PRESCRIBING GUIDELINES FOR LIPID LOWERING TREATMENTS
FOR SECONDARY PREVENTION

For guidance on Primary Prevention please see NICE guidance http://www.nice.org.uk/guidance/cg181

Before starting lipid lowering treatment

Although widely prescribed, lipid lowering agents can have numerous contraindications and peculiar drug interactions, even within the same class of drug. If a patient is being considered for drug treatment:

- Take care in ensuring the drug is appropriate to the individual patient, especially in patients with polypharmacy, multiple co-morbidities or in women of childbearing potential.
- Counsel the patient that the statin drugs are generally safe but, very rarely, they can cause muscle damage, so if they develop severe muscle aches or muscle weakness to discontinue all lipid lowering drugs and seek medical advice.

Secondary prevention of cardiovascular disease

This includes all patients with clinical evidence of established cardiovascular disease (CVD) including stable angina, peripheral vascular disease (PVD), stroke and transient ischaemic attacks (TIA). It also contains patients with an acute coronary syndrome i.e. unstable angina, ST or non ST elevation myocardial infarction (MI)

- Consider and manage all other modifiable CVD risk factors concurrently, including lifestyle advice.
- Consider starting atorvastatin 80mg once daily, or a lower dose such as 20mg if indicated e.g. in patients with eGFR <30 ml/min/1.73 m², if there are potential drug interactions or a high risk of adverse effects.
- Most patients able to tolerate atorvastatin 80mg will achieve the non-HDL cholesterol target of <2.5mmol/L. Measure LFTs or CK as indicated for primary prevention.
- See section on ‘Other agents’ if targets cannot be reached for reason other than adherence.
- See section on ‘Statin intolerance’ if this is an issue with atorvastatin.
- Consider addition of Ezetimibe 10 mg once daily to Atorvastatin 80 mg once daily (or maximal tolerated dose of statin therapy) if LDL-C ≥ 1.8 mmol/L

Chronic kidney disease

In patients with chronic kidney disease (CKD) whose eGFR is <60 ml/min/1.73m²:

- Start atorvastatin 20mg once daily for secondary and primary prevention (irrespective of the current QRISK equation score).
- Aim for a non-HDL cholesterol <2.5mmol/L OR a non-HDL cholesterol reduction of at least 40%. Consider increasing the statin dose if these targets are not met.
- If eGFR is <30 ml/min/1.73m² only increase atorvastatin dose from 20mg following renal specialist advice.
Diabetes patients

Treat patients with type 2 diabetes but without known CVD according to their risk calculated by the current QRISK equation. In those found to be at >10% risk of CVD over 10 years:

- Start **atorvastatin 20mg** once daily in addition to management of their other diabetes risk factors.
- Liver function tests (LFTs) should be repeated within 3 months. Creatine kinase (CK) need only be measured in patients with muscle symptoms.
- Aim for a non-HDL cholesterol <2.5mmol/L OR a non-HDL cholesterol reduction of at least 40%. Consider increasing the statin dose if these targets are not met.
- See section on ‘Statin intolerance’ if this is an issue with atorvastatin.

In type 1 patients, consider statin treatment if over 40 years OR with known diabetes microvascular complications (nephropathy, neuropathy or retinopathy) OR a >10 year duration of diabetes OR at increased cardiovascular risk, such as due to hypertension, smoking, family history of premature cardiovascular disease in first degree relatives or features of the metabolic syndrome.

Consider statin treatment in type 2 patients not already identified by QRISK as high risk if they have known microvascular complications or a >10 year duration of the disease.

Diabetes patients with marked hypertriglyceridemia may benefit from a fibrate in addition to or instead of statin treatment (see ‘Fibrates’ section).

Legacy patients

For patients already who are already taking previously popular lipid lowering treatment, such as simvastatin 40mg, consider at review changing to atorvastatin 20mg or higher as indicated above, especially if they have not achieved their lipid target.

Statin intolerance

Patients with severe side effects of myositis (CK>5x upper reference limit) or abnormal liver function tests (ALT>3x upper reference limit), should have their statin discontinued.

In patients who unequivocally justify statin treatment but have less severe side effects (such as myalgia (without myositis), GI upset, sleep disturbance) on atorvastatin or simvastatin, the following should be considered:

- Reducing the dose of the existing statin, if not already taking the minimum dose, assuming this is unlikely to breach any lipid target for the patient.
- Prescribing Pravastatin (initially at a dose of 10mg, increasing to 40mg if tolerated) or Rosuvastatin (initially at a dose of 5mg, increasing the dose as required to meet any target).
- Where the above options fail, consider referral to Lipid Clinic

Rosuvastatin is most likely to achieve target in patients with existing cardiovascular disease or diabetes.
Lipid modifying agents other than statins

Ezetimibe

This agent can be used in familial hypercholesterolemia and hypercholesterolemia resistant to high dose statins. Consider addition of **Ezetimibe 10 mg once daily** to Atorvastatin 80 mg once daily (or maximal tolerated dose of statin therapy) if LDL-C ≥ 1.8 mmol/L for secondary prevention of CVD.

