Sheffield Lipid Modification Guidelines v2 March 2017 (Adapted from NICE CG181, TA385, TA393 and TA394)

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Pre-existing CVD → **NO** → **Primary Prevention**

YES → **Secondary Prevention**
ACS, MI, angina, ischaemic stroke, TIA, PAD

- Commence **Atorvastatin 80mg** unless contraindicated* or CKD (see below).
- Use **lower dose** if potential drug interactions*, high risk of adverse effects* or patient prefers.
- In **CKD** (eGFR <60ml/min/1.73m^2 and/or albuminuria) commence **Atorvastatin 20mg**.
- In acute ischaemic stroke commence statin at 48 hours post-stroke.
- Perform **clinical assessment** and offer **lifestyle advice** (see BOX 2)
- Management of **modifiable risk factors** should be performed but must not delay statin treatment.
- Consider specialist referral for **PCSK9 inhibitor** therapy where appropriate; see appendix

High Risk of CVD Groups:
- **CKD** (eGFR <60ml/min/1.73m^2 and/or albuminuria)
- **Type I diabetes** (especially if >10 yr history, established nephropathy or other CVD risk factors)
- **Age ≥85 years**
- **10yr QRISK2 score ≥ 10% or** high risk by clinical judgement (see BOX 1).

NB1: Use QRISK2 to assess CVD risk in Type 2 diabetes.
NB: **Familial Hypercholesterolemia** – see NICE CG71 and STH Referral Pathway

Perform **clinical assessment**, offer **lifestyle advice** and manage **modifiable risk factors** (see BOX 2)

- Offer **Atorvastatin 20 mg** unless contraindicated* and involve patient in decision making process*.
- Use a **lower dose** only if potential drug interactions*, high risk of side-effects* or patient preference.

*See appendix for more information

BOX 1
QRISK2 may underestimate CV risk in those;
1. Treated for HIV.
2. With serious mental health problems.
3. On meds causing dyslipidaemia e.g. atypical antipsychotics, steroids, immunosuppressants.
4. With autoimmune disorder e.g. SLE, RA.
5. Taking antihypertensive or lipid therapy, or who have recently stopped smoking.
6. With BMI > 40 kg/m^2.
7. With raised triglycerides.

BOX 2
Clinical Assessment
- BP (see NICE pathway)
- BMI
- Smoking status
- Alcohol consumption
- Extended lipid profile, U&E, ALT.
- Consider HbA1c
- TSH (if hypothyroidism suspected)

NB If unexplained muscle pain before starting statin, check CK levels as well.

Lifestyle Advice
- Diet, weight and physical activity (aim for BMI <30 kg/m^2)
- Alcohol reduction (<14u/week with several alcohol free days/week)
- Smoking cessation

NB: Refer if:
- TC >9mmol/L,
- non-HDL-C >7.5mmol/L
- TG persistently >10mmol/L (urgently if TG >20mmol/L and not due to excess alcohol or poor glycaemic control)

Follow-up of patients taking statins
1. Efficacy monitoring
- Measure TC, HDL-C and non-HDL-C at 3 months after initiation of statin or dose change:
- If <40% reduction in non-HDL-C from baseline check adherence, timing of dose, diet and lifestyle measures and consider increasing dose of atorvastatin if <80mg and patient at high risk (do not increase above 20 mg if eGFR <30ml/min/1.73^2
- seek specialist advice from renal team).
- In **ACS and diabetics with CVD**, consider adding ezetimibe to max tolerated dose of statin if a 40% reduction in non-HDL is not achieved.
- Once stable, review patients annually and consider measuring non-HDL-C to inform discussion

2. Safety monitoring
ALT: Measure pre-statin treatment and 3 & 12 months after initiation or dose change; more often if abnormal. Stop if ALT > 3xULN.
CK: Routine testing unnecessary. Advise patients to report muscle pain, tenderness or weakness; measure CK if occurs. Stop if CK>5x ULN and discuss with specialist.
*See the **Common Blood Monitoring Schedules** for advice on routine monitoring of statins.

Statin Intolerance
CK>5xULN and/or ALT>3xULN?
Yes; Stop statin and seek specialist advice.
No; Discuss options with patient:
1. Stop statin & see if symptoms resolve +/- recur on restarting; if not, probably not statin related. Look for other cause.
2. Reduce dose or offer lower intensity statin e.g. simvastatin or pravastatin
If intolerant of 3 different statins seek specialist advice

Lipid Clinic referrals for specialist advice should be made to:
Dr Hannah Delaney,
Clinical Chemistry,
Northern General Hospital,
Herries Road,
Sheffield.
S5 7AU.

