

FATS3 – additional guidance : 2003

- *This is a lipid lowering drug strategy which should only be used within an overall lifestyle and clinical management strategy*
- *It is assumed that people with contraindications will be identified and excluded (refer to the BNF)*

This should be used with the FATS3 guidance and supporting documentation

People taking simvastatin 40 mg nocte with a total cholesterol ≥ 5 mmol/l

- Review compliance, diet (including alcohol consumption) and physical activity
- Measure total and HDL cholesterol, and triglycerides
- Review response to simvastatin 40 mg nocte
- Discuss options with the patient
- Consider changing to atorvastatin 40 mg nocte (see notes)
- Measure cholesterol at 8 weeks
- If cholesterol ≥ 5 mmol/l, increase atorvastatin to 80 mg nocte
- Measure cholesterol at 8 weeks
- If cholesterol ≥ 5 mmol/l, stop atorvastatin and treat with simvastatin 40 mg nocte and ezetimibe 10 mg daily
- Monitoring: Cholesterol at 8 to 12 weeks
Cholesterol at least annually thereafter

People intolerant of high dose statin

- Treat to maximum dose of statin tolerated
- Measure cholesterol when treated for 8 weeks at a stable dose
- If cholesterol ≥ 5 mmol/l, add ezetimibe 10 mg daily
- Monitoring: Cholesterol at 8 to 12 weeks
Cholesterol at least annually thereafter

People intolerant of any statin

- Measure total cholesterol, HDL cholesterol and triglycerides
- Prescribe if cholesterol ≥ 5 mmol/l
- Drugs: Fibrate eg fenofibrate micronised 267 mg daily
- Measure cholesterol at 8 weeks
- If cholesterol ≥ 5 mmol/l, consider stopping the fibrate and prescribing ezetimibe 10 mg daily

Notes:

1. Consider compliance with drugs and lifestyle, and patient wishes before changing / combining lipid lowering drugs
2. Consider discussion with local advisor if poor response to drugs
3. Ezetimibe is estimated to lower cholesterol by approximately 13% (19% reduction in LDL cholesterol)
4. In patients not able to tolerate any statin, review the cholesterol lowering achieved with a fibrate before changing to ezetimibe
5. Do not use a combination of a fibrate and ezetimibe

FATS3 – Additional Guidance 2003

This should be read in combination with the existing FATS3 summary and notes, and the supplementary laminate.

The FATS3 group was reconvened to discuss the role of some of the new lipid lowering drugs now available. The group also acknowledged that the new GP contract includes a quality marker which requires that patients with CHD have a total cholesterol below 5 mmol/l and it was felt that GPs would welcome additional guidance about appropriate action in patients taking simvastatin 40 mg daily who fail to meet this target. The target within the NSF for CHD and other national guidelines is also to lower the cholesterol below 5 mmol/l in high risk patients. If preferred LDL cholesterol can be used, calculated from a fasting lipid profile, aiming for a target less than 3 mmol/l. This additional guidance is not a revision of FATS3, but is intended to be supplemental.

Ezetimibe

The following was noted;

- Ezetimibe is a new class of drug which inhibits cholesterol absorption (approximately 20% cholesterol is obtained from absorption).
- It can be used in addition to a statin for more effective cholesterol lowering, or as a 'statin sparer' with lower doses of statin, or alone if a statin cannot be tolerated.
- It has low systemic exposure. The drug appears safe, but there is no long term data available.
- The evidence is that there are few side effects.
- There is no clinical outcome data.
- There is no evidence for use in combination with fibrates.
- Experience of its use in selected FH patients in the Newcastle lipid clinic has been favourable.
- In combination therapy ezetimibe is an additional drug, with additional costs.

The possibility of including rosuvastatin in the drug flow was considered. The consensus was that this offered little additional advantage to existing statins. It is not recommended and is not included on the local formulary.

FATS3 recommendations

Eligible patients should still be treated with simvastatin 40 mg daily as first line therapy (see FATS3).

Simvastatin is recommended in line with the evidence in the Heart Protection Study. The patent has now expired and cost savings are anticipated.

In all patients failing to reach a target cholesterol of less than 5 mmol/l, compliance with drugs and lifestyle should be reviewed and the response in cholesterol from baseline should be reviewed

People taking simvastatin 40 mg nocte with a total cholesterol \geq 5 mmol/l

- Review compliance, diet (including alcohol consumption) and physical activity
- Measure total and HDL cholesterol, and triglycerides
- Review response to simvastatin 40 mg nocte
- Discuss options with the patient
- Consider changing to atorvastatin 40 mg nocte (see notes)
- Measure cholesterol at 8 weeks
- If cholesterol \geq 5 mmol/l, increase atorvastatin to 80 mg nocte
- Measure cholesterol at 8 weeks
- If cholesterol \geq 5 mmol/l, stop atorvastatin and treat with simvastatin 40 mg nocte and ezetimibe 10 mg daily
- Monitoring: Cholesterol at 8 to 12 weeks
 Cholesterol at least annually thereafter

Average cholesterol lowering with atorvastatin 40 mg daily is greater than with simvastatin 40 mg daily, and further cholesterol lowering may be achieved by increasing the dose to 80 mg daily. However, doubling the dose of statin does not double the cholesterol lowering effect. Patients failing to meet the target with atorvastatin 80 mg can be considered for treatment with the combination of simvastatin 40 mg daily and ezetimibe 10 mg daily (table).

