Optimising Lipid Management for Secondary Prevention of Cardiovascular Disease in Barnsley

(adapted from the Accelerated Access Collaborative Summary of National Guidance for Lipid Management for Primary & Secondary Prevention of CVD Nov 21)

- Treatment with a statin should be offered to adults with established cardiovascular disease (CVD). This includes angina, previous myocardial infarction (MI), stroke or TIA, chronic kidney disease (CKD)*[See notes on dosing]* or symptomatic peripheral arterial disease.
- 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 if a person has Acute Coronary Syndrome (ACS).**
- **Patients Presenting with an acute CVD event should have the following tests done <u>within 24h of admission</u>:**

Full baseline lipid profile (total cholesterol (TC), HDL-C, non-HDL-C, triglycerides)	
U&E's and eGFR	Liver profile
Thyroid profile	HbA1c

- Creatinine kinase (CK) should be measured prior to statin treatment in patients with unexplained muscle pain

In adults with a <u>total cholesterol >7.5 mmol/L</u> ***and*** personal/family history of ***premature*** coronary heart disease (an event before 60y in an index or firstdegree relative refer to Referral pathway for adult patients with query Familial Hypercholesterolaemia (FH) and Simon Broome Diagnostic criteria for FH

Monitoring:

- Measure full lipid profile (non-fasting) 3 months after initiation or change of treatment.
- High intensity statin treatment should achieve non-HDL less than 2.5 (JBS 3 2014, QOF target) and reduction from baseline of at least 40% (NICE target. If baseline nHDL available).
  - NB. nHDL <2.5 approximately equivalent to LDL-C < 1.8mmol/L (JBS3, 2014)

If this is not achieved after 3 months:

- Discuss treatment adherence, timing of dose, diet and lifestyle measures
- If recommended statin treatment is contraindicated or not tolerated – follow AAC Statin Intolerance Algorithm

Barnsley Hospital NHS Foundation Trust

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NHS South Yorkshire Integrated Care Board

STEP 1

Atorvastatin 80mg ON GREEN

Reassess with non-fasting lipid profile after 3m

↓

STEP 2

ADD Ezetimibe 10mg OD GREEN

Reassess with non-fasting lipid profile after 3m

Or, (if statin intolerance confirmed):

Ezetimibe 10mg OD Monotherapy

Reassess with non-fasting lipid profile after 2m

↓ ↓ ↓

FASTING LIPID PROFILE and CONSIDER ADDITIONAL THERAPIES

Advice & Guidance or referral to Barnsley lipid clinic via ERS for primary care.

DO NOT OFFER a fibrate, nicotinic acid, bile acid binder or omega-3 fatty acids alone or in combination with statin, for the prevention of CVD (See NICE CG181 for exceptions).

Assess eligibility based on clinical criteria and shared decision making with the patient/carer.

STEP 3

If statin intolerance confirmed:
Ezetimibe 10mg and Bempedoic Acid 180mg
AMB 1 **(Amber-G)**

or

Inclisiran 284mg AMBER
Injections initially, again at 3 months, followed by every 6 months.

or

PCSK9i RED
- Alirocumab 75mg, 150mg
- Evolocumab 140mg

Injections every 2 weeks

Where patients still not to target, the addition of Bempedoic Acid to statin and/or ezetimibe to be considered (with specialist advice/referral):

- Where statin intolerance PLUS ezetimibe intolerance PLUS do not want injectables
- Refer to the lipid clinic if intolerant of statins and ezetimibe.

Do not delay high intensity/dose statin treatment in secondary prevention while managing modifiable risk factors:

- Use a lower dose of atorvastatin if there is a potential drug interaction, high risk of experiencing adverse events or patient preference.

Dosing in Chronic Kidney Disease (CKD)		
eGFR	**Initiation**	**Up-titration**
>30 to <60ml/min/1.73m^2	Atorvastatin 20mg ON	Increase dose and monitor for adverse effects
<30ml/min/1.73m^2	Atorvastatin 20mg ON	Agree use of higher doses with renal specialist before increasing

- If started on less than 80mg atorvastatin and the person is judged to be at higher risk (based on comorbidities, risk score and clinical judgement) consider increasing to 80mg atorvastatin
- 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** consider simvastatin 40mg or pravastatin 40mg, daily.
- Recheck lipid profile after 3 months and aim for non-HDL less than 2.5 (JBS 3 2014, QOF target) and reduction from baseline of at least 40% (NICE target. If baseline nHDL available).

