

Barnsley Lipid Management for Secondary Prevention of Cardiovascular Disease in Adults (adapted from the

Accelerated Access Collaborative Summary of National Guidance for Lipid Management for Primary & Secondary Prevention of CVD Sep 24)



(A separate Pathway for Primary Prevention of Cardiovascular Disease in Adults is available here).

INITIAL CONSIDERATIONS:

- Offer statin therapy to adults with CVD, this includes CHD, angina, Acute Coronary Syndrome (MI or unstable angina), revascularisation, stroke or TIA, or symptomatic peripheral arterial disease. Do not delay statin treatment if a person has acute coronary syndrome. Take a lipid sample on admission (within 24 hours).
- 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 within 24h of admission:

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

Familial Hypercholesterolaemia

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 <u>Referral pathway for adult patients with query Familial Hypercholesterolaemia (FH)</u> and <u>Simon Broome Diagnostic criteria for FH</u>

Monitoring:

- Measure full lipid profile (non-fasting) 2-3 months after initiation or change of treatment.
- High intensity statin treatment should achieve an LDL-C of < 2.0mmol/L, or non-HDL-C of < 2.6mmol/L (NICE target, QOF target).

If this is **not** achieved after 2 to 3 months:

- Discuss treatment adherence, timing of dose, diet and lifestyle measures
- If recommended statin treatment is contraindicated or not tolerated follow <u>AAC Statin Intolerance Algorithm</u>
- If started on less than atorvastatin 80mg and the person is judged to be at higher risk (based on co-morbidities or clinical judgment), consider increasing to 80mg atorvastatin or maximally tolerated dose.
- Consider escalation of lipid-lowering therapy



Barnsley Hospital

NHS Foundation Trust

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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*					Low intensity statins will produce an LDL-C reduction of 20-30%			
Statin dose mg/day	5	10	20	40	80	Medium intensity statins will		
Fluvastatin			21%	27%	33%	produce an LDL-C reduction of 31-		
Pravastatin		20%	24%	29%		40% High intensity statins will produce		
Simvastatin		27%	32%	37%	42%	an LDL-C reduction above 40%		
Atorvastatin		37%	43%	49%	55%	Simvastatin 80mg is not		
Rosuvastatin	38%	43%	48%	53%		recommended due to risk of muscle toxicity (MHRA 2014)		
Atorvastatin + Ezetimibe 10mg		52%	54%	57%	61%	*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 <u>BNF</u>). Note that rosuvastatin capsules have a significantly higher cost than the tablets, have a grey classification and should only be used in patients with swallowing difficulties or NG tubes when the capsules may be opened in line with the SPC.

• 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 <u>MHRA simvastatin drug</u> 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** AMB1 when combined with ezetimibe (<u>NICE TA694</u>) produces an additional LDL-C reduction of approximately 28% (range 22-33%). It is preferable to prescribe as a single-combination tablet with ezetimibe, see costs below.

Costs of Lipid Lowering therapies (Drug Tariff April 2025)

Cost / 28 days (£)					
Statin dose mg/day*	5	10	20	40	80
Fluvastatin capsules (20 & 40mg)			4.18	4.89	19.20
MR tablets (80mg)					
Pravastatin tablets		1.37	1.39	1.69	
Simvastatin tablets		0.62	0.84	0.84	1.76
Atorvastatin tablets		0.61	0.67	0.77	1.23
Rosuvastatin tablets	0.76	0.88	1.15	1.55	
Atorvastatin tablets + Ezetimibe 10mg tablets		3.14	3.20	3.30	3.76
Bempedoic acid 180mg / Ezetimibe 10mg tablets combination product (Nustendi®)	55.44				
Bempedoic acid 180mg (Nilemdo®)	57.97				
plus Ezetimibe 10mg tablets (separate products)	(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.





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Chronic Kidney Disease

Offer atorvastatin 20mg for the primary prevention of CVD to people with CKD (eGFR less than 60 mL/min/1.73m² and/or albuminuria)

Increase the dose if target not met, i.e. LDL-C of \leq 2.0 mmol/L, or non-HDL-C of \leq 2.6 mmol/L (NICE, QOF target) is not achieved and eGFR is 30 mL/min/1.73m² or more.

Agree the use of higher doses (greater than atorvastatin 20mg) with a renal specialist if eGFR is less than 30 mL/ min/1.73m²

Pregnancy and Lactation

Statins should be stopped 3 months before attempting to conceive and not be restarted until breastfeeding is finished. Stop statins if pregnancy is a possibility.

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 (<u>click</u> <u>here</u>).

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

	Secondary Prevention				
	Lipid Profile	ALT or AST			
Baseline	\checkmark	\checkmark			
3 months	\checkmark	\checkmark			
6-9months	If targets are not met (. LDL-C of ≤ 2.0 mmol/L, or non-HDL-C of ≤ 2.6 mmol/L) and up-titration is agreed, repeat full lipid profile and ALT or AST within 2-3 months of each up-titration of statin dose or addition of ezetimibe as required				
12 months	\checkmark	\checkmark			
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 nonadherence.

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.

