Lipid Management: Medicines Optimisation Pathways

South East London (SEL) Integrated Care System
September 2021 (updated November 2021)

Developed by SEL Cardiovascular Medicines Working Group on behalf of the SEL Integrated Medicines Optimisation Committee (IMOC) and following guidance from the National Institute for Health and Care Excellence (NICE), NHS England/Accelerated Access Collaborative (AAC) and UCL Partners.

Approval date: September 2021, updated November 2021  
Review date: September 2023 (or sooner if evidence or practice changes)

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Abbreviations used for lipid profiles:
TC = total cholesterol, TG = triglycerides, HDL-C = high density lipoprotein-cholesterol, LDL-C = low density lipoprotein-cholesterol, non-HDL-C = non-high density lipoprotein-cholesterol
Non-HDL-C = total cholesterol - HDL cholesterol

Definition of statin intolerance (NICE 2015):
Statin intolerance is defined as the presence of clinically significant adverse effects that represent an unacceptable risk to the patient or that may reduce compliance with therapy.

Please note: These pathways have been developed for use in adult patients in SEL and this guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patients, in consultation with the patient and/or guardian or carer.

Contra-indications for all pathways: the lipid management treatments listed are not recommended in patients who are pregnant or breastfeeding and in the 3 months prior to conception. Please check individual summary of product characteristics (SPC) for each medication and consider contra-indications before prescribing.
Primary Prevention: Medicines Optimisation for Lipid Management

**Lifestyle change and dietary measures** are key to CVD event reduction together with drug therapy.

In primary care check:
- bloods (non-fasting full lipid profile: TC, TG, HDL-C, LDL-C, non-HDL-C) liver function (LFTs), HbA1c (manage/review diabetes mellitus (DM) if ≥48mmol/mol) thyroid & renal function, blood pressure (BP), weight, smoking status and calculate QRisk2 score using EMIS template ([www.qrisk.org](http://www.qrisk.org)). Consider if lipid profile may indicate FH (see page 10).

Please note QRisk2 does not apply in the following conditions: familial hypercholesterolaemia (FH), type 1 diabetes mellitus (T1DM)- may be applied to QRisk3 calculations, chronic kidney disease CKD (QRisk3 has updated to eGFR <30ml/min; NICE states eGFR <60ml/min) and/or albuminuria- these patients are high CVD risk and require consideration for a high intensity (HI) statin. Offer HI statin to patients with Type 1 DM and age >40 years or DM >10 years or nephropathy or with other CVD risk factors (NICE).

Consider additional CVD risk factors, if present, together with with QRisk score: Severe obesity (BMI >40kg/m²), socio-economic status, human immunodeficiency virus (HIV) treatment, severe mental illness, medications that may cause dyslipidaemia (eg. antipsychotics, corticosteroids, immunosuppressants), autoimmune disorders eg. systemic lupus erythematosus (SLE), impaired fasting glycaemia, significant hypertriglyceridaemia (see page 9), recent change in risk factors eg change to smoking status, BP and lipid management.

**Consider options** with shared decision making (see page 6), education and lifestyle interventions to modify CVD risk.

For all patients consider the risk:benefit of therapy holistically: for example in patients aged ≥85 years consider frailty, life expectancy and co-morbidities.

Optimise management of BP and other co-morbidities. **Support** lifestyle interventions and medicines adherence.

If QRisk ≥10%: after addressing modifiable risk factors and following a shared decision: consider initiating or optimising statin therapy with a moderate dose of a high intensity drug:
- atorvastatin 20mg daily (alternative is rosuvastatin 10mg daily) - see page 6 for high intensity statin comparison table - consider drug interactions that may affect dosing (see BNF).

After 3 months, has non-HDL cholesterol fallen by ≥40% from baseline?

Check adherence to medication, timing of dose, statin adverse effects/intolerance/hesitancy & diet/lifestyle interventions.

