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Registration

SOR/2008-207 June 12, 2008

FOOD AND DRUGS ACT

Regulations Amending the Food and Drug Regulations (1508 2014; Schedule F)

P.C. 2008-1060 June 12, 2008

Her Excellency the Governor General in Council, on the recommendation of the Minister of Health, pursuant to subsection 30(1) (see footnote a) of the *Food and Drugs Act* (see footnote b), hereby makes the annexed *Regulations Amending the Food and Drug Regulations (1508 2014; Schedule F)*.

REGULATIONS AMENDING THE FOOD AND DRUG REGULATIONS (1508 2014; SCHEDULE F)

AMENDMENT

1. Part I of Schedule F to the *Food and Drug Regulations* (see footnote 1) **is amended by adding the following in alphabetical order:**

Nicotinic acid when sold in

(*a*) a modified-release oral dosage form that provides 500 mg or more per dosage unit or per daily dose; or

(*b*) an immediate-release oral dosage form that provides more than 500 mg per dosage unit or per daily dose

Acide nicotinique vendu sous l2019;une des forme suivantes :

a) *en forme posologique 00E0; lib00E9;ration modifi00E9;e fournissant, par unit00E9; posologique ou par dose quotidienne, 500 mg ou plus d2019;acide nicotinique administr00E9; par voie orale;*

b) *en forme posologique 00E0; lib00E9;ration imm00E9;diate fournissant, par unit00E9; posologique ou par dose quotidienne, plus de 500 mg d2019;acide nicotinique administr00E9; par voie orale*

COMING INTO FORCE

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

REGULATORY IMPACT ANALYSIS STATEMENT

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

Description

This amendment adds one medicinal ingredient to Part I of Schedule F to the *Food and Drug Regulations*.

Schedule F is a list of medicinal ingredients, the sale of which is controlled under sections C.01.041 to C.01.049 of the *Food and Drug Regulations*. Part I of Schedule F lists ingredients that require a prescription for human use and for veterinary use. Part II of Schedule F lists 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 Drug Schedule Status Committee determines the necessity for prescription status for medicinal ingredients on the basis of established and publicly available criteria. These criteria include, but are not limited to, concerns related to toxicity, pharmacological properties and therapeutic uses of the ingredients.

Description of the medicinal ingredient:

Nicotinic acid when sold in

(*a*) a modified-release oral dosage form providing 500 mg or more per dosage unit or per daily dose; or

(*b*) an immediate-release oral dosage form providing more than 500 mg per dosage unit or per daily dose

Nicotinic acid at these doses acts as a lipid metabolism regulating agent and is used for the treatment of patients with abnormally high levels of cholesterol in the blood. Diagnosis by a practitioner is required to rule out other causes of high blood cholesterol levels and to determine that other treatments have not been effective. Individualized instructions and direct supervision by a practitioner are required because nicotinic acid has been associated with liver toxicity when administered in modified-release formulations. Liver toxicity has also been associated with immediate-release formulations when administered at doses greater than 500 mg.

Modified-release dosage forms are defined in the Health Canada guidance document, ***Guidance for Industry 2014; Conduct and Analysis of Bioavailability and Bioequivalence Studies (Part B: Oral Modified Release Formulations)***, as drug formulations that differ from conventional formulations in the rate at which the drug is released. For the purpose of this guidance, modified release dosage

forms include formulations designed to meet one or more of the following objectives:

- To delay disintegration, de-aggregation, or dissolution so that the drug2019;s rate of degradation is altered;
- To delay or decrease the rate of absorption so that the likelihood of gastrointestinal or other adverse effects is diminished (e.g., enteric-coated forms);
- To provide effective drug concentrations for a longer period of time after a single dose;
- To deliver the drug initially at a rate similar to that obtained with the conventional form, and to provide effective drug concentrations for a longer period of time;
- To minimize fluctuations in drug concentrations during the dosing interval; and
- To provide, after single administration, multiple peaks and troughs in the serum concentration-time curves similar to those achieved after repeated dosing with the conventional formulation.

The degree of regulatory control afforded by Schedule F (prescription drug) status coincides with the risk factors associated with each medicinal ingredient. Oversight by a practitioner is necessary to ensure that appropriate risk/benefit information is considered before the drug containing the medicinal ingredient is administered and that the drug therapy is properly monitored.

Alternatives

The initial proposal, as part of Project No. 1451, included only the extended-release dosage form providing 500 mg or more per dosage unit or per daily dose. In response to comments received during the consultation process, the proposal was reconsidered and has been revised.

Any alternatives to the degree of regulatory control provided by this amendment would have to be established through additional scientific information and clinical experience.

Benefits and costs

The amendment impacts on the following sectors.

Public

Prescription access to drug products containing this medicinal ingredient will benefit Canadians by decreasing the opportuneities for improper use and by ensuring the guidance and care of a practitioner.

Another benefit is that drug products for human use containing medicinal ingredients listed on Schedule F may be covered by both provincial and private health care plans.

Health insurance plans

Drug products for human use containing medicinal ingredients listed

on Schedule F may be a cost covered by both provincial and private health care plans.

Provincial health care services

The provinces may incur costs to cover practitioners2019; fees for services. However, the guidance and care provided by the practitioners may reduce the need for health care services that may result from improper use of drug products for human use that contain medicinal ingredients listed on Schedule F. The overall additional costs for health care services should therefore be minimal.

Consultation

Direct notice of the regulatory proposal was provided to provincial and territorial ministers of health, medical and pharmacy licensing bodies, and industry, consumer and professional associations on July 28, 2006 with a 75-day comment period. This initiative was also posted on the Health Canada Web site and the 201C;Consulting With Canadians201D; Web site. The process for this consultation with stakeholders is described in the Memorandum of Understanding (MOU) to streamline regulatory amendments to Schedule F. The MOU signed by Health Canada, the Privy Council Office and the Department of International Trade on February 22, 2005, is posted on the Health Canada Web site. Comments were received from two respondents regarding the proposed amendment. One respondent had no objections to the regulatory proposal.

One respondent objected to the wording of the amendment, requesting that it be revised to provide prescription status for the immediate-release 500 mg oral dosage form. The respondent raised the following issues:

> 2014;00A0;the scientific basis for different prescription dose limits between immediate-release and modified-release dosage forms, especially concerning liver toxicity; and
>
> 2014;00A0;concerns about potential adverse effects, such as transient episodes of low blood pressure in the elderly, with the immediate-release 500 mg dose;

Response:

Liver toxicity

The scientific data indicates that a 500 mg dose of immediate-release nicotinic acid does not result in liver toxicity. However, some modified-release dosage forms of nicotinic acid do cause liver toxicity at a 500 mg dose.

Flushing and transient episodes of low blood pressure

While immediate-release nicotinic acid in doses of 500 mg or less has been associated with adverse or undesirable effects such as flushing, dizziness, increased heart rate and shortness of breath, these effects are not immediately life threatening and are reversible on

discontinuation of treatment and can be mitigated through labeling. The modified-release dosage forms generally produce less of the transient flushing side effect experienced with the immediate-release dosage form.

Compliance and enforcement

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

Contact

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Footnote a
2002;S.C. 1999, c. 33, s. 347

Footnote b
2002;R.S., c. F-27

Footnote 1
2002;C.R.C., c. 870

00A0;

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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Important notices

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