acid supplements (e.g. Omacor) have no role in angina, PAD or stroke, but refers back to CG 48 where a role post-MI in those unable to eat oily fish is endorsed (see *PACE Bulletin*, Vol1, No 2 (July 2007)).

Introduction

Last month NICE published on their website a document entitled *NICE Clinical Guideline (Draft for Consultation): Cardiovascular risk assessment: the modification of blood lipids for the primary and secondary prevention of cardiovascular disease (June 2007)*. It is the purpose of this special issue of the *PACE Bulletin* to summarize key proposals from the draft and to encourage debate and contribution to the NICE process. **Prescribers are advised that this is a draft for consultation and does not yet constitute NHS policy.** Local and national statins guidance will not change to reflect recommendations in the draft until they are confirmed in the final version to be published early in 2008. The Dept of Health has assured us that the QOF will not change until April 2008 at the earliest.

Key Recommendations

Primary and secondary prevention

- All modifiable cardiovascular risk factors should be considered and their management optimised (i.e. diet, physical activity, smoking status, BP, BMI, fasting total cholesterol (TC), fasting blood glucose, renal function, liver function, secondary causes of dyslipidaemia).
- People at high risk of cardiovascular disease (CVD) should modify their diet (total fat 30% or less of total energy intake; saturated fat 10% or less of total energy intake; dietary cholesterol < 300mg/day; saturated fats replaced by monounsaturated fat; at least 5 portions of fruit and vegetables per day; at least two portions of oily fish per week).
- Consideration should be given to potential compliance problems; adherence to statin treatment is problematic even in those who have experienced a CVD event; fewer than half of patients are still taking their statin 2 years after initiation.

Primary prevention

- Statin therapy is recommended first line as part of the management strategy for the primary prevention of CVD in adults who have a 20% or greater 10-year risk of developing CVD. This equates to half of men over 50 and 20% of women over 65.

PACEF Comment:
This is no change from advice given in NICE TA 94.

- Simvastatin 40mg or pravastatin 40mg, or a drug of comparable effectiveness and acquisition cost, is recommended as the treatment.

PACEF Comment:
This is more specific than the statin of 'low acquisition cost' advocated in NICE TA 94.

- Omega 3 fatty acid supplements should not routinely be recommended for primary prevention of CVD due to insufficient evidence.

PACEF Comment:
Practices should ensure that omega 3 fatty acid supplements such as Omacor are not in use for primary prevention.

- Higher intensity statins, such as atorvastatin and rosuvastatin should not routinely be offered to people for primary prevention.

PACEF Comment:
Practices should ensure that atorvastatin and rosuvastatin are not routinely in use for primary prevention.

- Targets for total or LDL cholesterol are not recommended for people treated with a statin for primary prevention. There are no clinical trials in primary prevention that have evaluated the relative and absolute benefits of cholesterol lowering to different total and LDL-C targets.

PACEF Comment:
Practices should ensure that they do not inadvertantly target chase in primary prevention. For the majority of patients, simvastatin 40mg once daily (unless poorly tolerated) will be sufficient.

- Fibrates, nicotinic acid and anion exchange resins should not routinely be recommended for primary prevention due to lack of trial evidence (nicotinic acid) or no reduction in total mortality in trials (fibrates, anion exchange resins).
- Ezetimibe is not recommended for primary prevention. This is due to lack of clinical effectiveness outcome data (trial outcomes were surrogates such as TC, LDL-C, triglycerides), short duration of trials (none greater than 12 weeks) and lack of long term safety data. Further guidance on ezetimibe is due to be published in a forthcoming NICE TA.
- Combination drug therapy is not recommended for primary prevention (e.g. anion exchange resin or ezetimibe or fibrate or nicotinic acid or omega 3 fatty acid supplement plus a statin).

PACEF Comment:
Practices should ensure that fibrates, nicotinic acid, ezetimibe and anion exchange resins are not in routine use for primary prevention.

Secondary prevention

- Statin therapy is recommended for adults with clinical evidence of cardiovascular disease (CVD).

PACEF Comment:
This is no change from advice given in NICE TA 94.

- Simvastatin 40mg should be initiated in the following patients: after MI or acute coronary syndrome or new-onset angina; in chronic stable angina; after ischaemic stroke or transient ischaemic episode; in peripheral arterial disease. Where there are potential drug interactions or simvastatin 40mg is contraindicated, a lower dose or alternative preparation may be chosen.

PACEF Comment:
Simvastatin 40mg is specifically endorsed as the first line agent of choice rather than a statin of 'low acquisition cost'. No guidance on the use of statins

in type 1 and type 2 diabetes is given as this is outside the scope of the guideline.