Titration thresholds / Targets

Secondary Prevention			
NICE titration threshold / QOF	JBS3**		
Aim for an LDL-C of \leq 2.0 mmol/L, or non-HDL-C of \leq 2.6 mmol/L at least*	non-HDL-C <2.5mmol/L (LDL-C < 1.8mmol/L)		

*Consider ezetimibe to reduce CVD risk further, even if the NICE lipid target for secondary prevention of CVD is met.



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**LDL-C and non-HDL-C levels should be reduced as much as possible in people with CVD. Consider a personalised target, as clinically indicated, e.g. JBS3 consensus recommendation

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.

Icosapent Ethyl (TA805) RED

Icosapent ethyl is recommended as an option for reducing risk of cardiovascular events in adults.

- Check fasting triglycerides levels.
- Manage secondary causes of hypertriglyceridaemia.
- Consider icosapent ethyl (TA805) if patient has established cardiovascular disease (secondary prevention) and on statins and fasting TG ≥ 1.7mmol/L and LDL-C* between 1.04‡ and ≤2.6mmol/L
- See table above and refer as appropriate.

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 (<u>Click here</u>)





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Referral to Barnsley lipid optimisation clinic

Conditions treated

- Hypertriglyceridaemia (triglycerides > 10mmol/L and not due to uncontrolled DM or alcohol excess)
- Mixed hyperlipidaemia (not due to alcohol excess or uncontrolled diabetes)
- Total cholesterol >9 mmol/l or non-HDL >7.5 (in the absence of a known secondary cause of raised lipids e.g. uncontrolled hypothyroidism, cholestatic liver disease, nephrotic syndrome, uncontrolled diabetes, alcohol excess) unless they fulfil the criteria for possible FH (these patients are seen under FHICC Service ID: 7946454 see Lipid Problems Referral Pathway (sheffieldccqportal.co.uk);
- Secondary prevention patients who are suitable for injectable therapies
- Secondary prevention patients who are intolerant of statins and Ezetimibe;
- Patients experiencing problems with lipid-lowering medication

Exclusions

- Genetic hyperlipidaemias e.g. Familial Chylomicronaemia Syndrome (FCS), Type III Hyperlipidaemia, Sitosterolaemia, Familial HDL deficiency, Polygenic Hypercholesterolaemia.
- Dyslipidaemia secondary to uncontrolled hypothyroidism, nephrotic syndrome, uncontrolled diabetes, alcohol excess. In most cases these should resolve on treatment/resolution of the cause
- Age <18
- Missing results/information on the referral form

Referrals are made via Choose and Book

Suggested investigations prior to referral

- Fasting lipid profile, fasting glucose, extended LFTs, U&E, TSH, CK, HbA1c
- BP
- Height and weight

Administrative requirements to be included in the referral:

- Patients full demographics
- Transport requirements
- Personal and family history of CVD
- Fasting lipid profile results, extended LFTs, U&E, TSH, CK & HbA1c
- Full list of medications and allergies
- Previous lipid lowering medications and when problems encountered (where appropriate)

Abbreviations and Definitions

ALT: alanine aminotransferase
AST: aspartate aminotransferase
CHD: coronary heart disease
CKD: chronic kidney disease
CVD: cardiovascular diseaseLDL-C: low density lipoprotein cholesterol
non-HDL-C: non-high density lipoprotein cholesterol
SLE: systemic lupus erythematosus
SPC: summary of product characteristics
TC: total cholesterolFH: familial hypercholesterolaemiaTC: 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. <u>NHS Accelerated Access Collaborative » Summary of national guidance for lipid management</u>





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Development Process

This guideline was endorsed by the Barnsley Area Prescribing Committee on 11th June 2025. Due for review June 2028.

References

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

Guidance

<u>NHS Accelerated Access Collaborative</u> - Summary of national guidance for lipid management for Primary and Secondary Prevention of CVD. Document first published: 9 April 2020 Page updated: 19 September 2024

<u>CG181</u> - Cardiovascular disease: risk assessment and reduction, including lipid modification. Clinical guideline [CG181] Published: 18 July 2014 Last updated: 10 February 2023

TA385 - Ezetimibe for treating primary heterozygous-familial and non-familial hypercholesterolaemia. Technology appraisal guidance [TA385] Published: 24 February 2016

<u>TA694</u> - Bempedoic acid with ezetimibe for treating primary hypercholesterolaemia or mixed dyslipidaemia. Technology appraisal guidance [TA694] Published: 28 April 2021

<u>TA733</u> - Inclisiran for treating primary hypercholesterolaemia or mixed dyslipidaemia. Technology appraisal guidance [TA733] Published: 06 October 2021

<u>TA393</u> - Alirocumab for treating primary hypercholesterolaemia and mixed dyslipidaemia. Technology appraisal guidance [TA393] Published: 22 June 2016

<u>TA394</u> - Evolocumab for treating primary hypercholesterolaemia and mixed dyslipidaemia. Technology appraisal guidance [TA394] Published: 22 June 2016

<u>TA805</u> – Icosapent ethyl with statin therapy for reducing the risk of cardiovascular events in people with raised triglycerides. Technology appraisal guidance [TA805] Published: 13 July 2022