Shropshire, Telford and Wrekin (STW) Lipid Management for Primary and Secondary Prevention of CVD (Summary of Guidance) V2.0

Approved by STW Area Prescribing Committee on 13th April 2022. Review March 2024

Adapted from the Accelerated Access Collaborative (AAC) National Lipid Pathway December 2021 https://www.england.nhs.uk/aac/wp-content/uploads/sites/50/2020/04/Summary-of-national-guidance-for-lipid-management-for-primary-and-secondary-prevention-of-cardiovascular-disea.pdf

NHS Shropshire, Telford and Wrekin Clinical Commissioning Group

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 pg 2. Measure BMI. Identify and exclude people with contraindications/drug interactions. If non-fasting triglyceride > 4.5mmol/L see pg 2.

PRIMARY PREVENTION

Statin therapy should be considered for adults who do not have established CVD but fall into the categories outlined below. Use QRISK risk assessment tool where appropriate (see pg 2)

- Age ≤84 & QRISK ≥10% over next 10 yrs
- Type 2 diabetes & QRISK ≥10% over next 10yrs
- Type 1 diabetes, if they have one or more of the following:
  - -Over 40 years
  - -Had diabetes for >10 yrs
  - -Have established nephropathy
  - -Have other CVD risk factors
- CKD eGFR < 60 mL/min/1.73m2 and/or albuminuria
- Age ≥85 years if appropriate consider comorbidities, frailty & life expectancy

Identify and address all modifiable risk factors - smoking, diet, obesity, alcohol intake, physical activity, blood pressure 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)

PRIMARY PREVENTION

If lifestyle modification is ineffective or inappropriate offer statin treatment.

Atorvastatin 20mg daily

· Measure full lipid profile again within 1-3 months (non-fasting).

· High intensity statin treatment should achieve reduction of non-HDL-C > 40% from baseline. If not achieved within 3 months:

- discuss treatment adherence, timing of dose, diet and lifestyle
- If at higher risk (based on comorbidities, risk score or clinical judgement – see pg 2 *'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'* (pg 2)

· If patients on a high-intensity statin have side effects, offer a lower dose or an alternative statin (see pg 2 *'Extent of lipid lowering with available therapies'*)

· If maximum tolerated dose of statin does not achieve non-HDL-C reduction > 40% of baseline value within 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
- Ezetimibe 10mg monotherapy may be considered. Assess response within 3 months.
- Ezetimibe 10mg/bempedoic acid 180 mg combination may be considered when ezetimibe alone does not control non-HDL-C/LDL-C well enough (NICE TA694).

If non-HDL-C reduction remains < 40% of baseline despite maximal tolerated lipid lowering therapy (including people with intolerances and contraindications) consider referral to specialist lipid management clinic

SEVERE HYPERLIPIDAEMIA

If TC>7.5mmol/L and/or LDL-C >4.9mmol/L and/or non-HDL-C >5.9mmol/L, a personal and/or family history of confirmed CHD (<60 years) and with no secondary causes: suspect familial hypercholesterolaemia (possible heterozygous FH) Do not use QRISK risk assessment tool

DIAGNOSIS AND REFERRAL

Take fasting blood for repeat lipid profile to measure LDL-C. Use the **Simon Broome** or **Dutch Lipid Clinic Network (DLCN)** criteria to make a **clinical diagnosis of FH**. Refer to Lipid Clinic for further assessment if **clinical diagnosis of FH** or if TC>9.0mmol/L and/or LDL-C >6.5mmol/L and/or non-HDL-C >7.5mmol/L or Fasting triglycerides > 10mmol/L (regardless of family history)-pg2

TREATMENT TARGETS IN FH

If clinical diagnosis of FH and/or other risk factors present follow the recommended treatment management pathway for primary or secondary prevention as for non-FH, **BUT**

Aim to achieve at least a 50% reduction of LDL-C (or non-fasting non-HDL-C) from baseline. **Consider specialist referral for further treatment and/or consideration of PCSK9i therapy IF**

-they are assessed to be at very high risk of a coronary event**

-OR therapy is not tolerated

-OR LDL-C remains >5mmol/L (primary prevention)

-OR LDL-C remains >3.5mmol/L (secondary prevention) despite maximal tolerated statin and ezetimibe therapy.