**PCSK9 inhibitors:**

Consider referral to lipid clinic for initiation of PCSK9 inhibitors.

Both Evolocumab and Alirocumab are indicated in familial hypercholesterolaemia if LDL – Cholesterol is persistently ≥ 5mmol/L and for secondary prevention if LDL –Cholesterol is persistently elevated ≥ 4mmol/L in patients at high risk of CVD and ≥ 3.5 mmol/L if at very high risk of CVD.

- High risk CVD is defined as a history of any of the following: acute coronary syndrome (such as myocardial infarction or unstable angina needing hospitalisation); coronary or other arterial revascularisation procedures; chronic heart disease; ischaemic stroke; peripheral arterial disease.

- Very high risk of CVD is defined as recurrent cardiovascular events or cardiovascular events in more than 1 vascular bed (polyvascular disease).

All patients established on PCSK9 Inhibitor will have regular monitoring of BCP, CK, and Lipid Profile every 3 months, and are also monitored for any adverse effects.

**Fibrates**

Triglycerides are a risk factor for pancreatitis, particularly if greater than 10mmol/L, and can compound the risk of CVD, especially in diabetes patients.

Consider a fibrate (fenofibrate micronised as first-line):

- If a patient has marked hypertriglyceridaemia (>10mmol/L) despite lifestyle advice.
- If a diabetes patient remains hypertriglyceridaemic (above 4.5mmol/L) despite actions to address hyperglycaemia.
- In some circumstances, this will be before a statin has been started because of acute need (such as high risk of pancreatitis) or because of the undesirability of initiating two drugs at the same time.
- Combinations of a statin and fibrate may increase the risk of myopathy and rhabdomyolysis.
- Consider referring patients to a Lipid Clinic in severe or refractory hypertriglyceridaemia.

**Omega-3 fish oils, Colesevelam, Nicotinic acid and its derivatives**

There is now no strong clinical indication for prescribing these agents.
Ensuring treatment adherence

At reviews to discuss medicines adherence and lifestyle modification consider an annual non-fasting blood test for non-HDL cholesterol to inform the discussion.

Lipid measurement

Total and HDL cholesterol measurements are largely unaffected by not fasting, so primary prevention risk assessment can be made on non-fasting samples. Non-HDL cholesterol (total cholesterol – HDL cholesterol) can, unlike LDL, also be measured non-fasting and is now the preferred means of judging response to lipid lowering treatment. A fasting sample is preferred in patients with known hypertriglyceridaemia or where an accurate LDL estimate is required.

References

2. JBS3 Board. Joint British Societies’ consensus recommendations for the prevention of cardiovascular disease (JBS3). Available from http://heart.bmj.com/content/100/Suppl_2/ii1.full
4. Alirocumab for treating primary hypercholesterolaemia and mixed dyslipidaemia. NICE Technology appraisal guidance [TA393]. https://www.nice.org.uk/guidance/ta393/chapter/1-Recommendations
5. Evolocumab for treating primary hypercholesterolaemia and mixed dyslipidaemia. NICE Technology appraisal guidance [TA394]. https://www.nice.org.uk/guidance/ta394/chapter/1-Recommendations

APPROVAL PROCESS

Written by: Guidance modified by Dr.Deepa Narayanan, Consultant Chemical Pathologist & Lipid Specialist. Yvonne Holloway, Senior Principal Pharmacist Cardiology Medicines Optimisation and Cardiology Lead, HEY Hospitals NHS Trust Updated by Antonio Ramirez, Interface Pharmacist (Jul 2018)

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Familiar Hypercholesterolemia Identification and Cascade Testing Service. Primary Care referral pathway

Primary/secondary prevention of Cardiovascular disease

History and clinical examination
Fasting lipid profile

Review Lipids:
Simon Broome criteria
- Total Cholesterol ≥ 7.5 mmol/L and LDL ≥ 4.9 mmol/L (adults)
- Total Cholesterol ≥ 6.7 mmol/L and LDL ≥ 4.00 mmol/L (children)

Yes

No

Review family history of hypercholesterolaemia or premature coronary artery disease <60 yrs in first degree relatives and <50 yrs in second degree relatives

Yes

No

Possible Familial Hypercholesterolaemia

Refer to dedicated Familial Hypercholesterolaemia and cascade screening service

Total Cholesterol ≥ 9 mmol/L and non HDL-C ≥ 7.5 mmol/L

Yes

No

Refer to lipid clinic

Consider other cardiovascular risk factors and secondary causes of dyslipidaemia. Qrisk3 if appropriate

Serum Triglycerides ≥ 4.6 mmol/L

Yes

No

Secondary causes of dyslipidaemia
- Alcohol excess
- Suboptimal glycaemic control
- Hypothyroidism
- Liver disease
- Proteinuria

Review other cardiovascular risk factors
Consider secondary causes of dyslipidaemia
CVD risk underestimated in Qrisk 2 score (if used)
Refer to lipid clinic if non HDL-C ≥ 7.5 mmol/L or TG ≥ 20 mmol/L

Prescribing Guideline for Lipid Lowering Treatments
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