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 from industry 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 issued by the **Marketed Health Products Directorate** and the **Therapeutic Products Directorate.**

IMPORTANT SAFETY INFORMATION REGARDING THE DISPENSING OF CLOZAPINE

November 11, 2003

Dear Pharmacist,

The Marketed Health Products and Therapeutic Products Directorates (MHPD and TPD) seek your collaboration by drawing your attention to **an essential element in the dispensing of the currently marketed clozapine brands, as set out in the INDICATIONS[1] Section of the approved Product Monographs;**

The switching of a patient from one brand of clozapine to another **should not be done unless** the pharmacist obtains a **new, registry-specific** patient registration form filled out by the prescribing physician.

This is necessary because the monitoring systems for the clozapine products are independent, one for each sponsor. Since it is the prescribing physician who is ultimately responsible for verifying a patient's hematological/non-rechallengable status as stated in the "Indications" section of the PM[1], the physician must know which monitoring system the patient is registered in, so as to be able to send and/or request a patient's hematological / non-rechallengable status to the appropriate system.

In addition, when starting a new patient on clozapine, Health Canada encourages the dispensing pharmacist to verify the patient's hematological/non-rechallengeable status with **all** existing clozapine registries[2].

Health Canada's regulatory role is to establish conditions and essential safety requirements for the use of drugs, which are indicated in the official Canadian Product Monograph (PM). In contrast to most other drug products, the safe dispensation of clozapine requires registration of treating physicians, dispensing pharmacists and patients in manufacturer-specific distribution systems[1]. Therefore, the switching of clozapine brands in a multi-source environment necessitates specific steps to ensure safety. The principles behind these steps have been set out in the PM, with the statement that details on distribution systems can be obtained from the manufacturers who administer these systems.

It is Health Canada's position that the safe dispensing of clozapine in the context of multiple distribution registries relies on the cooperation of prescribing physicians, dispensing pharmacists and on an efficient exchange of information between Health Professionals and the registries. The need for this DHPL, which identifies the specific area in the PM where expansion is required, was recognized following actual marketing experience with clozapine in a multisource environment.

original signed by

Robert Peterson, MD MPH PhD
Director General
Therapeutic Products Directorate

original signed by

David Clapin, BSc, PhD for
Christopher Turner, MD FRCPC
Director General
Marketed Health Products Directorate

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1 ***"INDICATIONS***
. . . BRAND-NAME clozapine is available only through a distribution system (SYSTEM NAME) that ensures weekly or every-fwo-week hematological testing prior to the dispensing of the next period's supply of BRAND NAME clozapine (see WARNINGS).

This requires.

- registration of the patient, their current location, treating physician, testing laboratory and dispensing pharmacist in the SYSTEM NAME.

- maintenance of a national SPONSOR-specific database that enables the monitoring of the hematological results of all patients on BRAND-NAME clozapine and provides timely feedback (within 24 hours of receipt of the blood test results) to the treating physician and dispensing pharmacist/or pharmacy.

- the ability to identify patients who have been assigned "Non-rechallengeable Status" (see WARNINGS). This requires that SPONSOR both provide to. and obtain from all other ***approved suppliers**** *of clozapine, the Non-rechallengeable Status/Hematological Status of all patients (see DOSAGE AND ADMINISTRATION). SPONSOR must be able to provide this information within 24 hours of receiving a written request. "*

"Physicians should not prescribe BRAND NAME clozapine until the non-rechallengeable status and the hematological status of the patient has been verified.

For the distribution system to be effective, treating physicians must ensure that the hematological testing is performed at the required frequency (see WARNINGS) and that the hematological results are sent to SYSTEM NAME ."

**** : " approved supplier" is a manufacturer who holds a valid Notice of Compliance (NOC) for clozapine***

2 *Novartis Canada Inc. CSAN® - distribution registry 1-800-267-2726*
Genpharm Inc. GenCAN®-distribution registry 1-866-501-3338, http://www.gencan.ca

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*.