**Step 1 in primary care**: Consider up-titration of statin to a maximum dose atorvastatin 80mg (alternative is rosvastatin 20mg to 40mg)*- see HI statin table page 6

**Step 2 in primary care**: If intolerant to higher dose of statin, consider adding ezetimibe 10mg daily (SPC- check contra-indications) to maximal tolerated statin.

**Step 3 in primary care with secondary care support**: If intolerant to any statin, start ezetimibe 10mg daily, and refer to lipid clinic to consider adding bempedoic acid 180mg daily ▼ (SPC) (see statin intolerance pathway on page 5 for further information).

After 3 months, has non-HDL cholesterol fallen by ≥40% from baseline? Check adherence to medication, adverse effects/intolerance/hesitancy and lifestyle interventions.

**Review annually** for adherence to medications, diet and lifestyle, check required bloods eg lipids. Refer for support as required from specialist teams.

**Refer to lipid clinic (see page 7 for SEL contact details)**

*Please note* that for rosuvastatin 40mg specialist supervision is recommended when this dose is initiated (see SPC).
**Secondary Prevention: Medicines optimisation for Lipid Management**

1. **Check baseline bloods** (non-fasting full lipid profile, LFTs, HbA1c, thyroid and renal function)- also consider if lipid profile may indicate FH (see page 10)

2. **Offer high dose high intensity statin** therapy with atorvastatin 40-80mg (alternative is rosuvastatin 20-40mg)* to adults with CVD: this includes acute coronary syndromes (ACS), angina, previous myocardial infarction (MI), revascularisation, stroke or transient ischaemic attack (TIA), symptomatic peripheral arterial disease (PAD) or abdominal aortic aneurysm (AAA)

3. **Support the self-management** (see page 6) of modifiable risk factors eg. smoking, diet, obesity, alcohol intake, physical activity, blood pressure and glycaemic control (HbA1c)

In primary care check: Is patient on high dose, high intensity statin? atorvastatin 40-80mg (alternative is rosuvastatin 20mg-40mg)*-consider dose adjustments: eGFR<30ml/min, drug interactions, intolerance

- Has non-HDL-C reduced by 40% or more from baseline at 3 months? **NICE** (if no baseline value: consider a target of non-HDL-C < 2.5mmol/L or LDL-C <2.0mmol/L: JBS)
  - After 3 months check non-fasting full lipid profile (TC, TG, HDL, LDL-C); LFTs

**Please see page 9 for a summary of lipid lowering options to discuss with your patient. In SEL it is recommended to prescribe high intensity statin with ezetimibe for at least 3 months before considering other options or referring to lipid clinic.**

*Please note* that for rosuvastatin 40mg specialist supervision is recommended when this dose is initiated (see SPC)
Statin intolerance pathway/options if not achieving lipid lowering targets

In primary care: Discuss with the patient if signs and symptoms are statin intolerance or due to a statin reluctance/non-adherence. Consider that a statin at any dose reduces CV risk- if a patient cannot tolerate a high intensity statin, aim to treat with a maximum tolerated dose of a statin, but if symptoms persist consider alternative options/lipid clinic referral (see below)

For Statin Related Muscle (SRM) symptoms: symmetrical pain/weakness in large proximal muscle groups, worsened by exercise. Measure creatine kinase (CK): if > 4x and <10x ULN with intolerable symptoms: stop statin for 4 to 6 weeks*

If CK normalises and symptoms have resolved for at least 2 weeks, then rechallenge: Offer a low/moderate dose of HI statin eg atorvastatin 10 to 20mg daily or rosuvastatin 5 to 10mg daily. Please note: Non-standard dosing may be prescribed by specialist clinics eg rosuvastatin 5mg weekly or three times a week (off label use but accepted practice)

No recurrence of muscle symptoms:
Titrates dose at 8 week intervals to achieve appropriate targets- continue to monitor for symptoms and continue therapy

If recurrence of muscle symptoms: recheck CK* and consider alternative options or add-on therapy if not tolerating statin/ achieving lipid lowering targets:
1) Continue maximal tolerated dose of statin (if not tolerated -stop the statin)
2) Add in ezetimibe 10mg daily (SPC)- review adherence/tolerance and full lipid profile in 3 months

