Sheffield Teaching Hospitals NHS
NHS Foundation Trust

NHS Sheffield
Clinical Commissioning Group

Lipid optimisation for the primary prevention of cardiovascular disease in adults: A 3 Step Approach

High risk CVD group? (Yes/No)

- **CKD** (persistent albuminuria and/or eGFR <60ml/min/1.73m^2)
- **Type 1 diabetes**
- **Age ≥85 years**

See separate guidance for people with Early Onset Type 2 Diabetes*.

No →

QRISK2/3 score ≥10%? Yes/No

NB: Please note that QRISK2/3 may underestimate CVD risk in certain groups (see **Box 1** overleaf).

No →

Recheck QRISK 2/3 score at appropriate intervals (e.g. annually).

Yes ↓

Yes ↓

Perform clinical assessment as per the following:

- **Blood pressure (NG136)**
- **BMI (CG189)**
- **Smoking status**
- **Alcohol consumption** (see cautions and contraindications)
- **Baseline blood test**

⇒**Non-fasting lipid profile**. If TC>9mmol/L or non-HDL-C>7.5mmol/L, see FH referral criteria. Also if raised TG(>10mmol/L), recheck with fasting sample, exclude common secondary causes of dyslipidaemia and seek specialist advice if still >10mmol/L. NB TG>20mmol/l requires urgent referral to specialist service. **See the managing raised triglycerides guidelines for further information.**

⇒**HbA1c, U&Es, LFTs and TSH**. If hypothyroid, correct hypothyroidism and reassess CVD risk

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Offer lifestyle advice and manage modifiable risk factors, such as– diet and weight loss (CG189), exercise, reducing alcohol intake (less than 14units/week with several alcohol free days) and smoking cessation.

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Step 1- Offer a **high intensity statin,** preferably **Atorvastatin 20mg** for the primary prevention of CVD either in addition to lifestyle modification or when lifestyle modification alone has not been sufficient to achieve goals agreed with the patient.

Consider using tools such as the NICE patient decision aid for statins and the QRISK3 risk calculator as part of the conversations for statin initiation. Also, take into consideration issues such as polypharmacy and drug interactions when discussing statin initiation with patients.

Measure **TC, non-HDL-C and HDL-C** 3 months after treatment initiation. If <40% reduction in non-HDL-C from pre-statin level then check adherence, timing of dose, diet and lifestyle measures and consider **increasing dose** of atorvastatin (do not increase above 20 mg if eGFR <30ml/min/1.73^2 - seek specialist advice from renal team). **If previously on a medium or low-intensity statin please see Box 2 overleaf for the relative reductions in non-HDL-C.**

If side effects, **revert to max tolerated dose** of high intensity statin or previous low-medium intensity statin. Switch to a cost effective dose of low-medium intensity statin if not previously on statin treatment.

Step 2- Add Ezetimibe to max tolerated statin treatment if <40% reduction in non-HDL-C. If unable to tolerate 3 different statins then consider **ezetime monotherapy** in line with NICE TA385.

Step 3- Consider **Bempedoic acid + Ezetimibe** (available as combination product) in those intolerant of statins and in whom ezetimibe monotherapy has not resulted in a >40% reduction in non-HDL-C (NICE TA694).

Efficacy Monitoring– Check Lipid profile 3 months after each dose or treatment change.

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Statin intolerance- This is defined as the presence of clinically significant adverse effects that represent an unacceptable risk to the patient or that may affect compliance with therapy. If patient reports intolerance consider the following options:

1. Stop statin & see if symptoms resolve +/- recur on restarting; if not, probably not statin related. Look for other cause.
2. Consider **rosuvastatin** (see BNF for dosage in different patient groups), which is also a high intensity statin as 2nd-line in those unable to tolerate atorvastatin 20mg. If tolerated, follow recommendations for efficacy monitoring as above.
3. Reduce dose or offer lower intensity statin e.g. simvastatin or pravastatin, if 1st and 2nd line statins are not tolerated.
4. If intolerant of 3 different statins, then consider **Ezetimibe monotherapy** in line with NICE TA385.
5. If ezetimibe monotherapy does not sufficiently lower non-HDL-C by 40% from baseline then consider adding bempedoic acid (NICE TA694), preferably as a single combination-tablet with ezetimibe.

