Summary of National Guidance for Lipid Management for Primary and Secondary Prevention of CVD

INITIAL CONSIDERATIONS:
- Measure non-fasting full lipid profile (total cholesterol, HDL-C, non-HDL-C, triglycerides) and HbA1c as part of an initial baseline assessment.
- Consider secondary causes of hyperlipidaemia and manage as needed.
- Ensure appropriate baseline and follow up tests as detailed on page 2. Measure BMI.
- Identify and exclude people with contraindications/drug interactions.
- If non-fasting triglyceride above 4.5mmol/L see page 2.

PRIMARY PREVENTION
Consider statin therapy for adults who do not have established CVD but fall into the categories below. Use QRISK risk assessment tool where appropriate (see page 2, Primary Prevention Risk Assessment).

If lifestyle modification is ineffective or inappropriate offer statin treatment. Atorvastatin 20mg daily

- Measure full lipid profile again after 3 months (non-fasting).
- High intensity statin treatment should achieve reduction of non-HDL-C > 40% from baseline. If not achieved after 3 months - discuss treatment adherence, timing of dose, diet and lifestyle
- If at higher risk (based on comorbidities, risk score or clinical judgement – see page 2 – Additional Risk Factors) consider increasing to 80mg atorvastatin. For how to increase in people with CKD see ‘Special Patient Populations’ (page 2).
- If patients on a high-intensity statin have side effects, offer a lower dose or an alternative statin.

SECONDARY PREVENTION
Offer statin therapy to adults with CVD, this includes CHD, angina, Acute Coronary Syndrome (MI or unstable angina), revascularisation, stroke or TIA, or symptomatic peripheral arterial disease. Do not delay statin treatment if a person has acute coronary syndrome. Take a lipid sample on admission (within 24 hours).

Identify and address all modifiable risk factors - smoking, diet, obesity, alcohol intake, physical activity, blood pressure and HbA1c.

SECONDARY PREVENTION
Do not delay statin treatment in secondary prevention while managing modifiable risk factors. Prescribe a high intensity statin: Atorvastatin 80mg daily

If maximum tolerated dose of statin does not control non-HDL-C/LDL-C well enough after 3 months confirm statin adherence, then consider the following options based on shared decision making* with the patient.

SECONDARY PREVENTION

- Measure full lipid profile again after 3 months (non-fasting).
- High intensity statin treatment should achieve reduction of non-HDL-C > 40% from baseline. If not achieved after 3 months - discuss treatment adherence, timing of dose, diet and lifestyle measures
- If started on less than atorvastatin 80mg and the person is judged to be at higher risk (based on comorbidities, risk score or clinical judgement – see page 2 – Additional Risk Factors), consider increasing to 80mg atorvastatin. For how to increase in people with CKD see ‘Special Patient Populations’ (page 2).
- If non-HDL-C baseline value is not available, consider target non-HDL-C < 2.5mmol/L (approximately equivalent to LDL-C < 1.8mmol/L) as recommended by Joint British Societies (JBS3).
- This scenario is not currently covered by NICE CG181. NICE will consider this as part of the guideline update with publication currently expected September 2023.
- If patients on a high-intensity statin have side effects, offer a lower dose or an alternative statin (see page 2 ‘Extent of lipid lowering with available therapies’).

SEVERE HYPERLIPidaemia
If TC>7.5mmol/L and/or LDL-C >4.9mmol/L and/or non-HDL-C >5.9mmol/L, a personal and/or family history of confirmed CHD (<60 years) and with no secondary causes: suspect familial hypercholesterolaemia (possible heterozygous FH).

Do not use QRISK risk assessment tool.

DIAGNOSIS AND REFERRAL
Take fasting blood for repeat lipid profile to measure LDL-C.

Use the Simon Broome or Dutch Lipid Clinic Network (DLCN) criteria to make a clinical diagnosis of FH.

- Refer to Lipid Clinic for further assessment if clinical diagnosis of FH or if TC>9.0mmol/L and/or LDL-C >6.5mmol/L and/or non-HDL-C >7.5mmol/L or Fasting triglycerides >10mmol/L (regardless of family history) (page 2).

TREATMENT TARGETS IN FH
If clinical diagnosis of FH and/or other risk factors present follow the recommended treatment management pathway for primary or secondary prevention as for non-FH, BUT Aim to achieve at least a 50% reduction of LDL-C (or non-fasting non-HDL-C) from baseline.

Consider specialist referral for further treatment and/or consideration of PCSK9i therapy if - they are assessed to be at very high risk of a coronary event** - OR therapy is not tolerated - OR LDL-C remains >5.5mmol/L (primary prevention) - OR LDL-C remains >3.5mmol/L (secondary prevention) despite maximal tolerated statin and ezetimibe therapy.

