

## Guidance on Prescribing Statins

*This guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.*

Please also refer to [South London Lipid Management for the Primary and Secondary Prevention of Cardiovascular Disease \(CVD\) in Adults](#)

The following issues need to be considered when prescribing a statin:

- Have an informed discussion with the patient about the benefits and risks of statin treatment. This should include factors such as benefits from lifestyle modification, informed patient preference, co-morbidities, adherence, polypharmacy, general frailty and life expectancy
- Contraindications and cautions
- Drug interactions
- Baseline and follow up monitoring

### Seek further advice before initiating statins in patients with:

- Renal impairment (eGFR <30ml/min/1.73m<sup>2</sup>)<sup>1</sup>
- Liver disease (cirrhosis or hepatitis)
- Untreated hypothyroidism
- Patients with excess alcohol intake (higher-risk drinking)- regularly consuming over 50 alcohol units per week (adult men) or over 35 units per week (adult women)
- For patients with prior haemorrhagic stroke or lacunar infarct the balance of risks and benefits of atorvastatin 80 mg is uncertain and the potential risk of haemorrhagic stroke should be carefully considered before initiating this dose

### General Contraindications and Cautions

- Hypersensitivity to the individual statin or to any of the excipients
- Active liver disease (Alanine aminotransferase (ALT) or Aspartate aminotransferase (AST) level > 100iu/L, unexplained persistent isolated elevations of serum transaminases and history of liver disease (see table 3 for further details)
- **SIMVASTATIN** - In patients with severe renal impairment (Creatinine Clearance (CrCl) < 30 ml/min)<sup>2</sup>, dosages above 10 mg/day should be carefully considered and, if deemed necessary, implemented cautiously. Alternatively, atorvastatin could be used
- Statin use is contraindicated in both pregnancy and lactation. Women of child-bearing age must be advised of the potential teratogenic risk of statins and to stop taking them if pregnancy is a possibility. Consideration should be given to delaying statin treatment or addressing contraceptive needs. Those who are planning a pregnancy and are on a statin treatment should be advised to stop 3 months before they attempt to conceive and not to restart the statin until breastfeeding is finished
- If statin therapy is contraindicated, not tolerated or not effective:
  - Do not offer nicotinic acid or bile acid binder or omega-3 fatty acids to lower CV disease risk.
  - Do not routinely consider treatment with a fibrate. Concomitant use of fibrates and statins increases the risk of muscle toxicity. Seek specialist advice

### Managing statin intolerance

- Patient unable to tolerate high intensity statin should use the maximum tolerated dose
- Patient should be informed any statin at any dose will reduced the CVD risk
- If a patient reports adverse effects when taking high intensity statin, consider the following strategies:
  - Stopping the statin and re-starting treatment when the symptoms have resolved to determine if the symptoms were related to the statin
  - Reduce the dose within the intensity statin group,
  - Change to a lower intensity statin or consider a water soluble statin
  - Do not offer co-enzyme Q 10 or vitamin D to improve adherence to statin
- Seek specialist advice for patients at high risk of CVD including those with CKD, type 1 diabetes, type 2 diabetes or genetic dyslipidaemia and those with CVD, who are intolerant to 3 different statins

<sup>1</sup> Estimated Glomerular Filtration Rate (eGFR) used as per NICE guideline

<sup>2</sup> CrCl used as per simvastatin Summary of Product Characteristics (SPC)

### Baseline assessment prior to statin initiation

- Perform baseline blood tests, a clinical assessment and treat co-morbidities and secondary causes of dyslipidaemia. The following should be included in the assessment:
  - Smoking Status
  - Alcohol Consumption
  - Blood pressure
  - Body mass or other measures of obesity
  - Lipid profile: Total cholesterol (TC), non-HDL cholesterol (non-HDL), HDL cholesterol (HDL) and triglycerides
  - HbA<sub>1c</sub> (glycated haemoglobin)
  - Renal function and eGFR<sup>3</sup>
  - Transaminase level (alanine aminotransferase or aspartate aminotransferase)
  - Thyroid-stimulating hormone
  - Estimate risk of CVD for primary prevention