Bempedoic acid initiation: This is amber 2 in SEL and will be undertaken by specialist lipid services:
1. Check baseline eGFR (do not start if eGFR <30ml/min)
2. Check baseline LFTs and uric acid (do not start in severe hepatic impairment eg. Child-Pugh C or active gout)
3. Check baseline FBC (particularly haemoglobin- Hb level)
4. Consider drug interactions eg simvastatin (BNF) and contra-indications (SPC)
5. Prescribe with ezetimibe 10mg
6. Communicate to primary care: baseline information at initiation and recommendations for follow up in primary and/or secondary care (lipid clinics may also have capacity to schedule a review at 3 to 6 months)

Bempedoic acid monitoring in primary care within the first 3 months and annually:
1. Check LFTs- discontinue treatment if AST/ALT ≥3x ULN
2. Monitor for hyperuricaemia with gout symptoms- if present, discontinue bempedoic acid
3. Check FBC, stop if Hb decrease by ≥20g/L from baseline or < lower limit of normal (LLN), investigate other possible causes/refer to appropriate specialist
4. Monitor for myopathy symptoms- if present check creatine kinase (CK) >10x ULN confirms myopathy: stop bempedoic acid and statin)- reduce statin dose or change statin/lipid lowering therapy if symptoms persist (see above). Report any side effects to the yellow card scheme.

Patient information: Report any unexplained muscle pain, tenderness or weakness.

Patient information: Report any unexplained muscle pain, tenderness or weakness.

*For muscular symptoms: check CK: if >50x ULN stop statin and consider rhabdomyolysis, if 10-50xULN check renal function- if deteriorating, stop statin for 1 month to see if symptoms and CK resolves. Restart a lower dose and uptitrate or consider alternatives above. See: Statin-Intolerance-Pathway-NEW.pdf (england.nhs.uk)

If patients report symptoms that are not typical of SRM (e.g. asymmetric distribution, failure to resolve with de-challenge despite normal CK) consider other musculoskeletal disorders, metabolic, degenerative or inflammatory e.g. Vitamin D deficiency, polymyalgia rheumatica. Check Bone profile, Vitamin D, C-Reactive Protein.

Risk factors for intolerance: for all doses of all statins (except for simvastatin 80 mg), factors predisposing to these adverse effects are not well defined, but as with most drugs, older people appear to be more vulnerable. Hypothyroidism, pre-existing muscle disease, and renal impairment are also causative factors, and commencement of treatment with an interacting drug is a well-established precipitant. Other suspected risk factors include female sex, diabetes mellitus, and Chinese (and possibly East Asian in general) ancestry.5

For abnormal LFTs: If transaminases raised 3xULN stop and restart once LFTs normalised- consider other causes of abnormal LFTs. LFTs are checked at baseline and within 1 year of statin therapy.
Shared decision making concerning lifestyle and statins

Lifestyle interventions: There are many resources to support self-management eg Heart UK and British Heart Foundation, national support groups and local social prescribing options. Support the patient to review their diet, exercise, smoking cessation, alcohol intake and mental health considerations which are key to lipid management. In dietary intervention studies, CVD events were reduced by 12% over 5 years (NNT=95), and statins/lipid lowering therapies reduce CVD risk by 25% for each year of treatment per 1mmol/L LDL-C reduction -see table below (Lancet 2016)

Lifestyle management options and LDL reduction: Consider also the evidence of a benefit for CV risk reduction with each medicine