**Defined as any of the following:
- Established coronary heart disease
- Two or more other CVD risk factors

If recommended statin treatment is contraindicated or not tolerated - follow AAC Statin Intolerance Algorithm for advice regarding adverse effects (click here).

If statin intolerance is confirmed:
- Ezetimibe 10mg monotherapy. Assess response after 3 months (TA385)
- Ezetimibe 10mg/bempedoic acid 180 mg combination when ezetimibe alone does not control non-HDL-C (NICE TA894)

If non-HDL-C remains >2.5mmol/L despite other lipid lowering therapies consider Injectable therapies - arrange a fasting blood test and assess eligibility criteria (TA939/394, TA733)

Injectable therapies**
- If non-HDL-C > 2.5mmol/L; Arrange fasting blood test to measure LDL-C to assess eligibility
  - Inclisiran - if fasting LDL-C ≥ 2.6mmol/L despite maximum tolerated lipid lowering therapy (TA733) OR
  - PCSK9i - see overseal for LDL-C thresholds (TA383/4)

If eligibility criteria not met, consider ezetimibe 10mg daily (if not previously considered)

If non-HDL-C remains < 2.5mmol/L despite maximal tolerated lipid lowering therapy (including people with intolerances and contraindications) consider referral to specialist lipid management clinic according to local arrangements

If maximum tolerated dose of statin does not control non-HDL-C/LDL-C well enough after 3 months consider statin adherence, then consider the following options based on shared decision making* with the patient.

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If eligibility criteria not met, consider ezetimibe 10mg daily (if not previously considered)
This guidance applies to new patients and may also be taken into consideration for those already on statins at their annual review. If 40% reduction of non-HDL-C has not achieved, offer intensive statin therapy. Discuss with people who are st监护 on a low- or medium-intensity statin the likely benefits and potential risk of side effects if changed to a high-intensity statin when they have a medication review and agree with the person whether a change is needed.

Erlotinib, alirocumab, orvilcumb or inclisiran can be added when patients’ LDL-C levels are not lowered enough with the maximally tolerated dose of statins. Bempedoic acid with ezetimibe is an option when statins are contraindicated or not tolerated, and when ezetimibe alone does not control LDL-C well enough. Do not offer a fibrate, niacin, or nicotinic acid before starting a statin, omega-3 fatty acids alone or in combination with statin, for the prevention of CVD (check NICE CG181 and TA805 for exceptions).

### Additional Risk Factors

Note, standard CVD risk scores including QRISK may underestimate risk in people who have additional conditions or medical conditions or treatments. These groups include the following groups of people:

- severe obesity (BMI > 40 kg/m²) increases CVD risk
- treated for HIV
- serious mental health problems
- taking medicines that can cause dyslipidaemia such as antipsychotic medication, corticosteroids or immunosuppressant drugs
- autoimmune disorders such as SLE, and other systemic inflammatory disorders
- non-diabetic hyperglycaemia
- significant hypertriglyceridaemia (fasting triglycerides 4.5-9.9 mmol/L)
- recent risk factor changes e.g. quit smoking, BP or lipid treatment

Consider also socio-economic status as another additional factor contributing to CVD risk. If QRISK < 10% over the next 10 years - Give lifestyle advice and ensure regular review of CVD risk in line with guidance.

### SPECIAL PATIENT POPULATIONS

**Type 1 Diabetes**

While NICE recommends offering statins to patients with Type 1 diabetes as detailed in the algorithm, it also states to consider statins in all adults with type 1 diabetes.

**Chronic Kidney Disease**

Offer atorvastatin 20mg for the primary or secondary prevention of CVD to people with CKD (eGFR < 60 mL/min/1.73m² and/or albuminuria) Increase the dose if a greater than 40% reduction in non-HDL-C is not achieved and eGFR is 30 mL/min/1.73m² or more. Agree the use of higher doses with a renal specialist if eGFR is less than 30 mL/min/1.73m²

### EXTENT OF LIPID LOWERING WITH AVAILABLE THERAPIES

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### BASELINE MEASUREMENTS

**Baseline Measurements**

In addition to full lipid profile, measure renal, thyroid and liver profiles (including albumin) and HbA1c to exclude secondary causes and co-morbidities. Measure baseline liver transaminase (ALT or AST) before starting a statin. Measure CK if unexplained muscle pain before starting a statin.

**Specialist advice**

Consider an annual non-fasting full lipid profile to inform the discussion around effectiveness of lipid lowering therapy and any medicines non-adherence.

### MONITORING

Provide annual medical reviews for people taking statins to discuss effectiveness of therapy, medication adherence, adverse effects and modification of other risk factors, including lifestyle, hypertension, and diabetes. Consider an annual non-fasting full lipid profile to inform the discussion around effectiveness of lipid lowering therapy and any medicines non-adherence.

