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Vol. 138, No. 40 — October 2, 2004

## Regulations Amending the Food and Drug Regulations (1373 — Schedule F)

*Statutory authority*

*Food and Drugs Act*

*Sponsoring department*

Department of Health



### REGULATORY IMPACT ANALYSIS STATEMENT

*(This statement is not part of the Regulations.)*

#### *Description*

The Therapeutic Products Directorate (TPD) of Health Canada intends to update Schedule F to the *Food and Drug Regulations* of the *Food and Drugs Act* by adding 15 medicinal ingredients to Part I of Schedule F, and amending the listing for one medicinal ingredient in Part I of Schedule F.

Schedule F is a list of medicinal ingredients, the sale of which are controlled under sections C.01.041 to C.01.046 of the *Food and Drug Regulations*. Part I of Schedule F lists medicinal ingredients that require a prescription for both human and veterinary use in Canada. Part II of Schedule F lists medicinal ingredients that require a prescription for human use, but do

not require a prescription for veterinary use if so labelled or if in a form unsuitable for human use. The review and introduction of new drugs onto the Canadian market necessitates periodic revisions to Schedule F.

The Drug Schedule Status Subcommittee reviews the status of chemical entities proposed for marketing. A decision regarding the necessity for prescription versus nonprescription status was made for each of the medicinal ingredients listed in this proposed amendment on the basis of established and publicly available criteria. These criteria include, but are not limited to, concerns relating to toxicity, pharmacologic properties, and therapeutic applications. Proposed revisions to current listings on Parts I and II of Schedule F are also based on decisions made by this Subcommittee.

#### New listings

It is proposed that the following 15 medicinal ingredients be added to Part I of Schedule F:

1. Anti-thymocyte globulin — an immunosuppressant. Anti-thymocyte globulin (equine- and rabbit-sourced) is used to reduce the immune response in patients who have received skin, cardiac, liver, or bone-marrow transplants. Anti-thymocyte globulin will be administered as an adjunct to other immunosuppressant therapy to delay the onset of the first rejection episode of a transplant. Because of this, the safe use of anti-thymocyte globulin requires individualized instructions and direct practitioner supervision.
2. Bivalirudin — a direct thrombin inhibitor. Bivalirudin is used to prevent blood clotting in patients with unstable angina, specifically those who are undergoing procedures to eliminate areas of narrowing in cardiac blood vessels. Treatment with bivalirudin requires supervision by a physician during administration to monitor status and institute prompt supportive care if required.
3. Drotrecogin — an anti-thrombotic profibrinolytic anti-inflammatory enzyme. Drotrecogin is used to treat patients with severe sepsis (sepsis associated with acute organ dysfunction), who have a high risk of death. Sepsis is the presence of pathogenic microorganisms, or their toxins, in the blood or tissues. Medical surveillance is required during administration of drotrecogin due to the increased risk of

bleeding and other undesirable side effects.

4. Dutasteride — a Type I and II 5 Alpha-reductase inhibitor. Dutasteride is used for the treatment of benign prostatic hyperplasia, enlargement of the prostate, and for the prevention and control of urologic events caused by the enlarged prostate gland. Prior to treatment with dutasteride a thorough medical assessment must be carried out to rule out other urological diseases such as prostate cancer.

5. Enfuvirtide — an antiviral agent and HIV fusion inhibitor. Enfuvirtide is used for the treatment of the human immunodeficiency virus (HIV), a life-threatening illness that destroys critical parts of the immune system. Specialized knowledge is required to treat HIV disease and the many infections that characterize the advanced stages.

6. Ertapenem and its salts — an antibiotic. Ertapenem sodium is used for the treatment of certain infections when caused by susceptible bacteria in adults; for example, complicated intra-abdominal, urinary tract and skin and skin structure infections and acute pelvic infections. Ertapenem has the potential to cause hypersensitivity and other adverse reactions, and must therefore be used under the supervision of a medical practitioner.

7. Ezetimibe — a cholesterol absorption inhibitor. Ezetimibe is used in patients with various lipid (water-insoluble fats and fatlike substances) disorders. It acts by preventing the absorption of cholesterol from the gastro-intestinal tract. Effective treatment with ezetimibe requires diagnosis and monitoring by a physician.

8. Fondaparinux sodium — a synthetic antithrombotic. Fondaparinux sodium is used to prevent the formation of blood clots in the blood, specifically the blood vessels of the legs or lungs following orthopaedic surgery such as hip or knee surgery. Fondaparinux possesses the potential to cause severe side effects even at normal therapeutic dosage levels.