<table>
<thead>
<tr>
<th>Choice of statin or oral lipid lowering therapy/ daily dose</th>
<th>Approximate reduction in LDL-C</th>
<th>NNT</th>
<th>NNH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluvastatin (non-formulary)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5mg</td>
<td>21%</td>
<td>20</td>
<td>100</td>
</tr>
<tr>
<td>10mg</td>
<td>27%</td>
<td></td>
<td>200</td>
</tr>
<tr>
<td>20mg</td>
<td>33%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pravastatin (consider as a 3rd option statin if atorvastatin and rosuvastatin are inappropriate)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20%</td>
<td>24%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>29%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Simvastatin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-</td>
<td>37%</td>
<td>10</td>
<td>100</td>
</tr>
<tr>
<td>5mg</td>
<td>32%</td>
<td></td>
<td>200</td>
</tr>
<tr>
<td>10mg</td>
<td>37%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>20mg</td>
<td>42%</td>
<td></td>
<td></td>
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<tr>
<td>Atorvastatin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-</td>
<td>37%</td>
<td>10</td>
<td>100</td>
</tr>
<tr>
<td>5mg</td>
<td>32%</td>
<td></td>
<td>200</td>
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<tr>
<td>10mg</td>
<td>37%</td>
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<tr>
<td>20mg</td>
<td>42%</td>
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<tr>
<td>Rosuvastatin</td>
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<td></td>
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<tr>
<td>-</td>
<td>37%</td>
<td>10</td>
<td>100</td>
</tr>
<tr>
<td>5mg</td>
<td>43%</td>
<td></td>
<td>200</td>
</tr>
<tr>
<td>10mg</td>
<td>48%</td>
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<td></td>
</tr>
<tr>
<td>20mg</td>
<td>53% specialist initiation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atorvastatin with Ezetimibe 10mg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-</td>
<td>52%</td>
<td>10</td>
<td>100</td>
</tr>
<tr>
<td>5mg</td>
<td>54%</td>
<td></td>
<td>200</td>
</tr>
<tr>
<td>10mg</td>
<td>57%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>20mg</td>
<td>61%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ezetimibe 10mg with Bempedoic acid 180mg</td>
<td>approx. 38%*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10mg</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

NB. High intensity (HI) statins reduce LDL-C >40% (highlighted green) and are more effective at preventing cardiovascular events than low/medium intensity statins

NICE/AAC recommends atorvastatin and rosvastatin as HI statins

*simvastatin 80mg is not recommended due to muscle toxicity risk

Common and uncommon side effects for statins may be found here: Statins - Side effects - NHS (www.nhs.uk)

For contra-indications please refer to individual summary of product characteristics (SPC) for each medication: women of childbearing age need to ensure adequate contraception during statin treatment and for 1 month afterwards, and statins should be discontinued for 3 months before attempting to conceive

For 10,000 patients taking a statin for 5 years, achieving 2mmol/L LDL-C reduction: 1000 MVEs avoided (secondary prevention) and 500 MVEs avoided (primary prevention); 100 newly diagnosed diabetes, 5 cases of myopathy and 1 rhabdomyolysis, and <1 active liver disease

MVEs= major vascular events: MI, stroke, coronary revascularisation
Reference: AHA statin safety and associated adverse events, 2019

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MVEs= major vascular events: MI, stroke, coronary revascularisation
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Lipid Clinic Referral and PCSK9 Inhibitors (monoclonal antibodies-mABs)

If still not achieving targets, or following confirmed statin intolerance, refer to lipid clinic for consideration of initiation of PCSK9i (mAB). NICE eligibility criteria for alirocumab or evolocumab are established CVD or familial hypercholesterolaemia:

<table>
<thead>
<tr>
<th>NICE TA eligibility criteria for PCSK9i (mAB)</th>
<th>Without CVD</th>
<th>With CVD and high risk</th>
<th>With CVD and very high risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary non-FH or mixed dyslipidaemia</td>
<td>Not recommended</td>
<td>LDL-C &gt; 4.0mmol/L</td>
<td>LDL-C &gt; 3.5mmol/L</td>
</tr>
<tr>
<td>Primary heterozygous FH</td>
<td>LDL-C &gt; 5.0mmol/L</td>
<td></td>
<td>LDL-C &gt; 3.5mmol/L</td>
</tr>
</tbody>
</table>

High risk: history of ACS, coronary/arterial revascularisation, CHD, ischaemic stroke, PAD

Very high risk: recurrent CVD events or CVD events in multiple beds (polyvascular disease)

