NHSL Guideline for the Management of Cholesterol in adults

PRIMARY PREVENTION OF CHD AND STROKE IN HIGH RISK PATIENTS

1. Random non-fasting test for total cholesterol, HDL cholesterol (TC:HDL ratio) and LFTs.

2. If cholesterol > 7.5 mmol/l or LDL-C ≥ 5mmol/l, exclude secondary causes and consider familial hyperlipidaemia.

3. Calculate ASSIGN score.

4. Treat patient if 10 year cardiovascular event risk ≥ 20% using atorvastatin 20mg daily (SIGN 149).

See BNF for cautions, contra-indications and clinically important interactions.

NB. There is no target for cholesterol in primary prevention therefore there is no need for routine cholesterol testing once treatment is commenced unless clinically indicated. There is no evidence to support up-titration from atorvastatin 20mg or the use of additional drugs.

SECONDARY PREVENTION OF CORONARY HEART DISEASE AND ISCHAEMIC STROKE/TIA

Patients with established vascular disease are at high risk and should be treated with a statin regardless of total blood cholesterol.

- i.e. Established cardiovascular disease/ CKD ≥ stage 3 /micro- or macro- albuminuria/ Diabetic patients aged ≥ 40 years/ Diabetic patients <40yrs with additional factors SIGN 149

1. Random non-fasting test for total cholesterol, HDL cholesterol and LFTs.

2. If cholesterol >7.5mmol/l or LDL-C ≥ 5mmol/l, exclude secondary causes and consider familial hyperlipidaemia.

3. Treat all patients with statin regardless of baseline cholesterol concentration

Recommended drug & daily dose:
- Established cardiovascular disease: Atorvastatin 80mg
- CKD ≥ stage 3 /micro- or macro- albuminuria / diabetic patients: Atorvastatin 20mg initially

See BNF for cautions, contra-indications and clinically important interactions- Some statins potentially interact with other drugs.

For true statin intolerance (see below re rechallenge of statins) consider the prescribing of ezetimibe in high risk patients. This is off label prescribing.

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3 months after initiation of therapy retest cholesterol levels

**Statin therapy goal achieved**
Reduction in non HDL cholesterol of at least 1mmol/l or a 40% reduction – continue treatment. There is no requirement to routinely test once cholesterol target is reached.

**Statin therapy goal not achieved:**
No reduction in non HDL cholesterol of 1mmol/l or 40% reduction.

**Prescribed Atorvastatin 80mg:**
Discuss concordance and lifestyle measures.

**Prescribed Atorvastatin 20mg:**
Discuss concordance and lifestyle measures. Up titrate statin dose.

Consider the addition of ezetimibe for patients at maximum tolerated statin therapy and in whom LDL cholesterol is considered not adequately controlled. *SIGN 149*

Patients at very high risk, not achieving cholesterol reductions should be referred to the lipid clinic. (see below for treatment flow chart)
**Statin Intolerance**

Patients who report statin intolerance may be rechallenged, initially with the same dose/same statin unless there is significant creatinine kinase elevation. If reported intolerance persists then an alternative statin should be offered. SIGN 149 reports that 70%-90% of patients of patients who report statin intolerance are able to take some form of statin when rechallenged.

**NB** The evidence for the use of statins is much stronger than for other lipid-lowering agents for both primary and secondary prevention of cardiovascular disease. It is important to emphasise this to patients, and to ensure that there is genuine intolerance before considering an alternative.

**Primary Prevention (those with no diagnosis of CHD, stroke/TIA or diabetes)**

Ensure patient is truly intolerant of statin before any change to therapy (see above). Reinforce dietary and lifestyle measures. If familial hyperlipidaemia is suspected then the patient should be screened for such.

Ezetimibe can be considered for primary prevention in patients at elevated CVD risk in whom statin therapy is contraindicated.

**Secondary Prevention (those with a diagnosis of CHD, stroke/TIA or diabetes)**

Ensure patient is truly intolerant of statin (see above) before any change to therapy. Reinforce dietary and lifestyle measures. Consider alternative agents - for example ezetimibe, if necessary. (The use of ezetimibe as monotherapy in secondary prevention is off label use.)

**Patients with symptoms of muscle pain and CK>10 times the upper limit of normal should stop statin therapy.**

**Failure to reach Cholesterol Targets**

**Primary Prevention (those with no diagnosis of CHD, stroke/TIA or diabetes)**

There is no primary prevention target in SIGN 149, in NICE guidance, nor in this guideline. The MCN does not recommend further cholesterol checking once treatment has started, nor up titration from atorvastatin 20mgs.

**Secondary Prevention (those with a diagnosis of CHD, stroke/TIA or diabetes)**

Patients who fail to achieve a reduction of 1mmol/l or 40% from baseline of non HDL cholesterol should be considered for the addition of ezetimibe once the maximum tolerated statin dose is reached.

**Lipid-lowering Drugs - Formulary Options**

Statins listed in the NHSL formulary: atorvastatin (preferred), simvastatin and rosvastatin.