**defined as any of the following:

· Established coronary heart disease

· Two or more other CVD risk factors

SECONDARY PREVENTION

Offer statin therapy to adults with CVD, this includes angina, previous MI, 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)

Identify and address all modifiable risk factors - smoking, diet, obesity, alcohol intake, physical activity, blood pressure and HbA1c

· Measure full lipid profile again within 1-3 months (non-fasting).

· High intensity statin treatment should achieve reduction of non-HDL-C > 40% from baseline. If not achieved within 3 months:

- discuss treatment adherence, timing of dose, diet and lifestyle measures
- If started on less than atorvastatin 80mg and the person is judged to be at higher risk (based on comorbidities, risk score or clinical judgement – pg2 *'Additional Risk Factors'*), consider increasing to 80mg atorvastatin. For how to increase in people with CKD see pg2

· If non-HDL-C baseline value is not available*, consider target non-HDL-C < 2.5mmol/L (approximately equivalent to LDL-C < 1.8mmol/L) as recommended by Joint British Societies (JBS3). **this scenario is not covered by NICE CG181*

· If patients on a high-intensity statin have side effects, offer a lower dose or an alternative statin (see pg 2 *'Extent of lipid lowering with available therapies'*)

If maximum tolerated dose of statin does not control non-HDL-C/LDL-C well enough within 3 months confirm statin adherence, then consider the following options based on shared decision making (see pg2 for information to support this) with the patient

If recommended statin treatment is contraindicated or not tolerated – follow AAC Statin Intolerance Algorithm for advice regarding adverse effects

If statin intolerance is confirmed, consider:

- **Ezetimibe 10mg** monotherapy. Assess response within 1-3 months (TA385)
- **Ezetimibe 10mg/bempedoic acid 180 mg** combination when ezetimibe alone does not control non-HDL-C sufficiently. (NICE TA694)

If non HDL-C remains > 2.5mmol/L despite other lipid lowering therapies, consider Injectable therapies-arrange a fasting blood test and assess eligibility criteria (TA393/394, TA733)

Ezetimibe 10mg daily (NICE TA385). Reassess within three months. If non-HDL-C remains > 2.5mmol/L; consider **injectable therapies** arrange a fasting blood test and assess eligibility

Injectable therapies*

Inclisiran – ***suitable for prescribing in primary care***. If fasting LDL-C ≥ 2.6mmol/L despite maximum tolerated lipid lowering therapy (TA733) **OR**

PCSK9i – ***secondary care prescribing only***. See overleaf for LDL-C thresholds. (TA393/4)

***Inclisiran and PCSK9i should not be prescribed concurrently**

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.

When patients cholesterol levels are not lowered enough with maximum tolerated dose of statins, Ezetimibe should be recommended, and thereafter consider injectable therapies with inclisiran, alirocumab or evolocumab if further LDL-C reduction is required. Bempedoic acid with ezetimibe is an option when statins are contraindicated or not tolerated, and when ezetimibe alone does not control LDL-C well enough. **NB: Ensure patient compliance with oral therapy checked prior to escalation of therapy.** 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).

PRIMARY PREVENTION RISK ASSESSMENT

QRISK3 is the current version of the QRISK calculator. www.qrisk.org/three

- 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 60 mL/min/1.73 m2 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/m2) 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 or secondary prevention of CVD to people with CKD (eGFR less than 60 mL/min/1.73m2 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/1.73m2 or more.

Agree the use of higher doses with a renal specialist if eGFR is less than 30 mL/min/1.73m2

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.