Lipid clinic will initiate, monitor and supply a PCSK9i mAB (red formulary status, hospital only medications), either:

- **ALIROCUMAB** usual starting dose is 75mg subcutaneous (SC) injection once every 2 weeks (or if LDL-C reduction of >60% required start on 150mg SC injection once every 2 weeks or 300mg SC once every 4 weeks) or

- **EVOLOCUMAB** 140mg SC injection every 2 weeks or 420mg once monthly (for FH, after 12 weeks of treatment, the dose may be uptitrated to 420mg every 2 weeks if a clinically meaningful response is not achieved)

Continue existing oral lipid lowering therapy and assess response within 3 months of initiation. For primary care: see SEL Guide to reconciling hospital only medicines in primary care.

Please ensure that, prior to referral to lipid clinic, patients have potential secondary causes of hyperlipidaemia excluded such as uncontrolled diabetes mellitus, obesity, excess alcohol consumption, untreated hypothyroidism, proteinuria and some medications, for example, thiazide diuretics and ciclosporin:

<table>
<thead>
<tr>
<th>SEL Lipid Clinic</th>
<th>Lipidologist for referrals</th>
<th>Contact Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>GSTT</td>
<td>Prof AS Wierzbicki/Prof MA Crook</td>
<td>via Choose &amp; Book or <a href="mailto:gst-tr.diabetesandendocrine@nhs.net">gst-tr.diabetesandendocrine@nhs.net</a></td>
</tr>
<tr>
<td>KCH</td>
<td>Dr Nandini Rao</td>
<td>via Choose &amp; Book or to book an appointment/query re appointment/blood test request forms Tel: 02032994181 or email: <a href="mailto:Laura.Gonzalez@nhs.net">Laura.Gonzalez@nhs.net</a></td>
</tr>
<tr>
<td>PRUH</td>
<td>Dr Nandini Rao</td>
<td>via Choose &amp; Book or <a href="mailto:kch-tr.br-referrals@nhs.net">kch-tr.br-referrals@nhs.net</a></td>
</tr>
<tr>
<td>LGT</td>
<td>Prof MA Crook</td>
<td>via Choose &amp; Book or <a href="mailto:tll-tr.LewishamReferrals@nhs.net">tll-tr.LewishamReferrals@nhs.net</a> or endocrinology at QEH: lipidology clinics at the Bromley diabetes centre, Outpatients QEH: Tel 02088364969</td>
</tr>
<tr>
<td>Community</td>
<td>Prof AS Wierzbicki for Lambeth, Southwark and Bexley boroughs</td>
<td>Forms on DXS and/or email: <a href="mailto:gst-tr.KHPCommunityCVD@nhs.net">gst-tr.KHPCommunityCVD@nhs.net</a></td>
</tr>
</tbody>
</table>
Inhibits PCSK9 production by interfering with RNA, thus reducing LDL-cholesterol levels

Added to maximally tolerated statin and dietary measures if not achieving treatment targets in secondary prevention

NICE recommends for:
- Patients with a history of cardiovascular disease e.g. ACS, coronary/arterial revascularisation, CHD, ischaemic stroke or peripheral arterial disease (PAD)
- with persistent LDL-C levels >2.6 mmol/l despite having the maximum tolerated lipid-lowering therapy (HI statins and/or ezetimibe)
- Alone or in combination with lipid lowering medication if statin intolerant/contra-indicated

NOT recommended by NICE (unless research) for: primary prevention (no history of CV events)

Dosing: 284mg subcutaneous injection by HCP into abdomen, upper arm or thigh: baseline, after 3 months, and then every 6 months

Monitoring: baseline LDL-C (fasting sample if possible), after 3 months, then every 6 months:
- Full lipid profile (to calculate LDL-C), liver profile and renal profile
- checking adherence to other medications
- side effects/intolerances
- if LDL-C remains ≥ 2.6 mmol/L despite inclisiran therapy for 9 to 12 months following initiation—refer to lipid clinic

Use with caution in severe renal impairment (e.g. CrCl <30 ml/min) or requiring haemodialysis (avoid 72 hours after inclisiran dosing)

