The Marketed Health Products Directorate (MHPD), Therapeutic Products Directorate (TPD) and Biologics and Genetic Therapies Directorate (BGTD) post safety alerts, public health advisories, press releases and other notices as a service to health professionals, consumers, and other interested parties. Although MHPD, TPD and BGTD approve therapeutic products, MHPD, TPD and BGTD do not endorse either the product or the company. Any questions regarding product information should be discussed with your health professional.

This is a letter issued by the **Marketed Health Products Directorate** and the **Therapeutic Products Directorate**

IMPORTANT SAFETY INFORMATION regarding repaglinide (GlucoNorm®)

June 16, 2003

Dear Health Professionals,

EMEA contraindicates the concomitant use of repaglinide and gemfibrozil.

The Marketed Health Products and Therapeutic Products Directorates wish to draw your attention to new information **regarding important safety concerns on the use of repaglinide.**

On May 21, 2003, the European Agency for the Evaluation of Medicinal Products (EMEA) posted a warning on its website contraindicating the concomitant use of repaglinide and gemfibrozil, and recommending that physicians whose patients were already receiving the two drugs reassess and place these individuals on alternative combination treatment. Patients were warned about the risk of severe or prolonged hypoglycemia when gemfibrozil was added, even if previously stable on repaglinide, and were instructed to contact their treating physician.

These recommendations were based on a recent scientific publication[1], which indicated that the plasma concentrations of repaglinide were greatly increased by gemfibrozil (a lipid-lowering agent) and the blood glucose-lowering effect was enhanced and prolonged. This increases the risk of severe hypoglycemia and five reports of serious hypoglycemic episodes in patients on concomitant repaglinide and gemfibrozil treatment have been received by EMEA.

Repaglinide, a blood glucose-lowering drug, is indicated in the management of type 2 diabetes. Severe hypoglycemia, which can be fatal, is a known complication of agents that increase the secretion of insulin. There is one repaglinide product that is currently marketed in Canada as GlucoNorm® by Novo Nordisk Canada Inc.

The complete text of the EMEA warning can be accessed:
http://www.emea.eu.int/pdfs/human/press/pus/1170003en.pdf

Health Canada has requested that Novo Nordisk Canada Inc. issue a Dear Health Professional Letter and a Public Advisory contraindicating the concomitant use of repaglinide and gemfibrozil.

References:

1 Niemi M, Backman JT, M. Neuvonen M, Neuvonen PJ **Effects of gemfibrozil, itraconazole, and their combination on the pharmacokinetics and pharmacodynamics of repaglinide: potentially hazardous interaction between gemfibrozil and repaglinide** *Diabetologia* 2003; 46: 347-351

Any suspected adverse reactions can also be reported to:

Canadian Adverse Drug Reaction Monitoring Program (CADRMP)
Marketed Health Products Directorate
HEALTH CANADA
Address Locator: 0201C2
OTTAWA, Ontario, K1A 1B9
Tel: (613) 957-0337 or Fax: (613) 957-0335
Toll free for consumers and health professionals:
Tel: 866 234-2345, Fax: 866 678-6789
cadrmp@hc-sc.gc.ca

The AR Reporting Form and the AR Guidelines can be found on the TPD web site or in *The Canadian Compendium of Pharmaceuticals and Specialties*.