Eligibility criteria for Injectable therapies

Inclisiran (TA733) AMBER

- Fasting LDL-C > 2.6mmol/L despite maximum tolerated lipid lowering therapy (TA 733)

PCSK9i (TA393, TA394) RED

- Non-FH or mixed dyslipidaemia:
  - Fasting LDL-C > 4.0mmol/L in high-risk patients (history of ACS, coronary or other arterial revascularization procedures, CHD, ischaemic stroke, PVD); or
  - Fasting LDL-C > 3.5mmol/L in very high-risk patients (recurrent CV events or CV events in more than one vascular bed).
- Familial Hypercholesterolaemia (*i.e. DNA confirmed genetic mutation*):
  - primary prevention if fasting LDL-C > 5.0mmol/L;
  - secondary prevention if fasting LDL-C > 3.5mmol/L.

NOTE: Inclisiran and PCSK9i should not be prescribed concurrently

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(adapted from the Accelerated Access Collaborative Summary of National Guidance for Lipid Management for Primary & Secondary Prevention of CVD Nov 21)

Initial considerations:

- Consider secondary causes of hyperlipidaemia and manage as needed.
- Identify and exclude people with contraindications/drug interactions
- Identify and address all modifiable risk factors (i.e. smoking, diet, obesity, alcohol intake, blood pressure, physical activity and HbA1c).
- If non-fasting triglycerides are > 4.5mmol/L, repeat with a fasting TG measurement.
- If TC > 7.5mmol/L +/- LDL-C > 4.9mmol/L +/- non-HDL-C > 5.9mmol/L +/- personal or family history of confirmed CHD (<60 years) with no secondary causes **suspect FH**.

Extent of Lipid Lowering with available therapies

Approximate reduction in LDL-C*					
Statin dose mg/day	5	10	20	**40**	**80**
Fluvastatin			21%	27%	33%
Pravastatin		20%	24%	29%	
Simvastatin		27%	32%	37%	42%
Atorvastatin		37%	43%	49%	55%
Rosuvastatin	38%	43%	48%	53%	
Atorvastatin + Ezetimibe 10mg		52%	54%	57%	61%

Low intensity statins will produce an LDL-C reduction of 20-30%

Medium intensity statins will produce an LDL-C reduction of 31-40%

High intensity statins will produce an LDL-C reduction above 40%

Simvastatin 80mg is not recommended due to risk of muscle toxicity (MHRA 2014)

*NICE CG181 groups statins into 3 different intensity categories according to percentage reduction in LDL-C.

- **Rosuvastatin** GREEN (second choice statin on the Barnsley Formulary) may be used as an alternative to atorvastatin if compatible with other drug therapy. Some people may need a lower starting dose (see BNF).
- Low/medium intensity statins (simvastatin or pravastatin) should only be used if intolerance or druginteractions. Avoid the use of fluvastatin where appropriate due to its high cost in relation to alternative statins (see costs below). Also see MHRA simvastatin drug interaction advice
- **Ezetimibe** GREEN when combined with any statin is likely to give greater reduction in non-HDL-C (or LDL-C) than doubling the dose of the statin.
- **Bempedoic acid** AMB 1 when combined with ezetimibe (NICE TA694) produces an additional LDL-C reduction of approximately 28% (range 22-33%) but no clinical outcome evidence is currently available (it is preferable to prescribe as a single-combination tablet with ezetimibe, see costs below).

Costs of Lipid Lowering therapies (Drug Tariff February 2022)

Cost / 28 days (£)					
Statin dose mg/day*	5	10	20	**40**	**80**
Fluvastatin capsules (20 & 40mg) MR tablets (80mg)			2.85	3.20	19.20
Pravastatin tablets		0.95	1.11	1.34	
Simvastatin tablets		0.80	0.83	0.93	
Atorvastatin tablets		0.72	0.97	1.03	1.42
Rosuvastatin tablets	0.96	1.09	1.33	1.76	
Atorvastatin tablets + Ezetimibe 10mg tablets		2.39	2.64	2.70	3.09
Bempedoic acid 180mg / Ezetimibe 10mg tablets **combination product** (Nustendi®)	55.44				
Bempedoic acid 180mg (Nilemdo®) **plus** Ezetimibe 10mg tablets **(separate products)**	57.11 (Bempedoic acid: £55.44, Ezetimibe: £1.67)				

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.

*Refer to colour key and table above for statin intensity.

Chronic Kidney Disease

Offer atorvastatin 20mg for the primary prevention of CVD to people with CKD (eGFR less than 60 mL/min/1.73m^2 and/or albuminuria)

Increase the dose if non-HDL greater than 2.5 (JBS 3 2014, QOF target) and reduction from baseline is less than 40% (NICE target. If baseline nHDL available) is not achieved and eGFR is 30 mL/min/1.73m^2 or more.

