



TAYSIDE PRESCRIBER

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STATIN INTERACTIONS UPDATE

Updated advice on simvastatin drug interactions and contraindications

The Medicines and Healthcare products Regulatory Agency (MHRA) has issued advice via [Drug Safety Update, Volume 6, Issue 1, August 2012](#) on prescribing of simvastatin with some other medicines associated with an increased risk of myopathy and/or rhabdomyolysis.

Key points to note are that:

- Simvastatin is now contraindicated with ciclosporin, danazol and gemfibrozil.
- The maximum recommended dose for simvastatin in conjunction with amlodipine or diltiazem is now 20mg daily.

The guidance in NHS Tayside is:

- ⇒ to review all patients taking contraindicated medicines and consider;
 - temporary suspension of the statin if interacting drug is taken for a short period e.g. short courses of antimicrobials such as clarithromycin,
 - the ongoing need for a statin,
 - whether atorvastatin would be a suitable alternative– see drug interactions table on page 2 or the relevant [Summary of Product Characteristics \(SPC\)](#) for specific advice.
- ⇒ to review all patients taking amlodipine, diltiazem, verapamil or amiodarone on simvastatin or requiring a statin at their next routine appointment. Recommended statins for these patients are:
 - primary prevention - simvastatin 20mg daily or atorvastatin 10mg daily;
 - secondary prevention - atorvastatin 20mg daily and titrate as necessary (ensure lowest necessary dose of atorvastatin used with diltiazem, verapamil or amiodarone).

There is an increased risk of myopathy associated with high dose (80mg) simvastatin. Prescribers are reminded that **simvastatin 80mg is non-formulary and should not be routinely used.**

Prescribing advice for interacting medicines with statins

Some statins (particularly simvastatin and atorvastatin) are metabolised by cytochrome P450 (CYP3A4) and thus co-administration of potent inhibitors of this enzyme (such as 'azole' anti-fungal agents or HIV protease inhibitors) is likely to increase plasma levels of these medicines and so increase the risk of dose-related side effects, including rhabdomyolysis.

Patients receiving any statin should be asked to report unexplained muscle pain, weakness or cramps immediately, and stop treatment until this has been investigated. If symptoms are severe or if creatine kinase is greater than 5 times the upper limit of normal, treatment should be withheld.

Any serious suspected reactions with simvastatin, fluvastatin, atorvastatin, rosuvastatin or pravastatin should be reported through the Yellow Card Scheme (<http://yellowcard.mhra.gov.uk/>).

Managing common drug interactions for simvastatin and atorvastatin

There are other important interactions for different statins, including medicines that interact with statins to reduce plasma concentrations of the statin. For further information refer to the manufacturer's [Summary of Product Characteristics \(SPC\)](#) for the specific medicine (s).

Pravastatin and **rosuvastatin** do not appear to be significantly metabolised by the cytochrome P450 system, and are alternatives in patients with concomitant long-term drugs that interact with simvastatin or atorvastatin.

Table 1 Prescribing recommendations for co-administering certain medicines with simvastatin or atorvastatin

Interacting drug or food	Simvastatin prescribing advice	Atorvastatin prescribing advice
Potent CYP3A4 inhibitors , including itraconazole, ketoconazole, posaconazole, erythromycin, clarithromycin, telithromycin, and HIV protease inhibitors	All are contraindicated with simvastatin (In practice: consider temporary suspension of simvastatin if interacting drug is taken for a short period e.g. short course of clarithromycin)	Avoid if possible: consider temporary suspension of atorvastatin if interacting drug is taken for short period Itraconazole: do not exceed 40mg atorvastatin daily Clarithromycin do not exceed 20mg atorvastatin daily HIV protease inhibitors: use the lowest therapeutic dose of atorvastatin and monitor carefully for adverse effects. Maximum recommended dose of atorvastatin depends on protease inhibitor used, see SPC .
Ciclosporin*	Contraindicated with simvastatin	Do not exceed 10mg atorvastatin daily
Danazol	Contraindicated with simvastatin	No specific restriction in SPC, however caution advised (use lowest therapeutic dose of atorvastatin and monitor carefully for adverse effects).
Gemfibrozil	Contraindicated with simvastatin	Increased risk of myopathy when used with fibrates. Use the lowest therapeutic dose of atorvastatin and monitor carefully for adverse effects.
Verapamil, amiodarone, diltiazem	Do not exceed 20mg simvastatin daily	Monitor lipid levels to ensure lowest necessary dose of atorvastatin is used and monitor carefully for adverse effects
Amlodipine	Do not exceed 20mg simvastatin daily	No specific recommendation
Grapefruit juice	Avoid grapefruit juice	Limit intake of grapefruit juice to very small quantities (or avoid altogether)
Warfarin/coumarins†	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
Other Fibrates†	Do not exceed 10mg simvastatin daily (except fenofibrate; use with caution)	Increased risk of myopathy when used with fibrates. Use the lowest therapeutic dose of atorvastatin and monitor carefully for adverse effects.
Ezetimibe†	Additive risk of myopathy cannot be ruled out	Additive risk of myopathy cannot be ruled out. Monitor carefully for adverse effects.
Fusidic acid	Patients should be closely monitored. Temporary suspension of simvastatin treatment may be considered.	Patients should be closely monitored. Temporary suspension of atorvastatin treatment may be considered.

*Ciclosporin interacts with all statins and is contraindicated with rosuvastatin

†Warfarin/coumarins, fibrates, and ezetimibe are important potential interactions to consider for all statins

References

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4. NHS Tayside Medicines Governance Unit. Statin Interactions. [Tayside Prescriber Issue 102](#), May 2009. Available from: Staffnet > Pharmacy > Medicines Governance > Prescribing Bulletins > Tayside Prescribers (NHS Tayside Staffnet intranet link only). (Accessed 31/8/12)
5. Merck, Sharp & Dohme Limited. [Summary of Product Characteristics](#) (SPC) [online], Zocor 10mg, 20mg, 40mg and 80mg film-coated tablets. SPC last updated on the eMC 18/9/12. (Accessed 3/9/12 and 24/9/12)
6. Pfizer Limited. [Summary of Product Characteristics](#) (SPC) [online], Lipitor 10mg, 20mg, 40mg, 80mg Tablets. SPC last updated on the eMC 25/6/12. (Accessed 3/9/12 and 24/9/12)

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