Disclaimer

This guideline is registered at North Central London (NLC) Joint Formulary Committee (JFC) and is intended solely for use by healthcare professionals to aid the treatment of patients within NCL. However, clinical guidelines are guidelines only, their interpretation and application remain the responsibility of the individual clinician. If in doubt, contact a senior colleague or expert. Clinicians are advised to refer to the manufacturer’s current prescribing information before treating individual patients.

The authors and NCL JFC accept no liability for use of this information from this beyond its intended use.

While we have tried to compile accurate information in this guideline, and to keep it updated in a timely manner, we cannot guarantee that it is fully complete and correct at all times. If you identify information within this guideline that is inaccurate, please report this to the admin@ncl-jfc.org.uk. If a patient is harmed as a consequence of following this guideline, please complete a local incident report and inform admin@ncl-jfc.org.uk.

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2. **Target audience**

Hospital clinicians, GPs, non-medical prescribers, specialist nurses and pharmacists.

3. **Purpose**

To provide guidance on appropriate prescribing of statins in different adult patient groups and use of other lipid modifying therapies e.g. ezetimibe.

4. **Introduction**

NICE issued updated guidance on lipid modification (CG181) in July 2014. This NCL JFC guidance reflects updated information based on NICE guidance, current pricing of statins and a search of interactions and contraindications.

5. **Cardiovascular Disease (CVD) Risk Assessment**

Be aware that all CVD risk assessment tools can provide only an approximate value for CVD risk. Interpretation of CVD risk scores should always reflect informed clinical judgement.

Use the QRISK2 risk assessment tool to assess CVD risk for primary prevention – available via [http://www.qrisk.org/](http://www.qrisk.org/) or automatically via GP prescribing systems. The following treatment groups are at higher baseline CVD risk, and therefore a further risk assessment is not required:

- patients ≥85 years old
- type 1 diabetic patients (see section 7.2.1)
- eGFR <60ml/min/1.73m² and/or albuminuria
- pre-existing CVD (secondary prevention)
- familial hypercholesterolaemia or other inherited disorders of lipid metabolism Refer to NICE CG181 ([http://www.nice.org.uk/guidance/cg181/](http://www.nice.org.uk/guidance/cg181/)) for further information on identifying patients and assessing CVD risk.

6. **Lifestyle Advice for Primary & Secondary Prevention of CVD**

Advise all patients to make lifestyle modifications to prevent CVD including cardioprotective diet, physical activity, weight management, reduced alcohol consumption and smoking cessation.

7. **Statin Treatment Guidance**

See Appendix 1 for flow chart and guidance on statin treatment in primary and secondary prevention. Common interactions of statins and management advice are listed in Appendix 2; please note that this list is not exhaustive and users should also refer to product Summary of Product Characteristics (SPCs) or ask a pharmacist for up-to-date advice.

7.1. **Statins in Patients with Renal Impairment**

For primary and secondary prevention of CVD in patients with chronic kidney disease (CKD) offer atorvastatin 20mg daily. The dose can be increased if >40% reduction in non-HDL cholesterol is not achieved and eGFR is ≥30ml/min/1.73m². Agree the use of higher doses with a renal specialist if eGFR is <30ml/min/1.73m².
7.2. Statins in Patients with Diabetes

7.2.1. Type 1 Diabetes

Consider statin therapy in all patients with type 1 diabetes as this patient group has a higher baseline CVD risk. Offer atorvastatin 20mg for primary prevention of CVD to adults with type 1 diabetes who have one or more of the following risk factors:

- Age >40 years
- Had diabetes for >10 years
- Established nephropathy
- Other CVD risk factors

7.2.2. Type 2 Diabetes

Offer atorvastatin 20mg for primary prevention of CVD to all type 2 diabetics with CVD risk ≥10% over next 10 years.

7.3. Statins in Pregnancy & Breastfeeding

Statins are contraindicated in pregnancy due to reports of congenital anomalies and effects on fetal development. Advise women of childbearing potential of the potential teratogenic risk of statins and to stop taking them if pregnancy is a possibility. Statins should ideally be discontinued 3 months before women attempt to conceive.

Statins are contraindicated in women who are breastfeeding.