9. Formoterol and its salts — long-acting beta-2 adrenergic receptor agonist. Formoterol fumarate is used for the treatment of asthma as well as chronic obstructive pulmonary disease. It helps dilate the larger air passages of the lungs (bronchi), causing relaxation of muscle fibres, as well as providing improvement in lung function. Formoterol has not been in

clinical use for a sufficient period of time to establish a pattern or frequency of long-term effects in humans, and thus requires direct medical supervision.

10. Levetiracetam — an anti-epileptic. Levetiracetam is used for patients with epilepsy whose seizures are not satisfactorily controlled by conventional therapy. As with all anti-epileptic drugs, it should be prescribed by a physician experienced in the treatment of seizures, and its administration and dosage should be supervised by a physician who can carefully determine the appropriate dose for the individual patient.

11. Pimecrolimus — an ascomycin macrolactam derivative to inhibit secretion of inflammatory cytokine (non-antibody proteins). Pimecrolimus is used for the treatment of mild to moderate atopic dermatitis (inflammation of the skin) in patients in whom the use of alternative, conventional therapies is deemed inadvisable because of potential risks, or in the treatment of patients who are not adequately responsive to or intolerant of alternative, conventional therapies. Long-term studies are lacking with pimecrolimus, and thus its toxicity profile cannot be fully assessed. Pimecrolimus must be administered under the supervision of a medical practitioner.

12. Rosuvastatin and its salts — a lipid metabolism regulator to be used for various lipid disorders (high levels of fatty substances in the blood). Rosuvastatin calcium is used in patients with excess cholesterol or other elevated levels of lipids in the blood. It is used as an adjunct to diet, to reduce elevated total cholesterol, particularly when patients' response to diet and exercise alone has been inadequate. The margin of safety is narrow in certain populations, and may produce undesirable or severe side effects at normal therapeutic dosages.

13. Telithromycin and its salts and derivatives — an antibacterial agent. Telithromycin is used for the treatment of select infections caused by susceptible bacteria; for example, community-acquired pneumonia, acute bacterial infections related to chronic bronchitis, and pharyngitis/tonsillitis. Telithromycin has the potential for adverse interactions with other drugs, and must therefore be administered under the supervision of a medical practitioner.

14. Tenofovir and its salts and derivatives — an antiretroviral agent. Tenofovir disoproxil fumarate is used for the treatment

of human immuno-deficiency virus (HIV), a life-threatening illness that destroys critical parts of the immune system. Specialized knowledge is required to treat HIV disease and the many infections that characterize the advanced stages.

15. Treprostinil and its salts — a vasodilator. Treprostinil sodium is used in the treatment of pulmonary arterial hypertension (PAH). PAH is a rare but serious blood vessel disorder of the lungs in which the pressure in the pulmonary artery rises above normal levels and may become life threatening. The dose of treprostinil sodium must be individualized, and therefore close medical supervision is required to monitor the pulmonary antihypertensive efficacy of the drug.

Metoprolol and its salts

It is proposed that the current English listing for "Metoprolol and its salts (*Métoprolol et ses sels*)" in Part I of Schedule F be amended to the appropriate spelling:

Metoprolol and its salts  
*Métoprolol et ses sels*

#### *Alternatives*

The degree of regulatory control coincides with the risk factors associated with each specific medicinal ingredient. The review of the information filed by the sponsor of these drugs has determined that prescription status is required at this time. Advice from a medical practitioner is necessary to ensure that consumers receive adequate risk/benefit information before taking the medication.

Any alternatives to the degree of regulatory control recommended in this regulatory initiative would need to be established through additional scientific information and clinical experience.

No other alternatives were considered.

#### *Benefits and costs*

The amendment would impact on the following sectors:

— Public

Prescription access to the drugs in Schedule No. 1373 would benefit Canadians by decreasing the opportunities for improper use and by ensuring professional guidance and care.

— Pharmaceutical industry

The classification of these drugs as prescription products would make their sale subject to professional intervention.

— Health insurance plans

These drugs, when assigned prescription status, may be covered by both provincial and private health care plans.

— Provincial health care services

The provinces may incur costs to cover physicians' fees for services. However, the guidance and care provided by the physicians would reduce the need for health care service that may result from improper use of these drugs. The overall additional costs for health care services should therefore be minimal.

