NHS South Yorkshire Integrated Care Board Doncaster Place

NHS Nottingham and Nottinghamshire Bassetlaw Place Based Partnership

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 and consider excluding secondary causes of high cholesterol when treatment options fail to reduce cholesterol to recommended levels.

Step 1

- Commence **atorvastatin 80mg daily** unless contraindicated (see overleaf and BNF)

In patients intolerant of atorvastatin consider **rosuvastatin** (see BNF for dosage in different patient groups). Up-titrate rosuvastatin dose at 4-weekly intervals.

In patients intolerant of atorvastatin AND rosuvastatin, offer maximum tolerated dose of any statin. Refer to statin intolerant pathway if unable to tolerate any statins.

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)

Non-HDL-C ≤ 2.5mmol/L

- Arrange annual review with non-fasting lipid profile.
- Consider further up-titration of statin dose if not yet at maximum tolerated dose, encouraging a "lower is better attitude to lipid optimisation.
- Continue to review and optimise lifestyle measures such as exercise, diet, weight loss, reduced alcohol intake and smoking cessation.

Non-HDL-C >2.5mmol/L

Step 2

ADD ezetimibe. Recheck lipids in 3 months.
If intolerant of statins, consideration for using **ezetimibe** monotherapy should be based on patient preference and CVD risk.

If non-HDL-C >2.5mmol/L, check adherence. **Request a fasting lipid profile** and consider the following options based on clinical criteria and shared decision making with the patient/ carer.

Routine use of injectable therapies as second-line treatment after statins is not encouraged unless extenuating circumstances or recommended by a specialist.

Step 3

- Review and optimise lifestyle measures such as diet, weight loss, reduced alcohol intake and smoking cessation.
- **Statin intolerance-** Offer **bempedoic acid + ezetimibe** (available as a combination product). Refer to the lipid clinic if patient is intolerant of statins and ezetimibe.

Step 3
Injectable therapies (secondary care) (PCSK9i)

LDL-C >4mmol/L– high risk CVD[1] OR **LDL-C >3.5mmol/L–** very high risk CVD[2]

- **Alirocumab 75mg, 150mg**
- **Evolocumab 140mg** injections, every two weeks

See Box 1 for full assessment criteria.

Step 3
Injectable therapies (primary care)

LDL-C ≥2.6mmol/L–

- **Inclisiran 284mg**, initially, again at 3 months, followed by every 6 months.

See NICE TA733 for full initiation criteria.

Safety Monitoring
Check LFTs at baseline and then at 3 and 12 months after initiating statin treatment or dose change. Monitor more frequently if abnormal results. LFTs should also be checked 3 months after starting treatment with bempedoic acid + ezetimibe (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.

Use of the other lipid lowering drugs included in this guidance is not recommended in pregnancy or breastfeeding unless recommended by a specialist, once the risks and benefits of treatment versus cardiovascular disease risk has been assessed.

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

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

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

Bempedoic acid with ezetimibe (Nustendi®) and inclisiran (Leqvio®) are black triangle (▼) and as such are subject to additional monitoring. Any suspected adverse effects to these drugs should therefore be reported under the Yellow Card scheme to the MHRA. **Please refer to the current BNF or SPC for full prescribing information.**

References

JBS3 (2014)- Joint British Societies' consensus recommendations for the prevention of cardiovascular disease (JBS3)
NHSE/AAC (2021)- 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 TA385 (2016)- Ezetimibe for treating primary heterozygous-familial and non-familial hypercholesterolaemia
NICE TA393 (2016)- Alirocumab for treating primary hypercholesterolaemia and mixed dyslipidaemia
NICE TA394 (2016)- Evolocumab for treating primary hypercholesterolaemia and mixed dyslipidaemia
NICE TA733 (2021)- Inclisiran for treating primary hypercholesterolaemia or mixed dyslipidaemia

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.

Adapted from Sheffield Joint Lipid optimisation in secondary prevention of CVD pathway.
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