**Prevention of atherosclerotic arterial disease requires control of all risk factors.**

- No single risk factor, including cholesterol concentration, should be viewed in isolation.
  - All other risk factors (e.g. smoking, blood pressure, diabetic control) should be addressed.
  - Dietary and other lifestyle advice (e.g. alcohol, obesity, physical activity, diet) should be given.
  - Addition of other medication should be considered in the secondary prevention of vascular disease (anti-platelet therapy, beta blockers, ACE inhibitors etc).
  - Ensure secondary causes of dyslipidaemia (hypothyroidism, renal impairment, liver disease, alcohol excess and diabetes) have been excluded.
While SIGN 149 has no defined cholesterol level targets but aims for a percentage reduction from baseline, acceptance for treatment with a PCSK9 inhibitor is subject to SMC restrictions, which defines LDL cholesterol levels.

Secondary Prevention non FH
- previous cardiovascular event or
- recurrent polyvascular disease

Maximum tolerated dose of statin

Statin intolerant?

Yes

Previous CV event - LDL < 4.0mmol/l
Recurrent/ polyvascular disease – LDL <3.5mmol/l

Add ezetimibe

No

Try reintroducing original statin or alternative

Yes

Previous CV event - LDL < 4.0mmol/l
Recurrent/ polyvascular disease – LDL <3.5mmol/l

Consider PCSK 9 inhibitor

No

Continue monitoring for treatment targets and safety
Primary/Secondary Prevention Heterozygous Familial Hypercholesterolaemia (Lipid Clinic)

Maximum tolerated dose of statin

Statin intolerant?

Try reintroducing original statin or alternative statin

Primary Prevention
LDL < 5.0mmol/l

No

Add/switch to ezetimibe

No

Secondary Prevention
LDL < 3.5mmol/l

Yes

Yes

Consider PCSK 9 inhibitor

No

No

Primary Prevention
LDL < 5.0mmol/l

Yes

Secondary Prevention
LDL < 3.5mmol/l

Yes

Continue monitoring for treatment targets and safety
Appendix 1 - PCSK-9 inhibitors

**Patient identification**
Treatment initiation decisions will be made by clinicians at the lipid clinic taking into consideration the eligibility of the patient within the SMC restrictions and precautions/contraindications and adverse effects of the treatment. (Patients with secondary causes of hyperlipidaemia or mixed hyperlipidaemias will not be considered for treatment with a PCSK-9 inhibitor.)

**Prescribing**
Prescribing will be on hospital prescriptions (‘blue pads’) from clinicians in the lipid clinic. This may be reviewed in future as confidence is gained in the use of these drugs.

**Administration**
Treatment will be administered by the patient in their own home. Patient education and training will be delivered by the lipid clinic.

**Monitoring**
Dose titration will be undertaken at the lipid clinic. Routine follow up of patients will be arranged by the lipid clinic and reviewed by the cardiologist who initiated treatment. This may be reviewed in future as confidence is gained in the use of these drugs.

**Medication**

**Medicine Name:**
Alirocumab (Praluent®) 75mg/1ml solution for injection prefilled pen
150mg/1ml solution for injection prefilled pen

**Licensed indication:**
- adults with primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia, as an adjunct to diet:
  - in combination with a statin or statin with other lipid lowering therapies in patients unable to reach LDL-C goals with the maximum tolerated dose of a statin or,
  - alone or in combination with other lipid-lowering therapies in patients who are statin-intolerant, or for whom a statin is contraindicated.

The effect of alirocumab on cardiovascular morbidity and mortality has not yet been determined.

**SMC Restriction:** for specialist use only in patients at high cardiovascular risk as follows:
- patients with heterozygous familial hypercholesterolaemia (HeFH) and LDL-C ≥5.0mmol/L, for primary prevention of cardiovascular events or,
- patients with HeFH and LDL-C ≥3.5mmol/L, for secondary prevention of cardiovascular events or,
- patients at high risk due to previous cardiovascular events and LDL-C ≥4.0mmol/L or,
- patients with recurrent/polyvascular disease and LDL-C ≥3.5mmol/L.
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**EVOLOCUMAB**

**Medicine Name:**
- Evolocumab (Repatha®) 140mg/1ml solution for injection prefilled syringe
- 140mg/1ml solution for injection prefilled disposable device (Repatha Sureclick®)

**Licensed Indication:**
Hypercholesterolaemia and mixed dyslipidaemia - adults with primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia, as an adjunct to diet:
- in combination with a statin or statin with other lipid lowering therapies in patients unable to reach LDL-C goals with the maximum tolerated dose of a statin or,
- alone or in combination with other lipid-lowering therapies in patients who are statin-intolerant, or for whom a statin is contraindicated.

Homzygous familial hypercholesterolaemia - adults and adolescents aged 12 years and over with homozygous familial hypercholesterolaemia in combination with other lipid-lowering therapies.

The effect of evolocumab on cardiovascular morbidity and mortality has not yet been determined.

**SMC restriction:** for specialist use only, when administered at a dose of 140mg every two weeks, in patients at high cardiovascular risk as follows:
- patients with heterozygous familial hypercholesterolaemia (HeFH) and LDL-C ≥5.0mmol/L for primary prevention of cardiovascular events or,
- patients with HeFH and LDL-C ≥3.5mmol/L for secondary prevention of cardiovascular events or,
- patients at high risk due to previous cardiovascular events and LDL-C ≥4.0mmol/L or
- patients with recurrent/polyvascular disease and LDL-C ≥3.5mmol/L