Gloucestershire Hospitals
NHS Foundation Trust

Statin Prescribing

Objective

These guidelines represent the views of the Gloucestershire Hospitals NHS Foundation Trust, 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.

This is a lipid lowering drug strategy which should only be used within an overall lifestyle and clinical management strategy.

Health professionals are asked to take these guidelines 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 carer.

Population to be treated[1, 2]

Treatment with a statin is recommended in the following people with:

- Total CVD risk ≥10% over 10 years (using QRISK®3), including people with type 2 diabetes
- Established CVD
- Type 1 diabetes who:
  - are older than 40 years, or
  - have had diabetes for more than 10 years, or
  - have established nephropathy, or
  - have other cardiovascular disease risk factors
- CKD stages 3–5
- Individuals with a high lifetime CVD risk estimated from heart age and other JBS3 calculator metrics, in whom lifestyle changes alone are considered insufficient by the physician and person concerned
- Familial dyslipidaemia: e.g. familial hypercholesterolaemia (FH) and other inherited disorders of lipid metabolism

Standard CVD risk scores will underestimate risk in people with: HIV treatment; serious mental health problems; antipsychotics, corticosteroids and immunosuppressant drugs; autoimmune and systemic inflammatory disorders; severe obesity (BMI>40).

Please also refer to the supporting notes regarding elderly patients on page 6 of this document.

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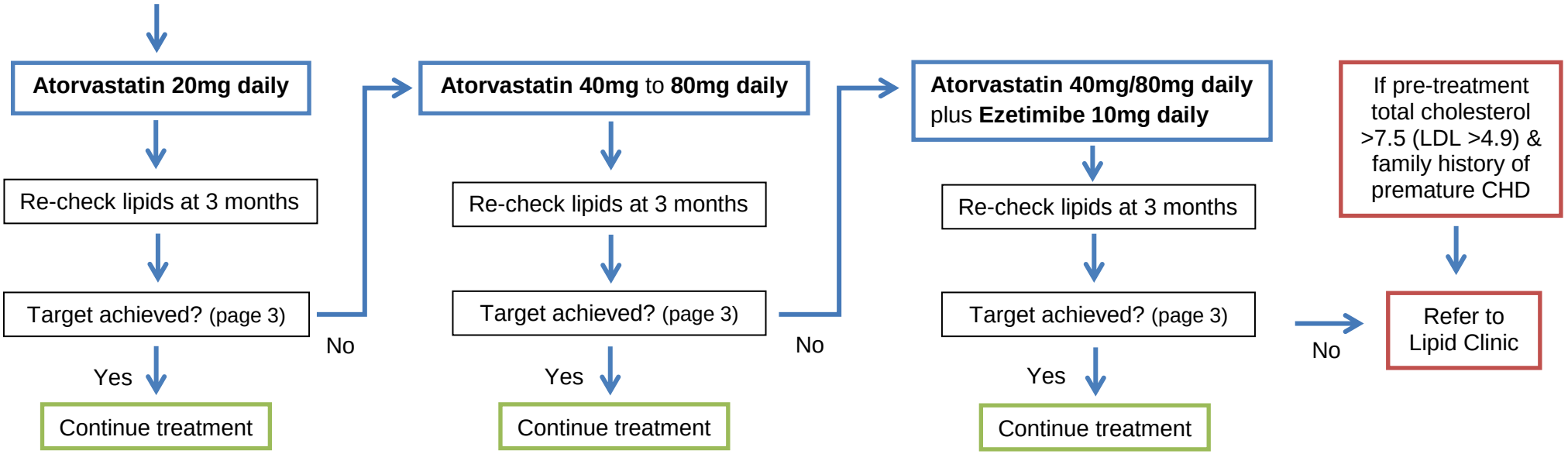
Indication for statin treatment
(see 'population to be treated' on page 1)

Investigate and treat **secondary causes** of hyperlipidaemia before starting statin treatment: excess alcohol, uncontrolled diabetes, hypothyroidism, nephrotic syndrome, liver disease and paraproteinaemia.



If intolerant of Atorvastatin, consider:
1. Simvastatin, Pravastatin, Rosuvastatin, (Fluvastatin), Rosuvastatin 5mg non-daily dose (1-3 tablets weekly);
   - Initiate at lowest dose.
   - Assess efficacy required (see Grouping of statins: Table 1 on page 3) & risk of potential drug interactions (see page 5).
   - Use lowest acquisition cost.
2. Ezetimibe (see restrictions on page 4).