**Table 1 Potency table for reduction in LDL cholesterol<sup>3</sup>**

Dose (mg/day)	% Reduction in LDL cholesterol				
	5	10	20	40	80
Fluvastatin	–	–	21	27	33
Pravastatin	–	20	24	29	–
Simvastatin	–	27	32	37	42 <sup>a</sup>
Atorvastatin	–	37	43	49	55
Rosuvastatin	38	43	48	53	–

<sup>a</sup> **Advice from the MHRA: there is an increased risk of myopathy associated with high-dose (80 mg) simvastatin. The 80 mg dose should be considered only in patients with severe hypercholesterolaemia and high risk of cardiovascular complications who have not achieved their treatment goals on lower doses, when the benefits are expected to outweigh the potential risks.**

**Low intensity statin:** Reduction in low-density lipoprotein cholesterol is 20% to 30%

**Medium intensity statin:** Reduction in low-density lipoprotein cholesterol 31% to 40%

**High intensity statin:** Reduction in low-density lipoprotein cholesterol is > 40%

**Table 2 Interactions with statins<sup>4</sup>**

Interacting drug or food	Simvastatin (for full details – see BNF or <a href="#">SPC</a> )	Atorvastatin (for full details – see BNF or <a href="#">SPC</a> )
CYP3A4 inhibitors including: Itraconazole Ketoconazole Posaconazole Erythromycin Clarithromycin Telithromycin and HIV protease inhibitors (e.g. nelfinavir). Nefazodone, Ciclosporin Danazol, Gemfibrozil	All are contraindicated with simvastatin	Avoid if possible: consider temporary suspension of atorvastatin if an interacting drug is taken for short period;  Advice on specific list: <b>Itraconazole:</b> do not exceed 40 mg atorvastatin daily; <b>Clarithromycin:</b> do not exceed 20 mg atorvastatin daily; <b>HIV protease inhibitors:</b> monitor lipid levels to ensure lowest necessary dose of atorvastatin is used. <b>Ciclosporin:</b> Do not exceed 10 mg atorvastatin daily <b>Danazol:</b> No restriction in Summary of Product Characteristics
Fluconazole	Avoid if possible. May increase plasma concentration of simvastatin when used concomitantly. There is no specific dose	Avoid if possible. May increase plasma concentration of atorvastatin therefore a lower maximum dose of atorvastatin should be considered with caution and

<sup>3</sup> eGFR used as per NICE guideline

<sup>4</sup> For details of other statin drug interaction information, please refer to their individual SPCs ([Fluvastatin](#), [Pravastatin](#) and/ or [Rosuvastatin](#)) or the BNF

