MEDSAFE
NEW ZEALAND MEDICINES
AND MEDICAL DEVICES
SAFETY AUTHORITY
A BUSINESS UNIT OF
THE MINISTRY OF HEALTH
www.medsafe.govt.nz

1 June 2010

Ms Michelle Palmer
Natural Products NZ
PO Box 358
BLENHEIM

Dear Ms Palmer

Classification of magnesium sulfate and red yeast rice

The Medicines Classification Committee (MCC) is a Ministerial advisory committee whose terms of reference are to make recommendations to the Minister of Health regarding the classification of medicines as prescription medicines, restricted medicines or pharmacy-only medicines.

At its 43rd meeting, on Tuesday 13 April 2010, the MCC considered classifying magnesium sulfate as a restricted medicine in divided oral preparations except when containing 1.5 g or less of magnesium sulfate per recommended daily dose. The MCC also considered classifying red yeast rice as a prescription medicine. Further details of the MCC's decisions will be published in the minutes from the 43rd meeting (http://www.medsafe.govt.nz/profs/class/minutes.asp). I have attached the relevant extract from the minutes for your convenience.

Following discussion the MCC recommended that the classification of magnesium sulfate should be added to the agenda of the next meeting to allow the sector time to submit data on whether there is significant risk of harm. The classification has the potential to affect dietary supplements in New Zealand that include magnesium sulfate.

The MCC also recommended that a proposal to classify red yeast rice, which contains 10 mg/kg or more of lovastatin (monacolin K), as a prescription medicine, be added to the agenda of the next meeting. Lovastatin (also known as monacolin K) is found in red yeast rice and it has been developed as a pharmaceutical medicine. In their deliberations the MCC encouraged the sector to submit information to allow it to consider whether the normal 10 mg/kg exemption from scheduling should be applied or whether there is evidence to support the safe use of lovastatin at a concentration above this point.

Could you inform members of Natural Products NZ regarding the potential classification of magnesium sulfate and red yeast rice, and ask that any information is submitted to me, by Friday 27 August 2010, at Medsafe, PO Box 5013, Wellington 6145. I will ensure that the MCC considers all submissions when considering the classification of both magnesium sulfate and red yeast rice at the next meeting.

Yours sincerely

ANDREA

Andrea Kerridge
Secretary, Medicines Classification Committee
Product Regulation

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EXTRACT FROM THE MINUTES OF THE 43rd MEETING OF THE MEDICINES CLASSIFICATION COMMITTEE HELD IN THE MEDSAFE BOARDROOM, LEVEL 6, DELOITTE HOUSE 10 BRANDON STREET, WELLINGTON ON TUESDAY 13 APRIL 2010 COMMENCING AT 9:30am

8.1 New chemical entities which are not yet classified in New Zealand

8.1.1 Magnesium sulfate

Magnesium sulfate is available as Epsom salts in the heptahydrate complex. In April 2008, the Adverse Drug Reactions Advisory Committee in Australia concluded that there was considerable risk to consumers from a 950 mg dried magnesium sulfate preparation, indicated for the relief of occasional constipation. The Australian National Drugs and Poisons Schedule Committee decided to include an entry for magnesium sulfate, for human therapeutic use in divided oral preparations except when containing 1.5 g or less of magnesium sulfate per recommended daily dose, in Schedule 3 (restricted medicine).

It was recognised that this agenda item had the potential to affect dietary supplements in New Zealand that included magnesium sulphate.

The Committee were concerned that Medsafe had not received any submissions about this agenda item as it could indicate that the Dietary Supplement sector in New Zealand was unaware of this proposal. The Committee was not prepared to discuss the proposal further until it was satisfied that the non-pharmaceutical sector had been given the opportunity to make submissions. To allow further consultation to occur the Committee supported foreshadowing the classification of magnesium sulfate as a restricted medicine as a separate agenda item for the next meeting of the Committee. It was agreed that this classification would be added to the agenda of the next meeting to allow the sector time to submit data on whether there is a significant risk of harm.

Recommendation

That the discussion of whether magnesium sulfate in divided oral preparations except when containing 1.5 g or less of magnesium sulfate per recommended daily dose should be added to the New Zealand Schedule as a restricted medicine be included in the agenda of the next meeting.