The FATS3 group felt this drug flow was preferable, minimising the number of drugs patients need to take, and using a drug on which the patent has expired where possible.

Before initiating these changes the response to simvastatin 40 mg should be reviewed. From the results of the Heart Protection Study and allowing for the fact that 17% of the patients taking placebo in that study were taking a statin, it can be estimated that the average cholesterol lowering effect from simvastatin 40 mg daily was 1.8 mmol/l, corresponding to a 26% reduction. This resulted in about a 25-30% reduction in the risk of vascular events. Clinicians may wish to discuss with patients the response that has been achieved on an individual basis, before deciding about changes in therapy.

Some patients may have above average HDL cholesterol. In these patients, clinicians may wish to estimate LDL cholesterol from a fasting lipid profile. If LDL cholesterol is less 3 mmol/l, treatment with simvastatin might be maintained.

Some patients, for example those with the metabolic syndrome or type 2 diabetes, may have higher triglycerides (measured from a fasting sample), and total cholesterol just above the target. These patients may respond less to switching to atorvastatin in preference to simvastatin. If necessary, clinicians can obtain advice about individual lipid profiles from the local advisors (e mail addresses are available on the FATS3 guidance).

Drug	Mean % change in total cholesterol	Mean % change in LDL cholesterol	Cost per 28 days (Dec 2003)
Simvastatin 40 mg	-28	-39	£21.00
Atorvastatin 40 mg	-36	-48	£29.69
Atovastatin 80 mg	-39	-51	£29.69
Ezetimibe 10 mg	-13	-19	£26.31
Fenofibrate 267 mg	-22	-26	£21.75

*Generic simvastatin became available in May 2003. Basic NHS prices are now beginning to fall.

People intolerant of high dose statin

- Treat to maximum dose of statin tolerated
- Measure cholesterol when treated for 8 weeks at a stable dose
- If cholesterol ≥ 5 mmol/l, add ezetimibe 10 mg daily
- Monitoring: Cholesterol at 8 to 12 weeks
Cholesterol at least annually thereafter

Some patients are not able to tolerate higher dose statins. In these patients, who still have a cholesterol above target, the addition of ezetimibe should be considered.

People intolerant of any statin

- Measure total cholesterol, HDL cholesterol and triglycerides
- Prescribe if cholesterol ≥ 5 mmol/l
- Drugs: Fibrate eg fenofibrate micronised 267 mg daily
- Measure cholesterol at 8 weeks
- If cholesterol ≥ 5 mmol/l, consider stopping the fibrate and prescribing ezetimibe 10 mg daily

Patients may not be able to tolerate a statin due to side effects. Some patients experience side effects with one statin, but not another and this should be considered when treating individual patients. Some patients have side effects with all statins and are not able to tolerate them. These patients may be able to take a fibrate, such as fenofibrate micronised 267 mg daily. If patients fail to reach target taking a fibrate, the percentage cholesterol lowering from base line that has been achieved should be reviewed. It may be preferable to change to ezetimibe which lowers cholesterol on average by approximately 13% (19% reduction in LDL cholesterol). However, the cholesterol may have been lowered more than this with the fibrate, in which case it is recommended that this is continued in preference (table). Fibrates and ezetimibe should not be combined.

Appendix

Members of the group

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Declared conflicts of interest

JSS has received travel grants and honoraria from various pharmaceutical companies that manufacture statins. PCA has received research support, travel grants, consultancy fees and honoraria from pharmaceutical companies that manufacture statins, including MSD the manufacturers of simvastatin, and was a HPS investigator. On behalf of the University of Newcastle PH provides advice to Merck Inc. from time to time. NL-B has received research support, travel grants and honoraria from pharmaceutical companies that manufacture statins and has been involved in original research into statins. ST has received research funding from Pfizer and AstraZeneca. PM was a HPS investigator. SHR was a HPS investigator. ML has until recently been a member of the Merck, Sharp and Dohme Advisory Board, is a member of the safety committee for the CARDS study (a study of atorvastatin), has received travel grants from various companies that make statins, and in the past has received research grants from various pharmaceutical companies, including from two that manufacture statins. RDGN has received research support, travel grants, consultancy fees and honoraria from various pharmaceutical companies that manufacture lipid lowering drugs. AZ has received grants to support the PCI clinic from the manufacturers of Atorvastatin and has received research funding from MSD for a non statin related study.