7.4. Relative Statin Intensities\(^1\)

<table>
<thead>
<tr>
<th>Statin Intensity</th>
<th>Daily Dose (reduction in LDL cholesterol)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>High-Intensity</strong></td>
<td></td>
</tr>
<tr>
<td>Atorvastatin</td>
<td>80mg (55%)</td>
</tr>
<tr>
<td>Atorvastatin</td>
<td>40mg (49%)</td>
</tr>
<tr>
<td>Atorvastatin</td>
<td>20mg (43%)</td>
</tr>
<tr>
<td>Simvastatin</td>
<td>80mg (42%)</td>
</tr>
<tr>
<td>Rosuvastatin (last line option)</td>
<td>40mg (53%)</td>
</tr>
<tr>
<td>Rosuvastatin (last line option)</td>
<td>20mg (48%)</td>
</tr>
<tr>
<td>Rosuvastatin (last line option)</td>
<td>10mg (43%)</td>
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<tr>
<td><strong>Medium-Intensity</strong></td>
<td></td>
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<tr>
<td>Atorvastatin</td>
<td>10mg (37%)</td>
</tr>
<tr>
<td>Simvastatin</td>
<td>40mg (37%)</td>
</tr>
<tr>
<td>Simvastatin</td>
<td>20mg (32%)</td>
</tr>
<tr>
<td>Rosuvastatin (last line option)</td>
<td>5mg (38%)</td>
</tr>
<tr>
<td><strong>Low-Intensity</strong></td>
<td></td>
</tr>
<tr>
<td>Pravastatin</td>
<td>40mg (29%)</td>
</tr>
<tr>
<td>Pravastatin</td>
<td>20mg (24%)</td>
</tr>
<tr>
<td>Pravastatin</td>
<td>10mg (20%)</td>
</tr>
<tr>
<td>Simvastatin</td>
<td>10mg (27%)</td>
</tr>
</tbody>
</table>

\(^1\) NB: Fluvastatin is not included in this table as it is not recommended or included on the NCL JFC formulary
8. Monitoring

Prior to initiating lipid modification therapy a baseline full lipid profile should be measured. This should include total cholesterol (TC), HDL cholesterol, non-HDL cholesterol and triglyceride levels. Secondary causes of dyslipidaemia should be excluded. The following groups should be referred to a lipid clinic (see contact details in section 10):

- Patients with baseline TC >7.5 mmol/L and family history of premature CHD
- Any patient with baseline TC >9.0mmol/L or non-HDL cholesterol >7.5mmol/L
- Patients with a triglyceride level >10mmol/L after two measurements (see NICE CG181 for further details).
- Urgently refer patients with triglyceride level >20 mmol/L that is not related to excess alcohol or poor glycaemic control.
- Patients at high-risk of CVD who are intolerant to 3 different statins

Lipid profiles should be measured at baseline and 3 months. Consider measuring every 12 months thereafter (or after 6 months if the dose/statin changes). The results should be used to inform annual medication reviews where adherence, lifestyle modifications and CVD risk factors can be discussed. Aim for ≥ 40% reduction in non-HDL cholesterol.

The most common adverse effects associated with statins include: muscle related adverse effects (see Section 8.1 below), headaches, gastrointestinal disturbances, nasopharyngitis and sleep disturbances. If significant; consider changing time of dose, reducing the dose or switching to an alternative agent.

8.1. Muscle-Related Adverse Effects

Muscle-related problems are the most frequently reported side effect of statins. All statins have a dose-dependent increased risk of myopathy. Interactions with other medications may also increase the risk of myopathy (see Appendix 2).

Patients should be counselled to report any unusual muscle pain, tenderness or weakness. CK levels should be measured in patients reporting these symptoms, and appropriate action taken as below.

- Where CK levels are (in the absence of strenuous exercise) >5x the upper limit of normal, stop/avoid statins. If symptoms resolve and CK levels return to normal, then re-introduction of the statin or of an alternative statin may be considered at the lowest dose and with close monitoring.
- Where CK levels are (in the absence of strenuous exercise) raised but <5x the upper limit of normal, consider a reduced statin dose.
- Where patients reporting muscle pain/weakness have previously tolerated statin therapy for >3 months, explore other possible causes of muscle pain/weakness.

There is a particularly high risk of myopathy associated with high dose (80mg) simvastatin, and it is therefore not recommended for patients newly initiated on a statin. For patients already established on simvastatin 80mg, continue only if the patient has not experienced muscle-related side effects.

8.2. Liver Function Tests

Measure liver transaminase enzymes at baseline, 3 months and 12 months. Thereafter only test if clinically indicated. Consider stopping/reducing statins when LFTs are raised >3x the upper limit of normal.
9. Lipid-Lowering Therapies

9.1. Ezetimibe

Ezetimibe is licensed and recommended by NICE (TA385) for patients with primary hypercholesterolaemia where a statin is contraindicated, not tolerated (consider referral to lipid specialist) or as an adjunct where high intensity statins have failed to sufficiently reduce cholesterol levels.

9.2. Therapies that are NOT Recommended

The following therapies should NOT be prescribed due to limited evidence of benefit.

- Fibrates (unless advised by a lipid specialist)
- Bile acid sequestrants (unless advised by a lipid specialist)
- Nicotinic acid
- Omega-3 fatty acid compounds
- Plant stanols and sterols
- Co-enzyme Q10 or vitamin D to increase adherence to statin

For patients established on these therapies, consider stopping and optimising statin therapy where appropriate. If patients wish to purchase omega-3 fatty acids, plant stanols/sterols, co-enzyme Q10 or vitamin D over the counter, there is no evidence of harm in this.