No/limited data in pregnancy and breast-feeding, severe liver impairment (Child-Pugh class C), child <18 years

ORION-10 and ORION-11 studies: reduced LDL-C by average of 52% and 50%, compared to placebo at month 17 (see lipid lowering options table page 9)

Adverse effects: Mild to moderate injection site reactions are transient and resolve: pain, erythema, rash
- Check for side effects/intolerances at each visit as this is a new medication
- Report all ADRs to yellow card scheme: https://yellowcard.mhra.gov.uk/

Amber 1 on SEL formulary as an interim measure: initiation in primary care on advice of a lipid specialist

Inclisiran checklist for initiation (add link) to be completed by primary care HCP before advice and guidance (A&G) is sought from a lipid specialist

Prescribing, administration and follow up is in primary care (unless the patient has been referred to a lipid clinic)

Missed doses: If a planned dose is missed by ≤ 3 months, administer inclisiran and continue dosing according to the patient’s original schedule.

If a planned dose is missed by > 3 months, a new dosing schedule should be started – inclisiran should be administered initially, again at 3 months, followed by every 6 months.
<table>
<thead>
<tr>
<th>Lipid management drug</th>
<th>Indication (NICE)</th>
<th>Administration</th>
<th>LDL lowering effect</th>
<th>CV outcome data</th>
<th>LT safety data</th>
</tr>
</thead>
<tbody>
<tr>
<td>High intensity statin (atorvastatin or rosuvastatin)</td>
<td>Adjunct to diet in hypercholesterolaemia, FH, CV risk reduction: primary and secondary prevention</td>
<td>One tablet daily (oral)</td>
<td>40-50%</td>
<td>Yes (primary and secondary prevention)</td>
<td>Yes</td>
</tr>
<tr>
<td>Ezetimibe</td>
<td>With statin to reduce CV risk: primary and secondary prevention, or if statin intolerance, FH</td>
<td>One tablet daily (oral)</td>
<td>24%</td>
<td>Yes (secondary prevention)</td>
<td>Yes</td>
</tr>
<tr>
<td>PCSK9i mAB (evolocumab or alirocumab)</td>
<td>FH if LDL&gt;5mmol/L, statin intolerance, CV risk reduction: secondary prevention if LDL&gt;3.5-4mmol/L</td>
<td>SC injection every 2 weeks (can be self administered)</td>
<td>60% +</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Bempedoic acid</td>
<td>With ezetimibe in statin intolerance</td>
<td>One tablet daily (oral)</td>
<td>28%</td>
<td>Awaited</td>
<td>Awaited</td>
</tr>
<tr>
<td>Inclisiran (PCSK9i)</td>
<td>Secondary prevention if LDL &gt;2.6mmol/L, statin intolerance</td>
<td>SC injection twice a year</td>
<td>52%</td>
<td>Awaited</td>
<td>Awaited</td>
</tr>
</tbody>
</table>

NB. This table will be updated following the publication of a national decision-making guide for inclisiran
Familial Hypercholesterolaemia (FH) Pathway

### In primary care case find age <30 years:
TC >7.5mmol/L or LDL-C >4.9mmol/L or non-HDL-C >6mmol/L

### In primary care case find age ≥30 years:
TC >9.0mmol/L or LDL-C >6.4mmol/L or non-HDL-C >7.5mmol/L

## In primary care check bloods:
repeat non-fasting lipid profile (TC, TG, HDL-C, LDL-C, non-HDL-C) plus LFTs, TFTs, renal function, HbA1c

### If TG > 2.3mmol/L
Unlikely FH: Investigate raised triglycerides-TG (refer if indicated) and aim to reduce non-HDL-C by 40% (see primary and secondary prevention pathways: pages 3 and 4).
Ensure appropriate SNOMED coding in primary care record: hypertriglyceridemia and/or hypercholesterolaemia, not FH.