***Early-Onset Type 2 Diabetes–** Type 2 Diabetes diagnosed before the age of 40 years. **CK–** creatine kinase, **FH–** familial hypercholesterolemia, **HDL-C–** high density lipoprotein cholesterol, **LDL-C–** low density lipoprotein cholesterol, **PAD–** peripheral artery disease, **PCSK9i-** Proprotein convertase subtilisin/kexin type 9 inhibitor, **TC**– total cholesterol, **ULN–** upper limit of normal.

Safety Monitoring- Recheck **LFTs** after initiating statin treatment or dose change at 3 and 12 months only; monitor more frequently if abnormal results. Stop if ALT is >3xULN and seek specialist advice. Routine CK testing is not required unless patient reports symptoms of unexplained muscle pain, tenderness or weakness. Stop if CK is >5xULN and seek specialist advice.

Cautions and Contraindications

Statins should be used with caution in those who are; elderly, have high alcohol intake (>50units/week), previous history of liver disease or deranged transaminases or at increased risk of muscle toxicity (e.g. those with a personal or family history of muscular disorders, previous history of muscular toxicity, renal impairment or hypothyroidism). For patients at increased risk of muscle effects baseline CK should be done and if levels are >5xULN levels should be rechecked in 7 days. Statin should not be started if CK level is still >5xULN.

Bempedoic acid is not recommended in people with moderate or severe liver impairment due to the unknown effect of prolonged exposure to ezetimibe. Discontinue if persistently high liver transaminases (>3xULN) or if hyperuricaemia accompanied with symptoms of gout appear.

Pregnancy- Statins are contraindicated in pregnancy and breastfeeding. Bempedoic acid with ezetimibe is also contraindicated in pregnancy and breastfeeding. These should be discontinued 3 months prior to conception or as soon as pregnancy is recognized.

Please refer to the current BNF or SPC for full prescribing information.

Box 1

QRISK2/3 may underestimate CV risk in those;

1. Treated for HIV.
2. With serious mental health problems.
3. On meds causing dyslipidaemia e.g. atypical antipsychotics, steroids and immunosuppressants.
4. With autoimmune disorder e.g. SLE, RA.
5. Taking antihypertensive or lipid therapy, or who have recently stopped smoking.
6. With BMI > 40 kg/m^2.
7. With raised triglycerides.

- Consider specialist referral for the assessment of CVD risk in these patients.

Box 2

Table 1 Switching between statins (adapted from NICE CG181)

It may not be possible to assess a 40% reduction in non-HDL-C in patients when switching from a low- or medium-intensity statin to a high-intensity statin. The boxes below are therefore meant to be used as a guide for healthcare professionals where pre-statin treatment cholesterol levels are not available.

	Atorvastatin 20mg			**Atorvastatin 20mg**
Fluvastatin 20mg	22%		Simvastatin 10mg	16%
Fluvastatin 40mg	16%		Simvastatin 20mg	11%
Fluvastatin 80mg	10%		Simvastatin 40mg	6%
Pravastatin 10mg	23%		Atorvastatin 10mg	6%
Pravastatin 20mg	19%		Rosuvastatin 5mg	5%
Pravastatin 40mg	14%			

Table 2

Statin grouping	
Low intensity	Pravastatin 40mg; Simvastatin 10mg; Pravastatin 20mg; Fluvastatin 20mg- 40mg;
Medium intensity	Atorvastatin 10mg; Rosuvastatin 5mg; Simvastatin 20mg- 40mg; Fluvastatin 80mg;
High intensity	Atorvastatin 20mg-80mg; Rosuvastatin 10mg– 40mg
Percentage reduction in LDL-C cholesterol- 20%–30%: low intensity. 31%–40%: medium intensity. Above 40%: high intensity. NB; Advice from the MHRA: there is an increased risk of myopathy associated with high-dose (80mg) simvastatin. Simvastatin 80mg is no longer recommended and therefore its use should be avoided. (Appendix A: NICE CG181)	

References

NICE CG181 (2014)-Cardiovascular disease: risk assessment and reduction, including lipid modification

NICE TA694 (2021)– Bempedoic acid with ezetimibe for treating primary hypercholesterolaemia or mixed dyslipidaemia

NICE TA 385 (2016)- Ezetimibe for treating primary heterozygous-familial and non-familial hypercholesterolaemia

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Approved by APG - July 2021

Review date - July 2026