Rosuvastatin remains the highest cost statin and is NOT recommended unless advised by a lipid specialist (for patients requiring high intensity statins who have not tolerated atorvastatin and simvastatin).

10. Lipid Clinic Contact Details

<table>
<thead>
<tr>
<th>Royal Free London NHS Foundation Trust</th>
<th>UCLH NHS Foundation Trust</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dr Devaki Nair</td>
<td>Dr Catherine Lunken</td>
</tr>
<tr>
<td>Clinical Lead for Lipids &amp; CVD Prevention</td>
<td>Department of Diabetes &amp; Endocrinology</td>
</tr>
<tr>
<td><a href="mailto:Devaki.nair@nhs.net">Devaki.nair@nhs.net</a></td>
<td>250 Euston Road, London NW1 2PG</td>
</tr>
<tr>
<td>Tel: 020 7472 6694 Ext 33489</td>
<td><a href="mailto:Catherine.lunken@uclh.nhs.uk">Catherine.lunken@uclh.nhs.uk</a></td>
</tr>
<tr>
<td>Clinical Nurse Specialist Tel: 0207 317 7723</td>
<td>Tel: 020 3447 9336</td>
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11. References


3) UKMI Q&A 125.7 What is the available evidence for the use of statins in patients with renal impairment? Jan 2015 Accessed online on 18/12/15 via [http://www.evidence.nhs.uk/search?q=%22What+is+the+available+evidence+for+the+use+of+statins+in+patients+with+renal+impairment%22](http://www.evidence.nhs.uk/search?q=%22What+is+the+available+evidence+for+the+use+of+statins+in+patients+with+renal+impairment%22)


12. Document control

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<tr>
<td>Dec 2015</td>
<td>1</td>
<td>New Guideline</td>
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Document management

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<tr>
<th>Groups / Individuals who have overseen the development of this guidance:</th>
<th>Sonali Sanghvi, UCLH Formulary Pharmacist</th>
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<tr>
<td>Groups which were consulted and have given approval:</td>
<td>Dr Catherine Lunken, UCLH Lipid &amp; Endocrinology Specialist</td>
</tr>
<tr>
<td></td>
<td>Dr Devaki Nair, RFH Clinical Lead for Lipids &amp; CVD Prevention</td>
</tr>
<tr>
<td></td>
<td>NCL JFC Formulary Pharmacists (UCLH, RFH, WH, MEH, NMUH, GOSH, RNOH, BEH &amp; C&amp;I MH Trusts)</td>
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<tr>
<td></td>
<td>NCL JFC CCG Representatives (Camden, Islington, Barnet, Haringey, Enfield)</td>
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<tr>
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<td>Statin Prescribing &amp; Lipid Modification Guideline</td>
</tr>
<tr>
<td>Version number:</td>
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</tr>
<tr>
<td>Disseminated to:</td>
<td>NCL JFC Formulary Pharmacists and CCG Leads</td>
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<td>Equality impact assessment:</td>
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<tr>
<td>NCL Joint Formulary Committee Approval date:</td>
<td>February 2016</td>
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<td>Review date:</td>
<td>February 2019</td>
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Appendix 1: Statin Guidelines

### Primary Prevention
- CVD risk ≥10% over next 10 years
- Age >85 years
- eGFR <60ml/min/1.73m² and/or albuminuria
- Adults with type 1 or type 2 diabetes (see guidance in Section 7.2)

Give lifestyle advice. Ensure regular review of CV risk and lipid levels.

Identify and address all modifiable risk factors: smoking, diet, alcohol intake, BP control and physical activity.

In secondary prevention, do not delay statin treatment to manage modifiable risk factors. Consider patient preference, concurrent medication, co-morbidities (see guidance in Section 7) and life expectancy before initiating statin.

Offer ATORVASTATIN 20mg daily

Repeat lipid profile after 3 months. >40% reduction in non-HDL cholesterol is an indicator of treatment effect. If this is not achieved consider adherence, tolerance and whether a higher statin dose is appropriate.

If intolerant (exclude other potential causes including drug interactions) either:
1. STOP & RETRIAL when symptoms are resolved to establish if symptoms are statin-related
2. Lower dose ATORVASTATIN, titrated up as tolerated
3. SIMVASTATIN 20mg and titrate up to 40mg as tolerated (check for interactions)
4. PRAVASTATIN 20mg and titrate up as tolerated - preferred option if on interacting drugs, but NB lower intensity statin

### Secondary Prevention
All patients with CVD or atherosclerotic vascular disease – ischaemic heart disease, stroke, TIA, peripheral artery disease, ACS

Initiate ATORVASTATIN 40mg daily
Or if tolerated, consider ATORVASTATIN 80mg daily
Max. 40mg at night in elderly, renal impairment, patients on interacting drugs and in those who have history of muscle disorders.