Interacting drug or food	Simvastatin (for full details – see BNF or <a href="#">SPC</a> )	Atorvastatin (for full details – see BNF or <a href="#">SPC</a> )
	adjustment and caution should be exercised with appropriate clinical monitoring	appropriate clinical monitoring of the patient
<b>Amiodarone, Amlodipine, Diltiazem, Verapamil</b>	Do not exceed 20 mg simvastatin daily (as these drugs increase plasma concentration of simvastatin)	Ensure lowest necessary dose of atorvastatin is used when co-administered with amiodarone, verapamil or diltiazem For co-administration with amlodipine, there is no specific recommendation
<b>Grapefruit or grapefruit juice</b>	Avoid grapefruit juice	Limit intake of grapefruit juice to very small quantities (or avoid altogether)
<b>Warfarin/coumarins</b>	Monitor INR before starting treatment and regularly during treatment, especially with dose changes	Monitor INR before starting treatment and regularly during treatment, especially with dose changes
<b>Fibrates (except fenofibrate)</b>	Concomitant use of fibrates increases risk of myopathy; do not exceed 10 mg simvastatin daily (except with fenofibrate, where the evidence suggests no clinical important interaction. Nevertheless, concurrent use should be undertaken only if the benefits of treatment outweigh the risks) <b>Co -administration with Gemfibrozil is contraindicated</b>	Concomitant use of fibrates increases risk of myopathy; use lowest starting dose and patient should be monitored and advised to report any signs of myopathy and possible rhabdomyolysis (i.e. otherwise unexplained muscle pain, tenderness or weakness or dark coloured urine).
<b>Ezetimibe</b>	Additive risk of myopathy cannot be ruled out with Concomitant use. There is no restriction in SPC and patient should be monitored and advised to report any signs of myopathy and possible rhabdomyolysis (i.e. otherwise unexplained muscle pain, tenderness or weakness or dark coloured urine)	Additive risk of myopathy cannot be ruled out with Concomitant use. There is no restriction in Summary of Product Characteristics (SPC) and patient should be monitored and advised to report any signs of myopathy and possible rhabdomyolysis (i.e. otherwise unexplained muscle pain, tenderness or weakness or dark coloured urine)
<b>Fusidic acid</b>	Concomitant use with systemic fusidic acid is not recommended. Temporary suspension of simvastatin should be considered for short courses of systemic fusidic acid and restart simvastatin 7 days after the last dose of fusidic acid. In-exceptional circumstances where prolonged systemic fusidic acid is needed, co-administration may be considered on an individual basis and under close medical supervision	Concomitant use of atorvastatin with systemic fusidic acid is not recommended. Temporary suspension of atorvastatin should be considered for short courses of systemic fusidic acid and restart atorvastatin 7 days after the last dose of fusidic acid. In-exceptional circumstances where prolonged systemic fusidic acid is needed, atorvastatin 10mg may be considered on an individual basis and under close medical supervision
<b>Niacin (nicotinic acid) (≥ 1 g/day)</b>	For Asian patients, not recommended with simvastatin	Risk of myopathy may be increased with concomitant use. If possible consider alternative non-interacting treatment

**Table 3. Monitoring Statin Therapy**

Parameter	Comments
<p><b>Lipid Levels</b> Total cholesterol (TC) High density lipoprotein (HDL) Non-HDL cholesterol (non-HDL) Triglycerides</p>	<p><b>Baseline lipid profile should be measured before starting a statin. Lipid profile should be measured and reviewed annually to check efficacy and on-going adherence to therapy</b></p> <p><b>Primary CVD prevention including people with type 2 diabetes or people with type 1 diabetes who meet criteria<sup>1</sup>:</b> Reinforce lifestyle issues and check adherence to medication. There are no specific lipid treatment targets for primary prevention, but if patient is considered higher risk due to the presence of multiple cardiovascular risk factors, consider increasing statin dose if necessary to reduce non-HDL cholesterol by 40% from baseline. Routine safety and efficacy monitoring should be undertaken. Patients should be reviewed annually, with lipid monitoring, to check efficacy and on-going adherence to therapy. Lifestyle issues should be revisited regularly.</p> <p><b>Acute coronary syndromes and secondary prevention of CVD or people with chronic kidney disease (CKD) (eGFR &lt; 60ml/min/1.73m<sup>2</sup> and/ or albuminuria)<sup>5</sup>:</b> Once statin therapy has been initiated - repeat lipid profile at 3 months. Reinforce lifestyle issues and check adherence to medication Aim to reduce non-HDL cholesterol by 40% from baseline</p> <ul style="list-style-type: none"> <li>• If baseline cholesterol is unknown, as a minimum, patients should be treated to achieve <i>at least</i> a total cholesterol <math>\leq</math> 5mmol/L and non-HDL cholesterol <math>\leq</math> 3.8mmol/L</li> <li>• Increase statin dose if not achieving adequate reductions in cholesterol (and not already on maximum dose) – seek specialist renal advice in renal disease (eGFR &lt; 30ml/min/1.73m<sup>2</sup>)<sup>6</sup></li> </ul> <p>Consider referral for specialist advice if patients not achieving a 40% fall in non-HDL cholesterol while on maximum tolerated dose of statin Routine safety and efficacy monitoring should be undertaken. Lifestyle issues should be revisited regularly</p>
<p><b>Thyroid Function Tests</b></p>	<p>Check before initiating a statin to exclude hypothyroidism</p>
<p><b>Liver Function Tests (LFTs)</b> ALT or AST</p>	<p><b>Baseline liver enzymes should be measured before starting a statin. Liver function (transaminases) should be measured within 3 months of starting treatment and at 12 month, but not again unless clinically indicated.</b></p> <p>If transaminases &gt;3x upper limit of normal (ULN) do not start a statin. If patient is already on treatment then discontinue the statin and re-test after 3 months. If still raised, refer to specialist</p> <p>For lesser increases in transaminases, which remain elevated at 6 months consider specialist advice</p>
<p><b>Creatine kinase (CK)</b></p>	<p><b>Routine CK monitoring after initiation is not recommended. CK should be measured during treatment when clinically indicated – i.e. where there are symptoms of muscle pain or tenderness, muscle weakness or muscle cramps.</b></p> <p>Before offering a statin, it is important to confirm if the patient has had persistent generalised unexplained muscle pain associated or not with previous lipid lowering treatment. If the patient has then measure baseline CK before starting a statin.</p> <ul style="list-style-type: none"> <li>• If CK levels are significantly elevated (&gt; 5 x ULN), re-measure CK after 7 days. If levels remain &gt;5 x ULN, statin treatment should not be started.</li> </ul>