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### SPECIALIST SERVICES

Scope of specialist service available locally may include; lipid clinic, PCSK9i clinic (offering initiation and subsequent follow up), FH diagnostic and cascade testing, lipoprotein apheresis service. NICE eligibility criteria for PCSK9i and fasting lipids thresholds are summarised below.

**NICE TA393 Alirocumab**

- **Primary non-FH or mixed dyslipidaemia**
  - Not recommended
  - LDL-C > 4.0 mmol/L
  - LDL-C > 3.5 mmol/L

**NICE TA394 Evolocumab**

- **Primary heterozygous-FH**
  - Not recommended
  - LDL-C > 5.0 mmol/L
  - LDL-C > 3.5 mmol/L

- **Secondary prevention**
  - LDL-C > 2.5 mmol/L (LDL-C = non-HDL-C minus (Fasting triglycerides ≤ 2.2 mmol/L) and < 40% reduction in non-HDL-C and LDL-C)

**Specialist advice**

- **PCSK9i may be available for prescribing in primary care:** see local initiation pathways.

### TRIGLYCERIDES

**Triglyceride concentration**

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<td>Refer to lipid clinic for urgent specialist referral if not a result of excess alcohol or poor glycaemic control. At risk of acute pancreatitis.</td>
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- **No-fasting triglycerides are greater than 4.5mmol/L, repeat with a fasting test.** Be aware that the CVD risk may be underestimated without consideration of LFTs. Consider the management of other CVD risk factors present and seek specialist advice if non-HDL-C concentration is > 7.5 mmol/L.

**Icosapent ethyl (TA805)**

- Check fasting triglyceride levels.
- Manage secondary causes of hypertriglyceridaemia.
- Consider icosapent ethyl (TA805) if patient has established cardiovascular disease (secondary prevention) and - on statins and fasting TG > 1.7mmol/L and LDL-C2 between 1.44 and ≤2.59mmol/L.
- See table above and refer as appropriate.

**Lipid-lowering drug therapy**

- LDL-C cannot be calculated using Friedewald’s formula to TG > 4.5 mmol/L. Discuss with your lab. Consider using an alternative equation (eg Sampson, doi: 10.1248/jpm.2004.0013) or beta-quantification. 1 laboratories do not report calculated LDL-C beyond one decimal point.

**Primary prevention**

- Intensify lipid lowering therapy if non-HDL-C reduction from baseline is less than 40% - LDL-C < 1.8mmol/L

- **Secondary Prevention**
  - Optimise lipid lowering therapy to achieve at least 50% reduction in LDL-C (or non-HDL-C).

**FH**

- Optimise lipid lowering therapy to achieve at least 50% reduction in LDL-C (or non-HDL-C).

If baseline cholesterol is unknown in the setting of secondary prevention use the use Joint British Societies’ JBS3 consensus recommendation.

- **Non-HDL-C = TG minus HDL-C**
- **LDL-C = non-HDL-C minus fasting triglycerides(≥2.2)**

- **Valid only when fasting triglycerides are less than 4.5 mmol/L.**

**NICE TA393 Alogliptin**

- **Primary non-FH or mixed dyslipidaemia**
  - Not recommended
  - LDL-C > 4.0 mmol/L
  - LDL-C > 3.5 mmol/L

- **Primary heterozygous-FH**
  - Not recommended
  - LDL-C > 5.0 mmol/L
  - LDL-C > 3.5 mmol/L

**NICE TA394 Dapagliflozin**

- **Primary non-FH or mixed dyslipidaemia**
  - Not recommended
  - LDL-C > 4.0 mmol/L
  - LDL-C > 3.5 mmol/L

- **Primary heterozygous-FH**
  - Not recommended
  - LDL-C > 5.0 mmol/L
  - LDL-C > 3.5 mmol/L

- **Secondary prevention**
  - LDL-C > 2.5 mmol/L (LDL-C = non-HDL-C minus (Fasting triglycerides ≤ 2.2 mmol/L) and < 40% reduction in non-HDL-C and LDL-C)

**Specialist advice**

- **PCSK9i may be available for prescribing in primary care:** see local initiation pathways.

### STATIN INTOXATION

Statin intoxication is defined as the presence of clinically significant adverse effects from statin therapy that are considered by the patient or their physician to represent an unacceptable risk to the patient or that may result in adherence to therapy being compromised. For people who are intolerant of the recommended statin treatment see the NHSE AAC statin intolerance algorithm, available on the NHSE AAC page (Click here)

**Authors:** Dr Rani Khatib & Dr Dermot Neely on behalf of the AAC Clinical Subgroup. Nov 2022. Review date: Nov 2023.

NICE confirmed that its guidance is accurately represented, Nov 2022.