- A target for total cholesterol or LDL cholesterol is not recommended for people with established CVD who are treated with a statin. Statins should be up-titrated if the patient does not reach a TC of 4mmol/l or LDL-C 2mmol/l on the initial dose. This decision should be made after considering the benefits/risks of treatment and informed patient preferences.
- The incremental cost effectiveness of lipid lowering from 5mmol/l to 4mmol/l is unknown.
- A fixed percentage reduction in total or LDL cholesterol is not recommended for individuals with established CVD treated with a statin.
- An 'audit level of TC of 5mmol/l can be used.

PACEF Comment:
The current draft is internally conflicted as evidenced by the apparent rejection of secondary prevention targets followed by a specific endorsement of 4mmol/l (TC) and 2mmol/l (LDL-C). Prescribers are reminded that current NHS policy endorses targets of 5mmol/l (TC) and 3 mmol/l (LDL-C) and that the DoH has given assurance in writing that this will remain the case until April 2008 at the earliest. The endorsement of an audit level of 5mmol/l (TC) may leave the QOF unchanged. The cost-effectiveness of more aggressive target chasing in the secondary prevention group remains unknown. Prescribers are urged to utilize targets secondary prevention only and to continue to utilize the 5mmol/l (TC) and 3 mmol/l (LDL-C) targets until the final version of the NICE CG is published in the New Year and PACEF issues Lincolnshire guidance on implementation.

- **Omega 3 fatty acid supplements (e.g. Omacor) should not routinely be recommended for the reduction of CV risk in patients with angina, PAD or stroke, although NICE have approved post-MI use (see CG48).** One randomized controlled trial (RCT) in **angina** showed that advice to increase consumption of oily fish or take omega 3 fatty acid supplements was not associated with reduction in all cause mortality or cardiac death. No RCTs relating to PAD or stroke currently exist.

PACEF Comment:
Prescribers are reminded that PACEF remain unconvinced of the cost-effectiveness of Omacor post-MI and the drug has been classified RED-RED. This draft guideline reinforces the view that omega 3 fatty acid supplements have no role in angina, PAD or stroke either.

- Fibrates, nicotinic acids and anion exchange resins may be considered in people with CVD intolerant of statins.
- Ezetimibe is not routinely recommended for secondary prevention but may be considered in people with CVD intolerance of statins. This is due to lack of clinical effectiveness outcome data (trial outcomes were surrogates such as TC, LDL-C, triglycerides), short duration of trials (none greater than 12 weeks) and lack of long term safety data. The recommendations of the forthcoming NICE TA on ezetimibe will be incorporated into the NICE CG.

PACEF Comment:
The forthcoming publication of the NICE TA on ezetimibe will be reviewed by PACEF shortly after publication and advice on implementation issued through the *PACE Bulletin*. In the meantime, the use of ezetimibe should be confined to secondary prevention patients only, specifically those intolerant of statins.

Percentage Reductions in LDL Cholesterol and Total Cholesterol

Statin	Daily Dose	28 day cost	Percentage reduction in LDL-C	Percentage reduction in total cholesterol
Atorvastatin	10mg	£18.03	37%	32%
Atorvastatin	20mg	£24.64	43%	36%
Atorvastatin	40mg	£28.21	49%	42%
Atorvastatin	80mg	£28.21	55%	47%
Pravastatin	40mg	£6.17	29%	29%
Rosuvastatin	5mg	£18.03	38%	33%
Rosuvastatin	10mg	£18.03	43%	37%
Rosuvastatin	20mg	£29.69	48%	40%
Simvastatin	**40mg**	**£3.22**	**37%**	**31%**
Simvastatin	80mg	£10.49	42%	35%

PACEF Comment:
The data in this table is compiled from the draft CG and provides an update on information previously circulated to prescribers countywide. In particular prescribers are asked to note the equipotency of simvastatin 40mg with atorvastatin 10mg and rosuvastatin 5mg and the six-fold cost difference. Simvastatin 40mg remains the preferred first-line agent and all prescriptions for atorvastatin 10mg and rosuvastatin 5mg should be considered for therapeutic switching to simvastatin 40mg unless there is good reason not to do so (e.g. known intolerance to simvastatin, contra-indication or potential interaction).

METHOTREXATE AND ANTICOAGULANT TREATMENT BOOKLETS

Prescribers are advised that patient held treatment record booklets for methotrexate are available through Stephen Gibson's office at LPCT. Order by telephone (01522 515387) or by e-mail from sandra.france@lpct.nhs.uk

Anticoagulant treatment booklets are available from LPCT Post Room.

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