### If TG ≤ 2.3mmol/L

#### Primary care check:
1. Family history: 1st degree relative MI <60 years old, 2nd degree relative MI <50 years old
2. Tendon xanthomata
If either are positive refer to lipid clinic for DNA testing for monogenic FH (Simon Broome criteria)

If confirmed FH*: aim to reduce LDL by >50%, lipid clinic will initiate/recommend options:
1. High intensity statin (atorvastatin or rosuvastatin- maximum tolerated doses- see high intensity statin table on page 6)
2. Add in ezetimibe 10mg daily
3. Refer to lipid clinic: Add in bempedoic acid 180mg daily (to ezetimibe) if not reaching target/statin intolerance or inclisiran if secondary prevention
4. Refer to lipid clinic for alirocumab or evolocumab (see PCSK9i mAB pathway on page 7)

Specialist service for monogenic FH: genetic counselling and DNA test for FH mutation and cascade testing for family members if indicated. This is available at all lipid clinics in SEL.

*Ensure correct coding in primary care record for confirmed FH. SNOMED: familial hypercholesterolaemia: 398036000, homozygous FH 238078005, heterozygous FH 238079000
### Management of triglycerides (TG)

SNOMED code: hypertriglyceridemia 302870006

<table>
<thead>
<tr>
<th>Triglyceride concentration</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>In all cases: Review secondary causes</strong></td>
<td>Exclude secondary causes of high triglycerides such as</td>
</tr>
<tr>
<td></td>
<td>- Excess alcohol intake</td>
</tr>
<tr>
<td></td>
<td>- Poorly controlled/new diabetes</td>
</tr>
<tr>
<td></td>
<td>- TG-raising medication (eg. high dose steroids)</td>
</tr>
<tr>
<td><strong>Greater than 20mmol/L</strong></td>
<td>• Refer to lipid clinic for urgent specialist review due to the risk of acute pancreatitis</td>
</tr>
<tr>
<td></td>
<td>• In selected patients omega 3 fatty acids may be initiated by lipid specialists for the control of triglycerides, but are not recommended for the secondary prevention of MI</td>
</tr>
<tr>
<td><strong>10 to 20 mmol/L</strong></td>
<td>Repeat TG with a fasting test (5 to 14 days after first test) and review potential secondary causes of hyperlipidaemia</td>
</tr>
<tr>
<td></td>
<td>• Seek specialist lipid clinic advice if TG remains &gt;10mmol/litre as risk of acute pancreatitis</td>
</tr>
<tr>
<td><strong>4.5 to 9.9 mmol/L</strong></td>
<td>If non-fasting TG &gt;4.5mmol/L repeat with a fasting TG. Optimise management of other CVD risk factors (check Qrisk)</td>
</tr>
<tr>
<td></td>
<td>• Seek specialist advice if non-HDL &gt; 7.5mmol/litre.</td>
</tr>
<tr>
<td></td>
<td>IF CVD risk (Qrisk) &lt;10% consider a fibrate such as fenofibrate 160mg daily <a href="https://www.nhs.uk/conditions/fenofibrate/">SPC</a> (if contra-indicated or not tolerated seek specialist advice)- recheck lipid levels within 3 months of initiation- aim for TG &lt;4.5mmol/L- monitor renal function and liver function with fibrate prescriptions at 3 months &amp; annually</td>
</tr>
<tr>
<td></td>
<td>IF CVD risk (Qrisk) ≥10% consider a HI statin for primary prevention (see page 3)</td>
</tr>
<tr>
<td></td>
<td>• Refer to lipid specialists if inadequate responses to therapy</td>
</tr>
<tr>
<td><strong>&gt;2 to &lt;4.5 mmol/L</strong></td>
<td>If CVD risk (Qrisk) &lt;10% address any lifestyle factors</td>
</tr>
<tr>
<td></td>
<td>If CVD risk (Qrisk) &gt;10% consider a HI statin for primary prevention (see page 3)</td>
</tr>
<tr>
<td>Hospital lipid clinic</td>
<td>Referral Criteria</td>
</tr>
<tr>
<td>----------------------</td>
<td>-------------------</td>
</tr>
<tr>
<td><strong>Severe hypercholesterolaemia</strong></td>
<td>Cholesterol &gt;9.0 mmol/L (or non HDL-C &gt; 7.5 mmol/L) regardless of existing heart disease / family history</td>
</tr>
<tr>
<td><strong>Suspected familial hypercholesterolaemia (FH)</strong></td>
<td>Cholesterol &gt;7.5 mmol/L and LDL-C &gt;5.0 mmol/L AND Premature CVD (age &lt;60yrs) in the patient OR Family history: 1st degree relative MI &lt; 60 years old, 2nd degree relative MI &lt;50 years old OR Presence of tendon xanthomata</td>
</tr>
<tr>
<td><strong>Family screening</strong></td>
<td>Cascade screening from identified patient with familial hypercholesterolaemia with a genetic diagnosis of FH</td>
</tr>
<tr>
<td><strong>Severe Hypertriglyceridemia</strong></td>
<td>• Triglyceride &gt; 20 mmol/L OR Triglyceride 10 - 20 mmol/L which persists on a fasting lipid profile (2 samples 1 week apart) OR Triglyceride 4.5 - 9.9 mmol/L WITH non-HDL cholesterol &gt; 7.5 mmol/L</td>
</tr>
<tr>
<td><strong>Statin intolerance</strong></td>
<td>Intolerance of 3 or more statins OR Severe adverse reaction to one statin AND non meeting target LDL-C/ non HDL-C on ezetimibe 10mg daily</td>
</tr>
<tr>
<td><strong>Secondary prevention of CVD</strong></td>
<td>Unable to meet target reductions in LDL-C or non HDL-C despite maximal doses of statins + ezetimibe</td>
</tr>
</tbody>
</table>

