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Subject: **Updated Hepatic Safety Information on Prexige™**

Dear Health Care Professional:

Prexige™ is a selective COX-2 inhibitor in the class of drugs called NSAIDs (non-steroidal anti-inflammatory drugs).

Novartis New Zealand Limited would like to inform you of important new safety information about serious liver side effects mainly observed with chronic use of doses higher than 100 mg of Prexige™ (lumiracoxib) tablets:

- In a recent review of international spontaneous post-marketing reports, eight cases of serious liver side effects have been reported, including two deaths, in patients on chronic treatment primarily at doses higher than Prexige™ 100 mg. Liver failure is a known rare but serious side effect of all COX-2 inhibitors and traditional non-steroidal anti-inflammatory drugs (NSAIDs).

- The 100 mg dose of Prexige™, which is the recommended dose worldwide for treatment of osteoarthritis, has not been associated with an unexpected increase in incidence of liver-related side effects for an osteoarthritis population treated with NSAIDs.

In order to manage the risk of liver toxicity with Prexige™, Novartis New Zealand Limited advises health professionals of the following:

- Prexige™ is now only available in the 100 mg tablets dosage form. Prexige™ is now only indicated for the symptomatic treatment of osteoarthritis (OA). The indications for primary dysmenorrhoea, acute pain and acute gout have been removed.

- Prexige 400 mg tablets are being recalled from pharmacies and must not be prescribed for any new patients. Prescribers should contact those existing patients taking the 400mg tablets and consider the use of other analgesics.

- The recommended dose of Prexige™ for osteoarthritis is 100 mg once daily, with or without food, for the shortest duration consistent with individual patient treatment goals. The 100 mg dose should not be exceeded as this does not provide any additional benefit and may increase the risk of adverse events. The patient's need for symptomatic relief and response to therapy should be re-evaluated periodically.

- Liver function monitoring is recommended at baseline and monthly thereafter while on therapy. Patients with a baseline AST/ALT > 1.5xULN should not be commenced on Prexige. Patient taking lumiracoxib who develop signs and/or symptoms suggestive of liver dysfunction should be investigated promptly. Prexige should be discontinued if elevations of AST/ALT > 3xULN occur.

- Patients who continue on Prexige™ 100 mg should return to their prescribing doctor as soon as possible for liver function monitoring, to be repeated at monthly intervals. Prescribers are asked to report any abnormal LFTs or hepatic reactions to CARM.

- Patients using Prexige 100mg tablets should be informed about the signs and symptoms of liver disease (i.e. nausea, vomiting, tiredness, weakness, loss of appetite, yellowing of skin or eyes (jaundice), easy bruising) and should be instructed to return to their doctor immediately if they have any of these signs and symptoms, rather than waiting until their next follow-up visit.

The clinical trial database for Prexige™ comprises approximately 40,000 patients from randomized, placebo and active controlled trials of up to one year duration, making it one of the largest bodies of evidence for any drug in its class. This includes the TARGET study involving more than 18,000 patients, which showed that Prexige™ significantly reduced serious gastrointestinal events without compromising cardiovascular safety compared to the NSAIDs naproxen and ibuprofen. In this study 6 cases (0.07%) of serious liver abnormalities were observed with Prexige. The abnormalities resolved on cessation of Prexige and no cases of liver failure, transplantation or death attributable to drug induced hepatitis were reported.

Since Prexige™ was first launched in July 2005, it is estimated that over seven million prescriptions have been issued worldwide. Prexige™ 100 mg once daily is approved for use in patients with osteoarthritis in more than 50 countries, including Canada, the European Union and Latin America.

Advice to Health Care Professionals:

Novartis New Zealand Limited is committed to ensuring that Prexige™ is prescribed appropriately with a full understanding of the risks and benefits of therapy. Patients taking Prexige™ who have any concerns about their medication should consult their healthcare provider.

Managing marketed health product-related adverse reactions depends on health care professionals and consumers reporting them. Reporting rates determined on the basis of spontaneously reported post-marketing adverse reactions are generally presumed to underestimate the risks associated with health product treatments. Any case of serious or unexpected adverse reactions, or abnormal liver function tests in patients receiving Prexige™ should be reported to Novartis or CARM at the following addresses

Novartis New Zealand Limited
Tel: 0800 650 555
Fax: 0800 650 493
e-mail address: nzsafety.phauno@novartis.com

Any suspected adverse reaction can also be reported to:

Centre for Adverse Reactions Monitoring (CARM)
Tel: 03 479 7247
Fax: 03 479 7150
e-mail address: carmnz@stonebow.otago.ac.nz

Should you have any questions or require additional information regarding the use of Prexige™, please contact Novartis Medical Information at 0800 650 422.

Sincerely,

Peter Sharpe General Manager Novartis New Zealand Limited		Martyn Gillam Regulatory Affairs & Quality Assurance Manager

CARM
CENTRE FOR ADVERSE REACTIONS MONITORING

Adverse Reactions to Medicines, Vaccines and Devices and all clinical events for IMMP

CARM fax: 03 479 7150
CARM phone: 03 479 7247

PATIENT DETAILS HP3442

Surname:	First Name/s:	NHI No.	
Address:		Date of Birth:	Sex:
		Ethnicity:	

ALL MEDICINES IN USE * ASTERISK SUSPECT MEDICINE/S * Include over-the-counter (OTC) & alternative medicines

Medicine or Vaccine+batch no.	Daily Dose	Route	Date Started	Date Stopped	Reason for Use

DESCRIPTION OF ADVERSE REACTION OR EVENT

Date of onset: .....

Recovered ☐ Not yet recovered but improved ☐ Not yet recovered ☐ Unknown ☐ Fatal ☐ - Date of Death: .....

Severe? - Yes ☐ No ☐ Rechallenged? - No ☐ Yes ☐ Result: .....

OTHER FACTORS - Please tick or specify as appropriate

Renal disease ☐ Allergy ☐: ..... Other Medical Conditions: .....

Hepatic disease ☐ Nutritional Suppl or OTC use ☐: ..... Industrial Chemicals ☐: .....

REPORTER - Please tick as appropriate: Doctor ☐ Pharmacist ☐ Dentist ☐ Nurse ☐ Other ☐:.....

Name:

Address: Signature: .....

Phone: ..... Date: .....