That Medsafe should write to the peak body of the sector (Natural Products NZ) asking them to inform their members of the Committees' interest in magnesium sulphate.

8.1.4 Red yeast rice

Red yeast rice is a reddish purple fermented rice. When produced using certain strains of *Monascus purpureus* it contains quantities of pharmacologically active substances, including monacolins, which can inhibit HMG-CoA reductase. Lovastatin (also known as monacolin K) is one of the more potent monacolins found in red yeast rice, and it has been developed as a pharmaceutical medicine. The United States Food and Drug Administration,

and several other regulators, have approved products containing lovastatin to treat hypercholesterolaemia. Lovastatin is classified as a prescription medicine in these countries. In view of the known pharmacological activity of lovastatin, the Australian National Drugs and Poisons Schedule Committee recently created an entry for red yeast rice, for human therapeutic use, in Schedule 4 (prescription medicine).

The Committee considered harmonising with the above classification at the 42nd meeting and agreed to delay making a recommendation until further information on the indications and side effect profile of red yeast rice extract, which contains lovastatin, and a literature review of lovastatin, could be considered.

The harmonisation was considered now that the following further information had been provided by Medsafe:

a. prescribing information for mevacor, an approved medicine in the United States which contains lovastatin as the active ingredient, which provided an overview of the safety profile and pharmacology of lovastatin
b. an evaluation of a red yeast rice containing complementary medicine (cholesen) conducted by the Australian Therapeutic Goods Administration in 2008 which contained an overview of the posology of red yeast rice products, and the safety profile of red yeast rice and lovastatin
c. a report regarding choleson clinical studies, dated February 2008
d. a memorandum providing a review of lovastatin for the period from 1 February 2008 to 30 January 2010.

The side effect profile and literature review of lovastatin, covering the period 1 February 2008 to 30 January 2010, supported scheduling all HMG-CoA reductase inhibitors as a class entry in harmony with the Australian Schedule 4 (prescription medicine). The World Health Organisation side effect profile suggested that lovastatin should be classified as a prescription medicine (as in the United States) in the same way as other statins in New Zealand. The literature review confirmed that foods and dietary supplement products sold on the basis of their lovastatin content, such as red yeast rice and oyster mushrooms, may contain sufficient lovastatin to warrant coverage by such a class entry.

A previous Committee member had passed on a paper, dated 28 October 2009, entitled "Red yeast rice and hyperlipidemia; how strong is the evidence?" from the Medscape Family Medicine, Best Evidence Review. The review made a number of conclusions:

a. treatment with statins is associated with a reduction in cardiovascular risk, even among low-risk patients
b. there are variable estimates with regard to the prevalence of myopathy among statin users, and there is no consensus about the best means to treat statin-associated myopathy
c. previous research found that red yeast rice is significantly superior to placebo in the treatment of hyperlipidemia
d. in the current study which focused on patients with a history of statin-induced myopathy, red yeast rice was effective in reducing total and LDL cholesterol values effectively and safety.

The level of lovastatin (also known as monacolin K), present in red yeast rice products is known to be in excess of 10 mg/kg (the New Zealand cut-off for exemption from scheduling). The Committee noted that there had been no

submissions from the Dietary Supplements sector on this reclassification proposal despite several products being sold in New Zealand. Once again the Committee were concerned that the agenda item had not been identified by the relevant sector of the industry and that a decision to reclassify could have unexpected consequences.

The Committee therefore discussed foreshadowing the classification of red yeast rice which contained 10 mg/kg or more of lovastatin as a prescription medicine. While the Committee agreed there was sufficient data to schedule lovastatin as a prescription medicine, the Committee encouraged the sector to submit information to allow it to consider whether the normal 10 mg/kg exemption from scheduling should be applied or whether there is evidence to support the safe use of lovastatin at a concentration above this point.

Recommendation

That a proposal to classify red yeast rice, which contains 10 mg/kg or more of lovastatin (monacolin K), as a prescription medicine, be added to the agenda of the next meeting.

That Medsafe request the peak body of the natural health care products sector (Natural Products NZ) to inform its members of this proposal and ask that they submit information on the effect of the proposal on products containing red yeast rice.