*Note: The aim of hospital and community clinics is to focus on patients with primary hyperlipidaemia, before referral please exclude:

- For hypercholesterolaemia exclude hypothyroidism (check TSH), chronic renal disease or nephrotic syndrome, variant diets (zero carbohydrate; protein supplements)
- For hypertriglyceridaemia exclude new/uncontrolled diabetes (check HbA1c) and excess alcohol intake*
References and supporting material


4) **Lancet 2016**: 388:2532-61; R Collins et al; Interpreting the evidence for the efficacy and safety of statin therapy; [https://www.thelancet.com/pdfs/journals/lancet/PIIS0140-6736(16)31357-5.pdf](https://www.thelancet.com/pdfs/journals/lancet/PIIS0140-6736(16)31357-5.pdf)

5) **AHA Scientific Statement**: Statin safety and associated adverse events; Arteriosclerosis, thrombosis and vascular biology 2019;39:e38-e81: [https://www.ahajournals.org/doi/10.1161/ATV.0000000000000073](https://www.ahajournals.org/doi/10.1161/ATV.0000000000000073)


8) **NICE TA694**: Bempedoic acid with ezetimibe for treating primary hypercholesterolaemia or mixed dyslipidaemia, Published: 28 April 2021: [https://www.nice.org.uk/guidance/ta694](https://www.nice.org.uk/guidance/ta694)

9) **NICE TA385**: Ezetimibe for treating primary heterozygous-familial and non-familial hypercholesterolaemia, Published: 24 February 2016: [https://www.nice.org.uk/guidance/ta385](https://www.nice.org.uk/guidance/ta385)

10) **NICETA394**: Evolocumab for treating primary hypercholesterolaemia and mixed dyslipidaemia, Published: 22 June 2016: [https://www.nice.org.uk/guidance/ta394](https://www.nice.org.uk/guidance/ta394)

11) **NICE TA393**: Alirocumab for treating primary hypercholesterolaemia and mixed dyslipidaemia, Published: 22 June 2016: [https://www.nice.org.uk/guidance/ta393](https://www.nice.org.uk/guidance/ta393)


13) **NICE TA733**: Inclisiran for treating primary hypercholesterolaemia or mixed dyslipidaemia; Published: 06 October 2021 [https://www.nice.org.uk/guidance/TA733](https://www.nice.org.uk/guidance/TA733)