IRISH MEDICINES BOARD

Notice Information: - 3rd Party Publications 03 December 2007

Part 1. Product Information

a)	Title:	HMG-CoA Reductase Inhibitors and muscular disorders-MIMS Publication
b)	Product Name/Type:	atorvastatin–Lipitor;fluvastatin– Lescol;pravastatin–Lipostat;rosuvastatin–Crestor;simvastatin–Zocor
c)	Reference:	MIMS Publication December 2007
d)	Product Classification:	HMG-CoA Reductase Inhibitors

Part 2. Problem/Issue

a) Problem/Issue:

HMG-CoA reductase inhibitors, commonly known as 'statins' are a class of medicines authorised as an adjunct to diet for the treatment of hypercholesterolaemia, when the response to diet and other non-pharmacological treatments (e.g. exercise, weight reduction) is inadequate. They are also authorised as an adjunct to treatment in the secondary prevention of major cardiac events in patients with cardiovascular disease.

The occurrence of muscle disorders including myalgia, myopathy and rarely rhabdomyolysis, in association with 'statins' is a dose-dependent, class effect, however, the potential for induction of these disorders varies across the individual products due to differences in pharmacokinetics and lipophilicity. The IMB has previously highlighted the risk of muscle disorders for some of the individual substances, as well as for this class of medicines in a previous issue of MIMS Ireland and its Drug Safety Newsletter in 2001, 2002 and 2004.While the risk of serious muscle toxicity and rhabdomyolysis occurs rarely, healthcare professionals are reminded of the precautionary measures to take prior to initiation and during the monitoring of patients treated with 'statins'.

Prior to Treatment

Clinicians should prescribe 'statins' with caution in patients with pre-disposing factors for myopathy/rhabdomyolysis. A creatine kinase (CK) level should be measured before starting treatment in the following situations:

- Renal impairment

- Hypothyroidism

- Personal or familial history of hereditary muscular disorders

- Previous history of muscular toxicity with a 'statin' or fibrate

- Alcohol abuse

- In elderly patients (age > 70 years), the necessity for such measur

measurement should be considered, according to the presence of other predisposing factors for rhabdomyolysis.

In these situations, the risk of treatment should be considered in relation to possible benefit. Clinical monitoring is recommended in these patients.

If CK levels are significantly elevated (> 5 x upper limit of normal) at baseline, treatment should not be started.

During Treatment

If muscle pain, weakness or cramps occur whilst a patient is receiving treatment, their CK levels should be measured. If these levels are found to be significantly elevated (> 5xULN), treatment should be stopped.

If muscle symptoms are severe and cause daily discomfort, even if CK levels are elevated to = 5 x ULN, treatment discontinuation should be considered.

If symptoms resolve and CK levels return to normal, then re-introduction of the product in question or introduction of an alternative ‘statin’ may be considered, at the lowest effective dose and with close monitoring.

Healthcare professionals are reminded that CK should not be measured following strenuous exercise or in the presence of any plausible alternative cause of CK increase as this makes interpretation of the values difficult. If CK levels are significantly elevated at baseline (> 5xULN), levels should be repeated within 5 to 7 days later, to confirm the results.

Healthcare professionals are reminded that suspected adverse reactions, including those associated with use of any of the ‘statins’ should be reported to the IMB, either on-line on the IMB website at ww

www.imb.ie or using a downloadable version of the adverse reaction report form also available from the IMB's website. Downloaded forms may be completed and sent by freepost to the IMB. Envelopes should be marked "Freepost", Pharmacovigilance Section, Irish Medicines Board, The Earlsfort Centre, Earlsfort Terrace, Dublin 2. Alternatively, completed forms may be submitted by fax (01- 6762517). Finally, post-paid report cards are also available from the Pharmacovigilance Section at the IMB (01- 6764971).

Part 3. Keywords

a) Keywords: torvastatin – Lipitor; fluvastatin – Lescol; pravastatin – Lipostat; rosuvastatin – Crestor ; simvastatin – Zocor