NHS
South London Cardiac and Stroke Networks

Guidance on Prescribing Statins

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

- Identifying patients in whom additional advice should be sought prior to initiation
- Contraindications and cautions
- Drug interactions
- Baseline and follow up monitoring

Seek further advice before initiating statins in patients with:

- Renal impairment (Cr >180µmol/l; CrCl<30ml/min)
- Liver disease (cirrhosis or hepatitis)
- Untreated hypothyroidism

General Contraindications and Cautions

- Hypersensitivity to the individual statin or to any of the excipients
- Active liver disease (AST or ALT level > 100iu/L) or unexplained persistent isolated elevations of serum transaminases
- Statin use is contraindicated in both pregnancy and lactation. Consideration should be given to delaying statin therapy or addressing contraceptive needs in women of child-bearing age
- Concomitant use of fibrates and statins increases the risk of muscle toxicity. Seek specialist advice. The co-administration of statins and nicotinic acid should be used with caution.
- Patients with excess alcohol intake (more than 50 units per week)

SIMVASTATIN (see SPC for full detail)

- In patients with severe renal insufficiency (creatinine clearance < 30 ml/min), dosages above 10 mg/day should be carefully considered and, if deemed necessary, implemented cautiously.
- Significant drug interactions occur with certain drugs (e.g. amiodarone, verapamil, diltiazem, erythromycin, clarithromycin, ciclosporin, itraconazole, ketoconazole, HIV protease inhibitors, nefazodone, ciclosporin). Dose reductions or cessation of therapy may be required – see FAQ / BNF for more details. Consider an alternative agent if necessary
- Advise patients to avoid consumption of grapefruit or grapefruit juice during simvastatin therapy
- International normalised ratio (INR) in patients on warfarin can be affected by concomitant simvastatin use. Monitor INR in patients before and more frequently during the early phase of treatment with simvastatin and after any dose changes

ATORVASTATIN (see SPC for full detail)

- 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
- For patients on interacting drugs, a lower starting dose may be required and lower maximum doses may need to be considered. Interacting drugs include ciclosporin, clarithromycin, diltiazem, amiodarone and verapamil, itraconazole, protease inhibitors - see BNF/ SPC for more details.
- Concomitant intake of large quantities of grapefruit juice and atorvastatin is not recommended
- International normalised ratio (INR) in patients on warfarin can be affected by concomitant atorvastatin use. Monitor INR in patients before and more frequently during the early phase of treatment with atorvastatin and after any dose changes

PRAVASTATIN (see SPC for full detail)

- Caution should be exercised where pravastatin is prescribed for patients treated with erythromycin or clarithromycin
- Start with a dose of 10mg daily in patients with creatinine clearance < 20ml/min.

Monitoring Statin Therapy

Lipid Levels Total cholesterol (TC) High density lipoprotein (HDL) Low density lipoprotein (LDL) Triglycerides	**Primary Prevention:** routine monitoring of lipid levels is not recommended, although clinicians should consider checking lipid levels occasionally throughout treatment to ensure on-going adherence to therapy **Secondary Prevention:** Lipid levels should be measured before therapy is initiated; at 12 weeks following initiation or change of dose and at 12 monthly intervals thereafter If total cholesterol remains persistently raised despite optimising statin therapy – follow local guidance
Thyroid Function Tests	Check before initiating a statin to exclude hypothyroidism
Liver Function Tests (LFTs)	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 monthly intervals thereafter. If transaminases >3x upper limit of normal (ULN) discontinue statin and refer. For lesser increases in transaminases, which remain elevated at 6 months consider specialist advice
Creatine kinase (CK)	Baseline CK should be measured before starting a statin. 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. **Patients should be counselled on initiation of statin to report any unusual muscle pain, tenderness or weakness during treatment** **IF MYOSITIS IS PRESENT OR SUSPECTED DISCONTINUE IMMEDIATELY** If muscle soreness occurs: • Rule out common causes (e.g. exercise) • Check TFTs (hypothyroidism predisposes to myopathy) • Measure CK - If CK elevated > 5 x ULN stop and seek advice - If CK elevated < 5 x ULN a) Monitor carefully by repeating CK level in one month b) If remains elevated, reduce dose and recheck CK level in one month c) If still remains elevated consider seeking advice • If symptoms continue STOP statin and consult a specialist before re-initiating *Note: Some Black African and Caribbeans have elevated baseline levels of CK. This is not a contra-indication to statin therapy. In these patients, after initiation if the CK > 5 x baseline - seek advice*
Other adverse effects	Headache, dyspepsia or insomnia. Evaluate symptoms at each visit. If symptoms not tolerated: • Consider changing time of dose (after food if nauseous, morning if sleep disturbed) • Consider decreasing dose • Consider using an alternative agent

References
1. Pasternak RC, Smith SC, Bairey-Merz CN, et al., ACC/AHA/NHLBI Clinical Advisory on the Use and Safety of Statins. *Circulation* 2002; 106:1024 – 1028
2. Summary of Product Characteristics for Simvastatin at www.emc.medicines.org.uk (accessed 23/01/2006)
3. NICE Technology Appraisal 94: Statins for the prevention of cardiovascular events. January 2006
4. NICE Technology Appraisal 94: Statins for the prevention of cardiovascular events. January 2006
5. NICE Clinical Guideline 67 (2008) Lipid Modification Cardiovascular risk assessment and the modification of blood lipids for the primary and secondary prevention of cardiovascular disease.

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