*Consultation*

The manufacturers affected by this proposed amendment were made aware of the intent to recommend these medicinal ingredients for inclusion in Part I of Schedule F at the time of market authorization for the drugs.

Direct notice of this regulatory proposal was provided to the provincial and territorial deputy ministers of Health, provincial and territorial drug program managers, deans of pharmacy, registrars of provincial medical and pharmacy associations, industry and consumer associations, regulatory and health professional associations, and other interested parties on December 8, 2003, with a 30-day comment period. This initiative was also posted on the Therapeutic Products Directorate Web site. Three comments were received regarding the proposed amendment in the Letter to the Stakeholders; the stakeholders had no objections to the regulatory proposal.

A 75-day comment period will be provided upon publication in

the *Canada Gazette*, Part I.

*Compliance and enforcement*

This amendment would not alter existing compliance mechanisms under the provisions of the *Food and Drugs Act* and the *Food and Drug Regulations* enforced by the Health Products and Food Branch inspectorate.

*Contact*

Ms. Georgina Georgilopoulos, Policy Division, Bureau of Policy, Therapeutic Products Directorate, Holland Cross, Tower B, 2nd Floor, 1600 Scott Street, Address Locator 3102C5, Ottawa, Ontario K1A 1B6, (613) 941-6226 (telephone), (613) 941-6458 (facsimile), georgina\_georgilopoulos@hc-sc.gc.ca (electronic mail).

**PROPOSED REGULATORY TEXT**

Notice is hereby given that the Governor in Council, pursuant to subsection 30(1) ([see footnote a](#)) of the *Food and Drugs Act*, proposes to make the annexed *Regulations Amending the Food and Drug Regulations (1373 — Schedule F)*.

Interested persons may make representations with respect to the proposed Regulations within 75 days after the date of publication of this notice. All such representations must cite the *Canada Gazette*, Part I, and the date of publication of this notice and be addressed to Georgina Georgilopoulos, Therapeutic Products Directorate, Department of Health, Address Locator 3102C5, Holland Cross, 1600 Scott Street, 2nd Floor, Tower B, Ottawa, Ontario K1A 1B6 (fax: (613) 941-6458; e-mail: georgina\_georgilopoulos@hc-sc.gc.ca).

Persons making representations should identify any of those representations the disclosure of which should be refused under the *Access to Information Act*, in particular under sections 19 and 20 of that Act, and should indicate the reasons why and the period during which the representations should not be disclosed. They should also identify any representations for which there is consent to disclosure for the purposes of that Act.

Ottawa, September 29, 2004

EILEEN BOYD  
*Assistant Clerk of the Privy Council*

**REGULATIONS AMENDING THE FOOD AND  
DRUG REGULATIONS (1373 — SCHEDULE F)**

AMENDMENTS

**1. The reference to**

**Metoprolol and its salts**  
***Métoprolol et ses sels***

**in Part I of Schedule F to the *Food and Drug Regulations***  
**[\(see footnote 1\)](#) is replaced by the following:**

Metoprolol and its salts  
*Métoprolol et ses sels*

**2. Part I of Schedule F to the Regulations is amended by  
adding the following in alphabetical order:**

Anti-thymocyte globulin  
*Sérum antithymocytes*

Bivalirudin  
*Bivalirudine*

Drotrecogin  
*Drotrécogine*

Dutasteride  
*Dutastéride*

Enfuvirtide  
*Enfuvirtide*

Ertapenem and its salts  
*Ertapénem et ses sels*

Ezetimibe  
*Ézétimibe*

Fondaparinux sodium  
*Fondaparinux sodique*

Formoterol and its salts  
*Formotérol et ses sels*

Levetiracetam  
*Lévétiracétam*

Pimecrolimus  
*Pimécrolimus*

Rosuvastatin and its salts  
*Rosuvastatine et ses sels*

Telithromycin and its salts and derivatives  
*Télithromycine et ses sels et dérivés*

Tenofovir and its salts and derivatives  
*Ténofovir et ses sels et dérivés*

Treprostinil and its salts  
*Tréprostiniil et ses sels*

#### COMING INTO FORCE

**3. These Regulations come into force on the day on which they are registered.**

[40-1-o]

#### [Footnote a](#)

S.C. 1999, c. 33, s. 347

#### [Footnote 1](#)

C.R.C., c. 870

**NOTICE:**

The format of the electronic version of this issue of the Canada Gazette was modified in order to be compatible with hypertext language (HTML). Its content is very similar except for the footnotes, the symbols and the tables.

  
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