NHS South West Yorkshire Partnership NHS Foundation Trust

NHS Barnsley Hospital NHS Foundation Trust

NHS South Yorkshire Integrated Care Board

Barnsley Lipid Management for Primary Prevention of Cardiovascular Disease in Adults

(A separate Barnsley Lipid Management Pathway for Secondary Prevention of Cardiovascular Disease in Adults is in development).

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 3 (including LFTs).** ● Measure BMI (NICE CG189) ● Identify and exclude people with contraindications/drug interactions. ● If non-fasting triglyceride above 4.5mmol/L see page 4. ● **If severe hyperlipidaemia** (TC>7.5mmol/L and/or LDL-C>4.9mmol/L and/or non-HDL-C>5.9mmol/L) **refer to separate Barnsley pathway.**

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 (use the current version QRISK3 where available, see page 3, *'Primary Prevention Risk Assessment'*)

- Age ≤84 & QRISK ≥10% over next 10 years
- Type 2 diabetes & QRISK ≥10% over next 10 years
- Type 1 diabetes, if they have one or more of the following:
  - Over 40 years
  - Had diabetes for >10 years
  - Have established nephropathy
  - Have other CVD risk factors
- CKD eGFR < 60 mL/min/1.73m^2 and/or albuminuria
- Age ≥85 years if appropriate consider comorbidities, frailty & life expectancy

Identify and address all modifiable risk factors - smoking, diet, obesity (NICE CG189), alcohol intake (less than 14units/week with several alcohol free days), physical activity, blood pressure (NG136
(Barnsley Hypertension guidelines are currently being updated)) and HbA1c.

Consider additional risk factors, if present, together with QRISK score (treated for HIV, severe mental illness, taking medicines that cause dyslipidaemia, systemic inflammatory disorder (e.g. SLE), impaired fasting glycaemia, recent change in risk factors)
(see page 3, *'Primary Prevention Risk Assessment'*)

PRIMARY PREVENTION

If lifestyle modification is ineffective or inappropriate offer statin treatment.

Atorvastatin 20mg daily

- Measure full lipid profile again after 3 months (non-fasting) and LFTs (ALT or AST). See page 3.
- **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 3 *'Additional Risk Factors'*) consider increasing the dose every 2-3 months up to a **maximum dose of atorvastatin 80mg daily.**
  - For how to increase in people with CKD see *'Special Patient Populations'* (page 3).

- 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' and 'costs of lipid lowering therapies'*)
- If maximum tolerated dose of statin does not achieve non-HDL-C reduction > 40% of baseline value after 3 months consider adding Ezetimibe 10mg daily (NICE TA385)
- **If statin treatment is contraindicated or not tolerated;**
  - See AAC Statin Intolerance Algorithm for advice regarding adverse effects (click here)
  - **Ezetimibe 10mg monotherapy** may be considered. Assess response after 3 months.
  - **Ezetimibe 10mg/bempedoic acid 180 mg combination** (available as a combination product which is more cost effective than the separate products, see costs on page 2) may be considered when ezetimibe alone does not control non-HDL-C well enough (NICE TA694)
    Bempedoic acid has an Amber-G classification in Barnsley.

Check lipid profile and LFTs (ALT or AST) 3 months after each dose or treatment change. *See page 3.*

If non-HDL-C reduction remains < 40% of baseline despite maximal tolerated lipid lowering therapy (including people with intolerances and contraindications) consider contacting medicine.information1@nhs.net (for attention of Lead Pharmacist, Medicines Information and Cardiology, BHNFT) for advice and guidance.

Management

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 not achieved, offer **high intensity statins**. Discuss with people who are stable 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.

Ezetimibe, can be added when patients' non-HDL-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 non-HDL-C well enough. 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 (Check NICE CG181 for exceptions).

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** (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 it's high cost in relation to alternative statins (see costs below). Also see MHRA simvastatin drug interaction advice
- **Ezetimibe** 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** **(Amber-G classification)** 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)

Statins

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	1.32
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

Refer to colour key and table above for statin intensity.

Ezetimibe 10mg / Bempedoic acid 180mg combination

Cost / 28 days (£)	
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)

Primary Prevention Risk Assessment

QRISK3 is the current version of the QRISK calculator. www.qrisk.org/three. Recheck QRISK score at appropriate intervals (e.g. annually)

- **Do not** use this risk assessment tool for people with established CVD or those who are at high risk of developing CVD because of FH or other inherited disorders of lipid metabolism.
- **Do not** use a risk assessment tool to assess CVD risk in people with type 1 diabetes, or eGFR less than 60mL/min/1.73m^2 and/or albuminuria.
- Consider people aged ≥ 85 at increased risk of CVD because of age alone particularly people who smoke or have raised BP.

Additional Risk Factors

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

- severe obesity (BMI>40kg/m^2) 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 4.5-9.9mmol/L)
- recent risk factor changes e.g. quit smoking, BP or lipid treatment

Consider socio-economic status as an 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 prevention of CVD to people with CKD (eGFR less than 60 mL/min/1.73m^2 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/1.73m^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 <40% non-HDL-C reduction, 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.*

Monitoring

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 (Refer to the current BNF or SPC for full prescribing information)

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]

Triglycerides

Triglyceride concentration	Action
Greater than 20mmol/L	**Requires urgent review** (contact medicine.information1@nhs.net (for attention of Lead Pharmacist, Medicines Information and Cardiology, BHNFT) for advice and guidance) 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. Contact medicine.information1@nhs.net (for attention of Lead Pharmacist, Medicines Information and Cardiology, BHNFT) for advice and guidance 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 contact medicine.information1@nhs.net (for attention of Lead Pharmacist, Medicines Information and Cardiology, BHNFT) for advice and guidance 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 13th July 2022.

References

1. EMC. Atorvastatin 20mg tablets SPC. Available at: Atorvastatin 20 mg film-coated tablets - Summary of Product Characteristics (SmPC) - (emc) (medicines.org.uk) Accessed <06.04.22>
2. EMC. Nustendi® 180mg/10mg tablets. Available at: Nustendi 180mg/10mg film-coated tablets - Summary of Product Characteristics (SmPC) - (emc) (medicines.org.uk) Accessed <06.04.22>