Sheffield Teaching Hospitals NHS
NHS Foundation Trust

NHS Sheffield
Clinical Commissioning Group

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

Offer statin therapy to adults with CVD, this includes angina, previous MI, revascularisation, ischaemic stroke or TIA or symptomatic peripheral arterial disease. Do not delay statin treatment if a person has acute coronary syndrome. In acute ischaemic stroke commence statin at 48 hours post-stroke.

Address all modifiable risk factors (smoking, diet, obesity, alcohol intake, physical activity, blood pressure and HbA1c) at every given opportunity. Do not delay statin treatment in secondary prevention while managing modifiable risk factors. See Lipid modification for primary prevention of CVD for more details on the requirements for baseline clinical assessment as well as providing lifestyle advice and managing modifiable risk factors. **Refer to the managing raised triglycerides guidelines in people with baseline serum triglyceride levels >10mmol/l.**

Step 1

- Commence **atorvastatin 80mg** unless contraindicated (see overleaf and BNF)
- Use lower dose if potential drug interactions (see BNF), high risk of adverse effects or patient prefers.
- In CKD (eGFR <60ml/min/1.73m^2 and/or albuminuria) commence atorvastatin 20mg and up-titrate. Do not increase above 20mg if eGFR<30ml/min/1.73m^2.

In patients intolerant of atorvastatin consider **rosuvastatin** (see BNF for dosage in different patient groups). Up-titrate rosuvastatin dose at 3-monthly intervals.

In patients intolerant of atorvastatin AND rosuvastatin consider simvastatin 40mg or pravastatin 40mg.

Recheck lipid profile after 3 months and aim for a target non-HDL-C < 2.5mmol/L (approximately equivalent to LDL-C < 1.8mmol/L) (JBS3, 2014)

Step 2

If non-HDL-C > 2.5mmol/l and on max tolerated dose of statin, **ADD Ezetimibe.**
If intolerant of statins, consider **ezetimibe** monotherapy.
Recheck non-fasting lipid profile in 3 months.

Non-HDL-C>2.5 and ≤4mmol/l

Step 3

Review and optimise lifestyle measures such as diet, weight loss, reduced alcohol intake and smoking cessation.

Offer **bempedoic acid + ezetimibe** (available as a combination product) in replacement of ezetimibe monotherapy in those intolerant of statins.
Refer to the lipid clinic if patient is intolerant of statins and ezetimibe.

Non-HDL-C>4mmol/L

Step 3

Check **fasting lipids** and assess eligibility (Box 1) for **PCSK9 inhibitor** treatment (alirocumab or evolocumab) using LDL-C result and refer to lipid clinic if eligible. If raised triglycerides (>4.5mmol/L) prevent measurement of LDL, refer to the Managing Raised Triglycerides guideline

If not eligible for PCSK9i treatment or patient does not consent to treatment or PCSK9i therapy not tolerated, consider **Bempedoic Acid+Ezetimibe** (available as a combination product) with max tolerated statin or without a statin, if statin intolerant.

Monitoring
Recheck lipid profile at 3 months after initiation and after each dose change. Recheck LFTs after initiating statin treatment or dose change at 3 and 12 months only; monitor more frequently if abnormal results. LFTs should also be checked 3 months after starting bempedoic acid + ezetimibe treatment (see also cautions below).

Statins: Stop if ALT is >3x upper limit of normal (ULN) 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 >5x ULN 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 prior to conception or as soon as pregnancy is recognized. Adequate contraception should be used in those taking statins or bempedoic acid with ezetimibe.

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

Box 1 : Refer for PCSK9i treatment if LDL meets these levels

	With CVD	
	High risk[1]	Very High Risk [2]
Non-FH	LDL-C > 4.0mmol/L	LDL-C > 3.5mmol/L
Primary heterozygous-FH	LDL-C > 3.5mmol/L	

[1] History of any of the following: ACS; coronary or other arterial revascularisation procedures; CHD, ischaemic stroke; PAD. [2] Recurrent CV events or CV events in more than 1 vascular bed (that is, polyvascular disease).

Box 2– Statin Intolerance
Statin intolerance is defined as the presence of clinically significant adverse effects from statin therapy that are considered to represent an unacceptable risk to the patient or that may result in adherence to therapy being compromised.

See the NHSE AAC statin intolerance pathway for establishing statin intolerance in people at high CVD risk and for whom a high intensity statin has been recommended.

References
JBS3 (2014)- Joint British Societies' consensus recommendations for the prevention of cardiovascular disease (JBS3)
NHSE/AAC (2020)- Summary of national guidance for lipid management for primary and secondary prevention of CVD
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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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, **ULN–** upper limit of normal.