- Check compliance before changing statin/ titrating dose.
- In HIV patients taking protease inhibitors, use pravastatin. Mixed hyperlipidaemia is common. Combination of statin with fibrate may be required. Refer to Lipid Clinic.
- For monitoring of lipids, LFT's, CK, see supporting notes on page 4.
- Patients with ACS may be initiated on intensive lipid lowering therapy i.e. atorvastatin 40mg/80mg daily.

CAUTIONS: (Please also refer to BNF for further prescribing information)

Initiate with a lower dose and avoid very high dose or high intensity statins if at increased risk of myotoxicity e.g. the elderly, severe renal impairment (eGFR<30), liver impairment, undertreated hypothyroidism, high alcohol intake, history of previous statin or muscle toxicity, trauma/major surgery, and concomitant medications (see page 5 for interactions).

All statins are contraindicated in active liver disease, pregnancy (adequate contraception required during treatment) and breast-feeding. Statins (except rosuvastatin) should be avoided in porphyria. Large quantities of grapefruit juice raise simvastatin and atorvastatin exposure.

Grouping of Statins

	Reduction in low-density lipoprotein cholesterol				
Dose (mg/day)	5	10	20	40	80
Fluvastatin	-	-	21%	27%	33%
Pravastatin	-	20%	24%	29%	-
Simvastatin	-	27%	32%	37%	*42%
Atorvastatin	-	37%	43%	49%	55%
Rosuvastatin	38%	43%	48%	53%	

*Advice from the MHRA: there is an increased risk of myopathy associated with high-dose (80 mg) simvastatin. The 80 mg dose should be considered only in patients with severe hypercholesterolaemia and high risk of cardiovascular complications who have not achieved their treatment goals on lower doses, when the benefits are expected to outweigh the potential risks.

Low intensity
Medium intensity
High intensity

Treatment targets

- JBS3[2] recommends the following new targets:

  Thresholds for treatment with statins based on 10-year CVD risk will be informed by National Institute for Health and Care Excellence (NICE) guidelines.

  For all patients with established CVD statins should be prescribed with a 'lower is better' approach to achieve values of at least <2.5 mmol/L for non-HDL-C (equivalent to <1.8 mmol/L for LDL-C).

- NICE Clinical Guidance CG181[1] recommends:

  Discuss with people who are stable on a low- or middle-intensity statin the likely benefits and potential risks of changing to a high-intensity statin when they have a medication review and agree with the person whether a change is needed.

  In all people who have been started on high-intensity statin treatment (both primary and secondary prevention, including atorvastatin 20 mg for primary prevention) aim for a greater than 40% reduction in non-HDL cholesterol.

- European Atherosclerosis Society (EAS) recommends[11]:

  - Low to moderate risk: LDL-C <3 mmol/L
  - High-risk: LDL-C <2.6 mmol/L or a reduction of at least 50% if the baseline is between 2.6 and 5.2 mmol/L
  - Very high-risk: LDL-C <1.8 mmol/L or a reduction of at least 50% if the baseline is between 1.8 and 3.5 mmol/L
    (see EAS guidelines for risk categories)

- We recommend that if resources allow, the JBS3 targets should be achieved especially in secondary prevention (for those with established cardiovascular disease and/or diabetes).

Monitoring

Lipids:

Measure both total and HDL cholesterol for CVD risk assessment. Before starting statin, take at least 1 non-fasting sample to measure a full lipid profile = total cholesterol, HDL-C, non-HDL-C and triglyceride concentrations.

If triglycerides = 10 – 20 mmol/L:

- Repeat test with fasting (after 5 days, but within 2 weeks) and review for potential secondary causes; refer to lipid clinic if triglyceride remains >10 mmol/L.

If triglycerides = 4.5 – 9.9 mmol/L:

- CVD risk may be underestimated by QRISK®3 and manage other risk factors present.
- Refer to lipid clinic if total cholesterol > 9.0 mmol/L or a non-HDLC >7.5 mmol/L even in absence family history of premature CHD; or if triglyceride >20 mmol/L that is not due to excess alcohol or poor glycaemic control.

Measure total cholesterol, HDL-C and non-HDL-C in all people on high-intensity statin at 3 months of treatment and once stable annually.