*See appendix for more information
Non-HDL Cholesterol- Non-HDL is total cholesterol minus HDL and is a measure of "bad" cholesterol.
CVD- cardiovascular disease, **CKD**- chronic kidney disease, **eGFR**- estimated glomerular filtration rate, **HIV**- human immunodeficiency virus, **SLE**- systemic lupus erythematosus, **RA**- rheumatoid arthritis, **BMI**- body mass index, **ALT**- alanine transaminase, **TSH**- thyroid stimulating hormone, **TC**- total cholesterol, **HDL**- high density lipoprotein, **TG**- triglyceride, **ACS**- acute coronary syndrome, **MI**- myocardial infarction, **TIA**- transient ischaemic attack, **PAD**- peripheral arterial disease, **ULN**- upper limit of normal, **CK**- creatine kinase

Appendix to Sheffield Lipid Modification Guidelines 2017

Statin Cautions and Contraindications:
Please refer to the current BNF or SPC for a full and up-to-date list.

- Patients with **hypothyroidism** should receive adequate thyroid replacement therapy; correcting hypothyroidism itself may resolve the lipid abnormality. Untreated hypothyroidism increases the risk of myositis with lipid-regulating drugs.
- Statins should be used with caution in those with a history of **liver disease** or with a **high alcohol** intake.
- Statins should be used with caution in those with risk factors for **myopathy or rhabdomyolysis**.
- Statins must be avoided in **pregnancy** (discontinue 3 months before attempting to conceive) and **breastfeeding**.
- Statins should be avoided in **haemorrhagic stroke**.
- Seek specialist advice if **eGFR < 30mL/minute/1.73m^2**.

Shared decision making
Involve the patient in discussions around their CVD risk management to make an informed decision regarding statin treatment. The NICE patient decision aid can be used or those available on the GP clinical systems.

High risk of side-effects with statins:

- Elderly, frail patients.
- Pre-statin myalgia +/- raised CK
- History of liver disease/raised ALT
- Hypothyroidism
- High alcohol intake
- Drug interactions (see table below)

Statin Drug Interactions: Please refer to the current BNF or SPC for a full and up-to-date list of drug interactions.

Drug interactions associated with increased risk of side-effects		
Interacting agents	**Simvastatin**	**Atorvastatin**
Ketoconazole Posaconazole Erythromycin Telithromycin Itraconazole Clarithromycin	Contraindicated	Avoid if possible; consider temporary suspension of atorvastatin if interacting drug is taken for a short period. If unavoidable a lower starting and maximum doses of atorvastatin should be considered and appropriate clinical monitoring is recommended. See SPC for maximum doses.
Ciclosporin	Contraindicated	Maximum dose 10mg daily atorvastatin
Danazol	Contraindicated	No specific recommendation
HIV protease inhibitors	Contraindicated	Avoid if possible. See SPC for maximum recommended doses
Gemfibrozil	Contraindicated	Lower starting dose and clinical monitoring is recommended
Other fibrates	Do not exceed 10 mg simvastatin daily (except fenofibrate)	Lower starting dose and clinical monitoring is recommended
Ezetimibe	Additive risk of myopathy can't be ruled out	Additive risk of myopathy cannot be ruled out
Amlodipine	Do not exceed 20 mg simvastatin daily	No specific recommendation
Amiodarone Verapamil Diltiazem		Consider lower maximum dose; appropriate clinical monitoring is required
Fusidic acid (systemic)	Patients should be closely monitored. Temporary suspension of simvastatin treatment may be considered.	Concurrent use is not recommended. Temporary suspension of atorvastatin may be considered.
Grapefruit juice	Avoid grapefruit juice when taking simvastatin	Concomitant intake of large quantities of grapefruit juice and atorvastatin is not recommended

PCSK9 Inhibitors (Alirocumab TA393, and Evolocumab TA394):

These are initiated, prescribed and monitored in secondary care only.

These groups of patients are eligible for PCSK9 inhibitors; they are for hospital initiation ONLY (via Lipid Clinic, NGH)

1. Primary non-familial hypercholesterolemia or mixed dyslipidemia with CVD (secondary prevention):
   High CVD risk* and LDL-C > 4.0 mmol/L despite max. tolerated dose of lipid-lowering therapy **or**
   Very high CVD risk** and LDL > 3.5 mmol/L despite max. tolerated dose of lipid-lowering therapy
2. Primary heterozygous familial hypercholesterolemia (as per genetic testing)
   i. Without CVD (primary prevention): LDL-C > 5.0 mmol/L despite max. tolerated dose of lipid-lowering therapy
   ii. With CVD (secondary prevention): LDL-C > 3.5 mmol/L despite max. tolerated dose of lipid-lowering therapy

NB. These drugs may be used in combination with a statin or with other lipid-lowering therapies, or alone in patients who are statin intolerant or for whom a statin is contraindicated (excluding pregnancy).

*High risk of CVD: History of any of the following: ACS; coronary or other arterial revascularisation procedures; chronic heart disease; ischaemic stroke; PAD.

** Very high risk of CVD: Recurrent cardiovascular events or cardiovascular events in more than 1 vascular bed (that is, polyvascular disease).

Related Pathway: STH referral pathway for adult patients with query Familial Hypercholesterolaemia (FH)
http://www.sheffieldccgportal.co.uk/pressv2/index.php/component/zoo/item/lipid-problems