Agree the use of higher doses (greater than atorvastatin 20mg) with a renal specialist if eGFR is less than 30 mL/ min/1.73m^2

Monitoring

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 ***(standard LFT monitoring in Barnsley only includes ALT and ALP enzymes, unless additional tests are requested).***

Measure CK if unexplained muscle pain before starting a statin. Refer to NHS AAC statin intolerance algorithm (click here).

CK should not be measured routinely especially if a patient is asymptomatic

	Primary Prevention	
	Lipid Profile	ALT or AST
Baseline	✓	✓
3 months	✓	✓
6-9months	if non-HDL greater than 2.5 (JBS 3 2014, QOF target) and reduction from baseline is less than 40% (NICE target. If baseline nHDL available), up titration required. Repeat full lipid profile and ALT or AST within 3 months of each up-titration of statin dose or addition of ezetimibe as required	
12 months	✓	✓
Yearly	✓**	

Provide annual medication reviews for people taking statins to discuss effectiveness of therapy, medicines adherence, lifestyle modification and address CVD risk factors.

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

Repeat full lipid profile is non-fasting.

Measure liver transaminase within 3 months of starting treatment and then within 3 months of every additional up titration and then again at 12 months, but not again unless clinically indicated (e.g. abnormal results).

If ALT or AST are greater than 3 times the upper limit of normal, then do not initiate a statin or discontinue statin therapy already prescribed and repeat the LFTs in a month.

If ALT or AST are elevated but are less than 3 times the upper limit of normal, then:

- Continue the statin and repeat in a month.
- If they remain elevated but are less than 3 times the upper limit of normal, then continue statin and repeat again in 6 months.

Cautions and contraindications

Statins should be used with caution in those at increased risk of muscle toxicity (e.g., renal impairment, hypothyroidism, personal or familial history of hereditary muscular disorders, previous history of muscular toxicity with a statin or fibrate, previous history of liver disease and/or where substantial quantities of alcohol are consumed, elderly (aged over 70 years), interactions with other medicines where plasma levels may be increased.[1]

Statins are contraindicated in patients with active liver disease or unexplained persistent elevations of serum transaminases exceeding 3 times the upper limit of normal.[1] Statins are contraindicated during pregnancy, while breast-feeding and in women of child-bearing potential not using appropriate contraceptive measures.[1]

Bempedoic acid with ezetimibe is contraindicated in pregnancy and breast-feeding. [2]

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

Triglycerides

Triglyceride concentration	Action
Greater than 20mmol/L	Refer to lipid clinic for urgent specialist review if not a result of excess alcohol or poor glycaemic control. At risk of acute pancreatitis.
10 - 20mmol/L	Repeat the TG measurement with a fasting test (after an interval of 5 days, but within 2 weeks) and review for potential secondary causes of hyperlipidaemia. Seek specialist advice if the TG concentration remains > 10mmol/litre. At risk of acute pancreatitis
4.5 - 9.9mmol/L	If non-fasting triglycerides are greater than 4.5mmol/L, repeat with a fasting TG measurement Be aware that the CVD risk may be underestimated by risk assessment tools, optimise the management of other CVD risk factors present and seek specialist advice if non- HDL-C concentration is > 7.5 mmol/litre.

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.

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)

Abbreviations and Definitions

ALT: alanine aminotransferase
AST: aspartate aminotransferase
CHD: coronary heart disease
CKD: chronic kidney disease
CVD: cardiovascular disease
FH: familial hypercholesterolaemia
LDL-C: low density lipoprotein cholesterol
non-HDL-C: non-high density lipoprotein cholesterol
SLE: systemic lupus erythematosus
SPC: summary of product characteristics
TC: total cholesterol

Non-HDL-C = TC minus HDL-C

LDL-C = non-HDL-C minus (Fasting triglycerides[a]/2.2)

[a] valid only when fasting triglycerides are less than 4.5 mmol/L

Acknowledgements

This guidance has been adapted from the NHS Accelerated Access Collaborative Summary of National Guidance for Lipid Management for Primary and Secondary Prevention of CVD. Summary-of-national-guidance-for-lipid-management-for-primary-and-secondary-prevention-of-cardiovascular-disea.pdf (england.nhs.uk)

Development Process

This guideline was endorsed by the Barnsley Area Prescribing Committee on 12th July 2023.

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Guidance

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