<sup>5</sup> eGFR used as per NICE guideline

<sup>6</sup> eGFR used as per NICE guideline

	<ul style="list-style-type: none"> <li>If CK are raised <math>&lt;5 \times \text{ULN}</math>, start a statin at a lower dose</li> </ul> <p>Baseline CK should also be measured before starting a statin in those who may already be taking medicines that will increase the risk of myopathy when used concomitantly, for example, fibrates.</p> <p>CK should not be measured following strenuous exercise or in the presence of any plausible alternative cause of CK increase as this makes value interpretation difficult. If CK levels are significantly elevated at baseline (<math>&gt; 5 \times \text{ULN}</math>), levels should be re-measured within 5 to 7 days later to confirm the results.</p> <p><b>Patients should be counselled on initiation of statin to report any usual muscle pain, tenderness or weakness during treatment.</b> If this occurs during treatment:</p> <ul style="list-style-type: none"> <li>Rule out common causes (e.g. exercise)</li> <li>Check TFTs (hypothyroidism predisposes to myopathy)</li> <li>Measure CK             <ul style="list-style-type: none"> <li>If CK elevated <math>&gt; 5 \times \text{ULN}</math> stop and seek advice</li> <li>If CK elevated <math>&lt; 5 \times \text{ULN}</math>, follow the strategy below:                 <ol style="list-style-type: none"> <li>Monitor carefully by repeating CK level in one month</li> <li>If remains elevated, reduce dose and recheck CK level in one month</li> <li>If still remains elevated consider seeking advice</li> </ol> </li> </ul> </li> <li>If symptoms continue STOP statin and consult a specialist before re-initiating</li> </ul> <p><i>Note: Some Black African and Caribbean's have elevated baseline levels of CK. This is not a contra-indication to statin therapy. In these patients, after initiation if the CK <math>&gt; 5 \times</math> baseline - seek advice</i></p> <p><b>IF MYOSITIS IS PRESENT OR SUSPECTED DISCONTINUE STATIN IMMEDIATELY</b></p>
<b>Other adverse effects</b>	<p>Headache, dyspepsia or insomnia. Evaluate symptoms at each visit.</p> <p>If symptoms not tolerated:</p> <ul style="list-style-type: none"> <li>Consider changing time of dose (after food if nauseous, morning if sleep disturbed)</li> <li>Consider decreasing dose</li> <li>Consider using an alternative agent</li> </ul>

#### References

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- SPC Fluvastatin 40mg tablets Actravis UK Ltd (updated 21/03/2016) [Online] available from <https://www.medicines.org.uk/emc/medicine/24469> accessed 21/07/2016
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