LFTs:

Measure ALT within 3 months of starting treatment and at 12 months, but not again unless clinically indicated. Do not routinely exclude from statin therapy people who have an ALT that is raised but less than 3 times the upper limit of normal.

CK:

Before offering statin treatment, ask the patient if they have had persistent generalised unexplained muscle pain, whether associated or not with previous lipid-lowering therapy. If they have, measure CK.

If CK is more than 5 times the upper limit of normal, re-measure CK after 7 days. If CK is still > 5 times the upper limit of normal, do not start statin treatment. If CK is raised but less than 5 times the upper limit of normal, start statin at a lower dose.

Do not measure CK in asymptomatic people who are being treated with a statin.

Ezetimibe

Ezetimibe should only be considered in the following circumstances:

- Monotherapy in patients who have demonstrated intolerance to at least 3 different statins (including pravastatin & rosuvastatin); or because of contraindications to all initial statins.
- In combination with an initial statin only when an inadequate response to maximum tolerated doses of statin monotherapy (avoid simvastatin 80mg) has been demonstrated.
- When decision has been made to treat with ezetimibe coadministered with a statin, ezetimibe should be prescribed on the basis of lowest acquisition cost (i.e. avoid proprietary combination preparations).

Statin Interactions

Note: This list is not exhaustive; please refer to the BNF / Summary of Product Characteristics for each individual drug

Interacting Drug	Simvastatin Prescribing Advice	Atorvastatin Prescribing Advice
Potent CYP3A4 inhibitors, including: Ciclosporin* Clarithromycin Danazol Erythromycin HIV protease inhibitors Itraconazole Ketoconazole Nefazodone Posaconazole Telithromycin	**Avoid simvastatin**	Avoid if possible: consider temporary suspension of atorvastatin if interacting drug is taken for short period **Ciclosporin:** do not exceed 10mg atrovastatin daily **Clarithromycin:** do not exceed 20mg atorvastatin daily **HIV protease inhibitors:** monitor lipid levels to ensure lowest necessary dose of atorvastatin is used **Itraconazole:** do not exceed 40mg atorvastatin daily
Amiodarone Amlodipine Diltiazem Verapamil	Do not exceed **20mg simvastatin**	Monitor lipid levels to ensure lowest necessary dose of atorvastatin is used
Fusidic Acid	Patients should be closely monitored. Temporary suspension of simvastatin may be considered.	Patients should be closely monitored. Temporary suspension of atorvastatin may be considered.
Grapefruit Juice	Avoid grapefruit juice when taking simvastatin	Limit intake of grapefruit juice to very small quantities (or avoid altogether)
Warfarin/courmarins†	Monitor INR before starting treatment and regularly during treatment, especially with dose changes	Monitor INR before starting treatment and regularly during treatment, especially with dose changes
Fibrates: Gemfibrozil Other fibrates (except fenofibrate)†	**Avoid simvastatin** Do not exceed **10mg simvastatin**	Increased risk of myopathy when used with fibrates; gemfibrozil increases systemic exposure to atorvastatin
Ezetimibe†	Additive risk of myopathy cannot be ruled out	Additive risk of myopathy cannot be ruled out

* Ciclosporin interacts with all statins and is contraindicated with rosuvastatin.
† Warfarin/courmarins, fibrates, and ezetimibe are important potential interactions to consider for all statins

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Elderly Patients (over age 85 years)

Based on guidelines written by the GHNFT Care of the Elderly Physicians and NICE CG18[11]

- Only measure the lipid profile when you would consider intervention.
- Consider people aged ≥ 85 to be at increased risk of CVD because of age alone, particularly people who smoke or have raised blood pressure.
- For people aged ≥ 85, statins may be of benefit in reducing the risk of non-fatal MI. Be aware of factors that may make treatment inappropriate.
- The decision whether to start statin therapy should be made after an informed discussion between the clinician and the person about the risks and benefits of statin treatment, taking into account additional factors such as potential benefits from lifestyle modifications, informed patient preference, comorbidities, polypharmacy, general frailty and life expectancy
- Do not consider statins in over 85 with any degree of disability, poor self rated health, in situations where drug compliance is unlikely or unreliable or where side effects and potential drug interactions are presenting as a clinical problem.
- Every patient is an individual and there may be cases when clinical judgement will result in prescribing of statins out with this guidance.
- If statin is indicated, avoid using very high dose or very potent statins (e.g. Simvastatin 80mg/Atorvastatin 80mg, Rosuvastatin ≥10mg).

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