New maternity referral guidelines released

In July 2011, the Ministry of Health updated its Referral Guidelines for Lead Maternity Carers (LMC). This updates and replaces the referral process as outlined in "The role of General Practice in the care of pregnant women", BPJ 35 (Apr, 2011). These guidelines have been designed to enhance communication, collaboration and documentation between all providers of clinical care for a pregnant woman.

For the full article, please visit www.bpac.org.nz keywords: maternity referral

Simvastatin: risk associated with high doses

The United States Food and Drug Administration (FDA) has issued a recommendation that the use of high-dose simvastatin (80 mg) is restricted, due to increased risk of myopathy. The recommendation states that simvastatin 80 mg should only be prescribed if a patient has previously been taking the medicine for longer than 12 months with no signs of myopathy. Furthermore, prescriptions for 80 mg simvastatin should not be issued to new patients and those already taking simvastatin should not have their dose increased to 80 mg per day.[1]

The FDA advice comes following the analysis of the SEARCH trial, which found that patients taking 80 mg per day of simvastatin had an increased risk of myopathy compared to patients taking lower doses of the same medicine, or other medicines of the same class.[1, 2] The study, which included over 12 000 people, found that 52 patients in the 80 mg group, and one in the 20 mg group, developed myopathy. Approximately 60% of reported cases of myopathy were due to a genetic variation affecting the uptake of simvastatin into the liver, resulting in increased plasma levels of simvastatin which in turn increases the risk of myopathy.[1] Most cases were likely to occur in the first year of treatment. Increased age and female gender were also found to increase the risk of myopathy.[1]

Symptoms of myopathy, which in severe cases can develop into rhabdomyolysis, include; muscle pain and tenderness, weakness and dark or red urine. Confirmation of diagnosis can be achieved by testing for elevated serum creatine kinase levels.[3]

Medsafe response

Medsafe is currently in the process of updating the data sheets for all medicines available in New Zealand that contain simvastatin.

For example, the changes to the Lipex data sheet include:

- In the **Dosing and Administration** section: The 80 mg dose of LIPEX should be used only for those patients who have not achieved their LDL-C goal utilising the 40 mg dose.
- The following **Contraindications** have been added:
  - Myopathy secondary to other lipid lowering agents
  - Concomitant administration of potent CYP3A4 inhibitors, e.g. itraconazole, ketoconazole, posaconazole, HIV protease inhibitors, erythromycin, clarithromycin, telithromycin and nefazodone)
  - Concomitant administration of gemfibrozil, cyclosporin or danazol
- The inclusion of additional information in the **Warnings and Precautions** section, including: The risk of myopathy is greater in patients on simvastatin 80 mg compared with other statin-based therapies with similar LDL-C lowering efficacy. Therefore the 80 mg dose of LIPEX should only be used in patients at high risk for cardiovascular

complications who have not achieve their treatment goals on lower doses and when the benefits are expected to outweigh the potential risks. In patients taking LIPEX 80 mg for whom an interacting agent is needed, a lower dose of LIPEX or an alternative statin regimen with less potential for drug-drug interactions should be used.

- The addition of information (including dose caps) in the drug interactions section of the **Warnings and Precautions** section
- Additional information in the **Interactions** section

A Prescriber Update will also be released shortly advising of restrictions to the 80 mg dose of simvastatin in New Zealand.

Use of high dose simvastatin

In New Zealand, simvastatin, combined with diet and exercise, remains the first-line cholesterol lowering treatment for patients with an estimated five year CVD risk of 15–20%. The usual dose is simvastatin 20–40 mg per day, which may be increased to 80 mg in patients who require intensive treatment. It is important to remember that the statin dose response is not linear, i.e. the 80 mg dose reduces LDL cholesterol by an additional 6% over the 40 mg dose.

In patients taking 80 mg simvastatin, consider switching to atorvastatin 40 mg daily, which is an equivalent dose. In addition, consider that the benefits of statin treatment for elderly people are less clear than in younger populations,[4] therefore older patients may benefit more from a reduction in dose.

For further information about prescribing statins see: "An update on statins", BPJ 30 (Aug, 2010).

To view previous Medsafe guidance on statin-induced myopathy see: "Statin interactions: reports of serious myopathy" Prescriber Update 2011;32(2), available from: www.medsafe.govt.nz.

References

1. U.S. Food and Drug Administration. FDA Drug Safety Communication: New restrictions, contraindications, and dose limitations for Zocor (simvastatin) to reduce the risk of muscle injury. Available from: www.fda.gov/Drugs/DrugSafety/ucm256581.htm (Accessed Aug, 2011).
2. SEARCH. Study of the Effectiveness of Additional Reductions in Cholesterol and Homocysteine. Available from: www.searchinfo.org (Accessed Aug, 2011).
3. MERCK. U.S. Prescribing information for simvastatin revised to include new limits on the use of the highest dose – 80 mg – and updated drug information. Available from: www.merck.com/newsroom/news-release-archive/prescription-medicine-news/2011_0608.html (Accessed Aug, 2011).
4. Mangin D, Sweeney K, Heath I. Preventive health care in elderly people needs rethinking. 2007 BMJ 335(7614):285-7.