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5th April 2013

Attention All: Consultants
Medical Officers
Pharmacists
Pharmacy Technicians
Nurses

Re: Simvastatin Tablets

Following the Medicines and Healthcare Products Regulatory Agency (MHRA) and the Food and Drug Administration (FDA) recommendations regarding simvastatin drug interactions and the recent Summary of Product Characteristics (SPC) update, the following information is being brought to your attention.

Simvastatin is a HMG CoA reductase inhibitor (statin) available in the Government Formulary List as 10mg, 20mg, 40mg and 80mg tablets. Simvastatin, like other statins, occasionally causes myopathy. Myopathy sometimes takes the form of rhabdomyolysis with or without acute renal failure secondary to myoglobinuria, and very rare fatalities have occurred. As with other statins, the risk of myopathy/rhabdomyolysis, is dose related. Hence, the risk of myopathy increases with higher plasma levels associated with high-dose therapy (simvastatin 80mg) and concurrent use of interacting drugs.
Prescribing recommendations for interacting agents are summarized in the table below.

Interacting agents	**Prescribing recommendations**
Itraconazole Ketoconazole Posaconazole Erythromycin Clarithromycin Telithromycin HIV protease inhibitors (e.g. nelfinavir) Nefazodone Ciclosporin Danazol Gemfibrozil	Contraindicated with simvastatin

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Other fibrates (except fenofibrate) Verapamil Diltiazen	Do not exceed 10mg simvastatin daily
Amiodarone Amlodipine	Do not exceed 20mg simvastatin daily
Fusidic acid	Patients should be closely monitored. Temporary suspension of simvastatin treatment may be considered.
Grapefruit juice	Avoid grapefruit juice when taking simvastatin

The key change is that when used with amlodipine, the maximum dose of simvastatin is now 20mg. For **patients taking amlodipine and simvastatin 40mg** consider:

1. **Reducing simvastatin dose to 20mg** – most patients can be managed this way as the interaction with amlodipine leads to an increase in simvastatin exposure that is similar to taking simvastatin 40mg alone.

2. **Staying on simvastatin 40mg** – discuss the risks and benefits of this 'off-label' option with the patient. Be aware that, due to the interaction with amlodipine, exposure to adverse effects is similar to that associated with simvastatin 80mg when given alone.

3**. Change to an alternative statin –** patient should be referred to a Consultant for a change to an alternative statin

4. **Change to an alternative calcium channel blocker** - do not change therapy in patients who are well controlled with amlodipine. Altering the calcium channel blocker is clinically less desirable. Note: the maximum dose of simvastatin is 10mg with verapamil and diltiazem.

Simvastatin 80mg should be used only in patients who have been taking this dose for 12 months or more without evidence of muscle myopathy. Simvastatin 80 mg should not be started in new patients, including patients already taking lower doses of the drug.

It is advisable that each patient is considered individually, and hence taking into account:

- multiple drug therapy and the possibility of drug interactions,
- co-morbidities, including liver function,
- following a change in therapy monitor patients for efficacy and adverse effects.

Thank you
For your attention, please

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Chief Medical Officer

References:

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