References:

JBS3. 2014. www.jbs3risk.com/pages/6.htm

Kirsten *et al*. 2005. Hospital Pharmacy 40(8):687-692

Navarese *et al*. 2015. Annals of internal medicine 163(1):40-51

Soon Jun Hong *et al*. 2018. Clinical therapeutics 40(2): 226-241.e4

NICE 2016. TA385 www.nice.org.uk/guidance/ta385

NICE 2016. TA393 www.nice.org.uk/guidance/TA393

NICE 2016. TA394 www.nice.org.uk/guidance/TA394

NICE 2014. CG181 www.nice.org.uk/guidance/CG181

NICE 2008. CG71 www.nice.org.uk/guidance/cg71

NICE 2021. TA694 www.nice.org.uk/guidance/TA694

NICE 2021. TA733 www.nice.org.uk/guidance/TA733

ABBREVIATIONS

ALT: alanine aminotransferase
LDL-C: low density lipoprotein cholesterol
non-HDL-C: non-high density lipoprotein cholesterol
CHD: coronary heart disease
PCSK9i: proprotein convertase subtilisin kexin 9
CKD: chronic kidney disease monoclonal antibody inhibitor
CVD: cardiovascular disease
SLE: systemic lupus erythematosus
FH: familial hypercholesterolaemia
SPC: summary of product characteristics **TC**: total cholesterol

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

- **Rosuvastatin** 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 should only be used if intolerance or drug interactions.
- **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.
- **PCSK9i** (NICE TA393, TA394) alone or in combination with statins or ezetimibe produce an additional LDL-C reduction of approximately 50% (range 25-70%).
- **Bempedoic acid** when combined with ezetimibe (TA694) produces an additional LDL-C reduction of approximately 28% (range 22-33%) but no clinical outcome evidence is currently available.
- **Inclisiran** (TA733) alone or in combination with statins or ezetimibe produces an additional LDL-C reduction of approximately 50% (range 48-52%) but no clinical outcome evidence is currently available.

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) before starting a statin.

Measure CK if unexplained muscle pain before starting a statin.

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

Ongoing monitoring

Repeat full lipid profile is non-fasting.

Measure ALT within 1-3 months of starting treatment and then within 1-3 months of every additional up titration and then again at 12 months once prescribed a stable dose, but not again unless clinically indicated.

Summary table of monitoring requirements

	Primary Prevention		Secondary prevention	
	Lipid Profile	ALT	Lipid Profile	ALT
Baseline	√	√	√	√
1-3 months	√	√	√	√
6-9months	If <40% non-HDL-C reduction, up titration required. Repeat full lipid profile and ALT within 1-3 months of each up-titration of statin dose or addition of ezetimibe as required			
12 months	√	√	√	√
Yearly	√*		√*	

Where compliance has been confirmed (with oral therapy) and expected response is not seen, consider seeking specialist advice.

Abnormal results and required actions

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

- Start/ 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. Further monitoring intervals to be determined by ALT result.

Abnormal results and required actions continued…

Where triglyceride levels are raised the following actions should be taken as described in the table below:

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 > 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.

TREATMENT TITRATION THRESHOLD/TARGETS

	NICE titration threshold	JBS3
Primary Prevention	Intensify lipid lowering therapy if non-HDL-C reduction from baseline is less than 40%	non-HDL-C <2.5mmol/L (LDL-C <1.8mmol/L)
Secondary prevention		
FH	Optimise lipid lowering therapy to achieve at least 50% reduction in LDL-C (or non-HDL-C)	

If baseline cholesterol is unknown in the setting of secondary prevention use the Joint British Societies' JBS3 consensus recommendation.

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

PATIENT MEDICATION REVIEW

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.

SPECIALIST SERVICES

Services available in STW include lipid clinic, PCSK9i clinic (offering initiation and subsequent follow up), FH genetic diagnosis and cascade testing in conjunction with West Midlands FH service. NICE eligibility criteria for PCSK9i initiation and fasting LDL-C thresholds are summarised below.

NICE TA393 Alirocumab NICE TA394 Evolocumab	Without CVD	With CVD	
		High risk [1]	Very high risk [2]
Primary non-FH or mixed dyslipidaemia	Not recommended	LDL C > 4.0 mmoL/L	LDL C > 3.5 mmoL/L
Primary heterozygous-FH	LDL C > 5.0 mmoL/L	LDL C > 3.5 mmoL/L	

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

Bempedoic acid/ezetimibe and inclisiran are available and suitable for prescribing in primary care and do not require initiation by specialist services. PCSK9i should only be prescribed in secondary care.

NB: this pathway applies to patients registered with a Shropshire, Telford and Wrekin GP. Patients in Wales will be considered separately