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North Central London
Joint Formulary Committee

Statin Prescribing & Lipid Modification Guideline
for the Prevention of Cardiovascular Disease

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Contents

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/ 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/1.73m^2 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/) 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/1.73m^2. Agree the use of higher doses with a renal specialist if eGFR is <30ml/min/1.73m^2

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]

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

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

Royal Free London NHS Foundation Trust	**UCLH NHS Foundation Trust**
Dr Devaki Nair Clinical Lead for Lipids & CVD Prevention Devaki.nair@nhs.net Tel: 020 7472 6694 Ext 33489 Clinical Nurse Specialist Tel: 0207 317 7723	Dr Catherine Lunken Department of Diabetes & Endocrinology 250 Euston Road, London NW1 2PG Catherine.lunken@uclh.nhs.uk Tel: 020 3447 9336

11. References

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12. Document control

Date	Version	Amendments
Dec 2015	1	New Guideline

Document management

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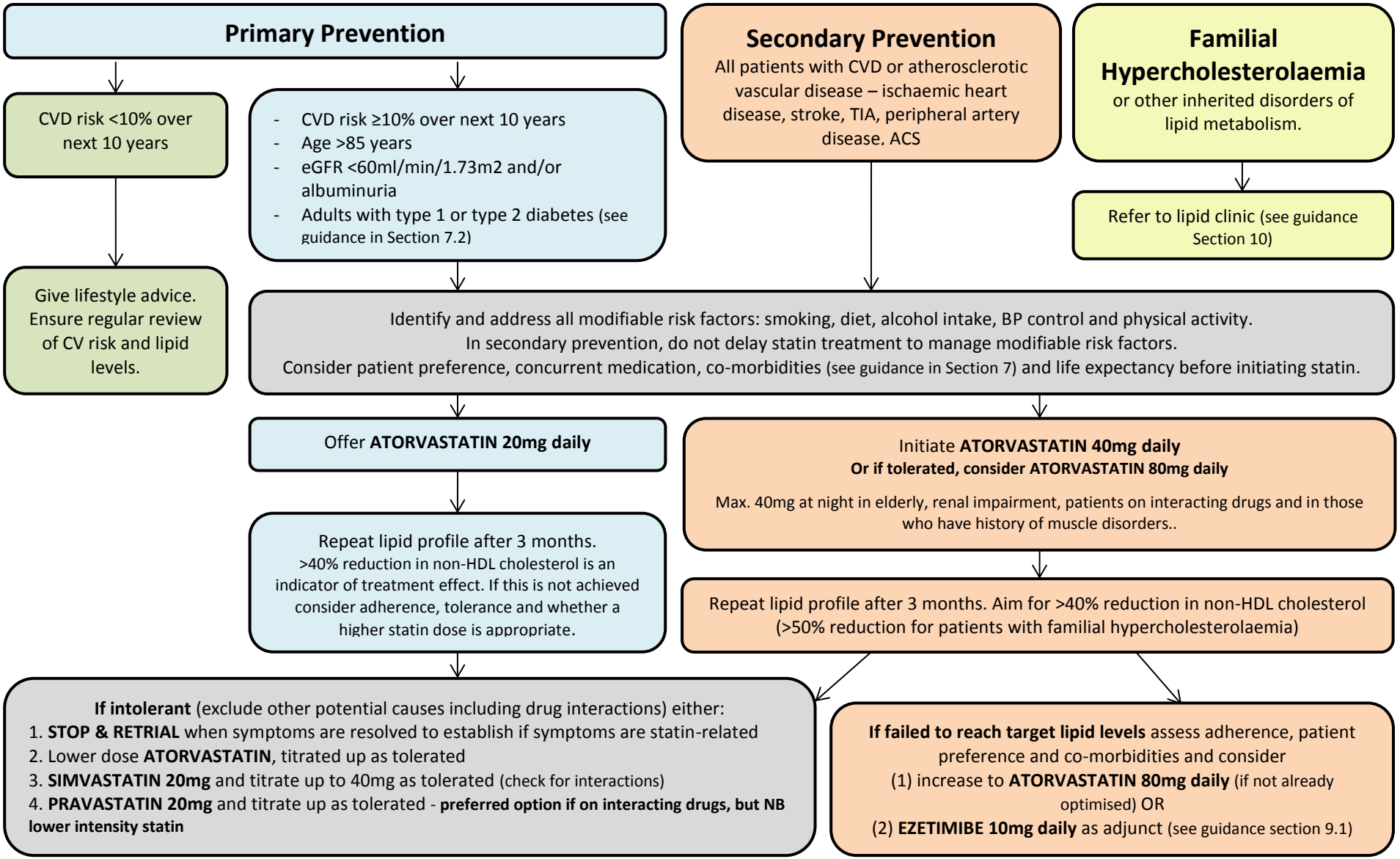
Appendix 1: Statin Guidelines



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)

Interacting Drug	Atorvastatin Advice	Simvastatin Advice	Pravastatin Advice
Macrolides - clarithromycin, erythromycin, telithromycin **Azoles – itraconazole, ketoconazole, posaconazole**	**Avoid if possible** (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. **Clarithromycin**: do not exceed 20mg daily **Itraconazole**: do not exceed 40mg daily.	Contraindicated with simvastatin	Nil significant interaction reported – dose as normal
Amiodarone, verapamil, diltiazem, amlodipine	May increase statin levels – counsel patient to report any symptoms of myopathy. Monitor lipid levels to ensure lowest necessary dose of atorvastatin is used.	Do not exceed simvastatin 20mg daily	Nil significant interaction reported – dose as normal
HIV Protease Inhibitors **e.g. tipranavir, ritonavir, nelfinavir, lopinavir**	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.	Contraindicated with simvastatin	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.
Ciclosporin, gemfibrozil, danazol, nefazodone	Do not exceed atorvastatin 10mg daily	Contraindicated with simvastatin	**Ciclosporin**: Initiate pravastatin 20mg daily and if tolerated titrate up to 40mg daily with caution. **Gemfibrozil**: 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.
Other fibrates **(for gemfibrozil see above)**	Counsel patient to report any symptoms of myopathy. Monitor lipid levels to ensure lowest necessary dose of atorvastatin is used.	Do not exceed simvastatin 10mg daily. (except **fenofibrate** - no dose alteration required, but monitor for adverse effects)	Counsel patient to report any symptoms of myopathy. Monitor lipid levels to ensure lowest necessary dose of pravastatin is used.
Fusidic Acid (systemic)	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 statin is used.		
Ezetimibe	Possible additive risk of myopathy. Counsel patient to report any signs of myopathy.		
Warfarin/Coumarins	Monitor INR on initiation and with dose changes.		Nil significant interaction reported
Grapefruit Juice	Limit to very small quantities or avoid if possible.	Avoid while taking simvastatin.	Nil significant interaction