Repeat lipid profile after 3 months. Aim for >40% reduction in non-HDL cholesterol (>50% reduction for patients with familial hypercholesterolaemia)

If failed to reach target lipid levels assess adherence, patient preference and co-morbidities and consider
(1) increase to ATORVASTATIN 80mg daily (if not already optimised) OR
(2) EZETIMIBE 10mg daily as adjunct (see guidance section 9.1)

### Familial Hypercholesterolaemia
or other inherited disorders of lipid metabolism.

Refer to lipid clinic (see guidance Section 10)

Familial Hypercholesterolaemia or other inherited disorders of lipid metabolism.

Refer to lipid clinic (see guidance Section 10)
**Appendix 2: Statin Interactions Table**

(please also refer to the most up to date SPC or ask a pharmacist for advice as this list is not exhaustive)

<table>
<thead>
<tr>
<th>Interacting Drug</th>
<th>Atorvastatin Advice</th>
<th>Simvastatin Advice</th>
<th>Pravastatin Advice</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Macrolides - clarithromycin, erythromycin, telithromycin</strong></td>
<td><strong>Avoid if possible</strong> (i.e. stop atorvastatin for duration if short course). If required, counsel patient to report any symptoms of myopathy. Monitor lipid levels to ensure lowest necessary dose of atorvastatin is used. <strong>Clarithromycin</strong>: do not exceed 20mg daily <strong>Itraconazole</strong>: do not exceed 40mg daily.</td>
<td>Contraindicated with simvastatin</td>
<td>Nil significant interaction reported – dose as normal</td>
</tr>
<tr>
<td><strong>Azoles – itraconazole, ketoconazole, posaconazole</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Amiodarone, verapamil, diltiazem, amlodipine</strong></td>
<td>May increase statin levels – counsel patient to report any symptoms of myopathy. Monitor lipid levels to ensure lowest necessary dose of atorvastatin is used.</td>
<td>Do not exceed simvastatin 20mg daily</td>
<td>Nil significant interaction reported – dose as normal</td>
</tr>
<tr>
<td><strong>HIV Protease Inhibitors e.g. tipranavir, ritonavir, nelfinavir, lopinavir</strong></td>
<td>See pravastatin as preferred option. If high risk patient or target lipid levels not achieved with pravastatin, consider low dose atorvastatin and seek advice from pharmacist/HIV team.</td>
<td>Contraindicated with simvastatin</td>
<td>Initiate pravastatin 20mg daily and if tolerated titrate up to 40mg daily with caution. Counsel patient to report any symptoms of myopathy. If high risk patient or target lipid levels not achieved with pravastatin – see atorvastatin.</td>
</tr>
<tr>
<td><strong>Ciclosporin, gemfibrozil, danazol, nefazodone</strong></td>
<td>Do not exceed atorvastatin 10mg daily</td>
<td>Contraindicated with simvastatin</td>
<td><strong>Ciclosporin</strong>: Initiate pravastatin 20mg daily and if tolerated titrate up to 40mg daily with caution. <strong>Gemfibrozil</strong>: Avoid combined use. If required, monitor lipid levels to ensure lowest necessary dose of pravastatin is used. Counsel patient to report any symptoms of myopathy.</td>
</tr>
<tr>
<td><strong>Other fibrates (for gemfibrozil see above)</strong></td>
<td>Counsel patient to report any symptoms of myopathy. Monitor lipid levels to ensure lowest necessary dose of atorvastatin is used.</td>
<td>Do not exceed simvastatin 10mg daily. (except fenofibrate - no dose alteration required, but monitor for adverse effects)</td>
<td>Counsel patient to report any symptoms of myopathy. Monitor lipid levels to ensure lowest necessary dose of pravastatin is used.</td>
</tr>
<tr>
<td><strong>Fusidic Acid (systemic)</strong></td>
<td>Avoid if possible (i.e. if short course stop statin until 7 days after course is finished). If required, counsel patient to report any symptoms of myopathy. Monitor lipid levels to ensure lowest necessary dose of atorvastatin is used.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Ezetimibe</strong></td>
<td>Possible additive risk of myopathy. Counsel patient to report any signs of myopathy.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Warfarin/Coumarins</strong></td>
<td>Monitor INR on initiation and with dose changes.</td>
<td></td>
<td>Nil significant interaction reported</td>
</tr>
<tr>
<td><strong>Grapefruit Juice</strong></td>
<td>Limit to very small quantities or avoid if possible.</td>
<td>Avoid while taking simvastatin.</td>
<td>Nil significant interaction</td>
</tr>
</tbody>
</table>