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Publication of Schedule of Amendments

Publication d'une liste de modifications

Please be advised that the following Schedule appears in the *Canada Gazette*, Part II of:

Veillez prendre note que l'annexe qui suit apparaît dans la Partie II de la *Gazette du Canada*, du :

DATE 19 May, 2004

DATE 19 mai 2004

REGISTRATION: SOR/2004-108 4 May, 2004

ENREGISTREMENT : DORS/2004-108 4 mai 2004

SCHEDULE

Food and Drugs Regulations - Amendment - Schedule F - Schedule 1329

ANNEXE

Règlement sur les aliments et drogues - Modification - annexe F - annexe 1329

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Policy Division/Division de la politique

Attachments

Pièces jointes

(SOR/DORS)

Her Excellency the Governor General in Council, on the recommendation of the Minister of Health, pursuant to subsection 30(1)¹ of the *Food and Drugs Act*, hereby makes the annexed *Regulations Amending the Food and Drug Regulations (1329 – Schedule F)*.

REGULATIONS AMENDING THE FOOD AND DRUG REGULATIONS (1329 –
SCHEDULE F)

AMENDMENTS

1. The reference to

Amfebutamone and its salts
Amfébutamone et ses sels

in Part I of Schedule F to the *Food and Drug Regulations*² is repealed.

2. The reference to

Melarsomine and its salts, for human use, or for veterinary use
in the treatment of heartworm in dogs

Mélarsomine et ses sels, destinés à l'usage humain ou à l'usage vétérinaire dans le traitement du ver du coeur chez le chien

in Part I of Schedule F to the Regulations is replaced by the following:

Melarsomine and its salts, when sold for the treatment of heart worm in dogs

Mélarsomine et ses sels, s'ils sont vendus pour le traitement du ver du coeur chez le chien

3. The reference to

Omeprazole
Oméprazole

in Part I of Schedule F to the Regulations is replaced by the following:

Omeprazole and its salts

Oméprazole et ses sels

4. The reference to

Praziquantel
Praziquantel

in Part I of Schedule F to the Regulations is replaced by the following:

Praziquantel, except when sold for the treatment of the tapeworm *Anoplocephala perfoliata* in horses

*Praziquantel, sauf s'il est vendu pour le traitement du ver solitaire *Anoplocephala perfoliata* chez les chevaux*

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

Alteplase and its salts and derivatives
Altéplase, ses sels et dérivés

Anakinra and its salts and derivatives
Anakinra, ses sels et dérivés

Atipamezole and its salts
Atipamézole et ses sels

Bimatoprost and its derivatives
Bimatoprost et ses dérivés

Bupropion and its salts
Bupropione et ses sels

Carprofen and its salts and derivatives
Carprofène, ses sels et dérivés

Ganirelix and its salts and derivatives
Ganirélix, ses sels et dérivés

Glimepiride
Glimépiride

Ivermectin and its derivatives, for human use or for veterinary use when sold for intramuscular injection into horses or for oral administration to dogs and cats
Ivermectine et ses dérivés, destinés à l'usage humain ou à l'usage vétérinaire, s'ils sont vendus pour injection intramusculaire aux chevaux ou pour administration par voie orale aux chiens et aux chats

Medetomidine and its salts
Médétomidine et ses sels

Moxidectin and its derivatives, when sold for the prevention of heartworm in dogs
Moxidectine et ses dérivés, s'ils sont vendus pour la prévention du ver du coeur chez le chien

Orbifloxacin and its salts and derivatives
Orbifloxacine, ses sels et dérivés

Palivizumab
Palivizumab

Romifidine and its salts
Romifidine et ses sels

Tegaserod and its salts
Tégasérod et ses sels

Thyrotropin alfa
Thyrotropine alfa

Tiotropium bromide
Tiotropium (bromure de)

Tolfenamic acid and its salts and derivatives
Tolfénamique (acide), ses sels et dérivés

Unoprostone and its salts and derivatives
Unoprostone, ses sels et dérivés

Valdecoxib and its salts
Valdécoxib et ses sels

Valganciclovir and its salts and derivatives
Valganciclovir, ses sels et dérivés

6. The reference to

Ivermectin, except when sold or recommended for intramuscular injection into horses or for administration to dogs
Ivermectine, sauf si elle est vendue ou recommandée pour injection intramusculaire aux chevaux ou pour administration aux chiens

in Part II of Schedule F to the Regulations is repealed.

COMING INTO FORCE

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

REGULATORY IMPACT ANALYSIS STATEMENT

(This statement is not part of the regulation)

Description

This amendment updates Schedule F to the *Food and Drug Regulations* of the *Food and Drugs Act* by adding 19 medicinal ingredients to Part I of Schedule F, amending 4 medicinal ingredients in Part I of Schedule F, and transferring 1 medicinal ingredient from Part II to 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 which require a prescription for both human and veterinary use. Part II of Schedule F lists medicinal ingredients which 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 may require periodic revisions to Schedule F.

The Therapeutic Products Directorate's Drug Schedule Status Subcommittee reviews the status of medicinal ingredients contained in new drugs 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 a review of evidence against 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

The following 19 medicinal ingredients are being added to Part I of Schedule F:

1. **Alteplase and its salts and derivatives** -an enzyme used to dissolve blood clots. It is used to restore function to certain intravenous devices by dissolving obstructive blood clots. It is also used as a treatment for acute myocardial infarction (heart attack)and stroke. The safe use of alteplase requires initial physician diagnosis and assessment followed by monitoring for adverse reactions such as bleeding.
2. **Anakinra and its salts and derivatives** - an interleukin-1 receptor antagonist. Anakinra is used to treat adults with

active rheumatoid arthritis to reduce the signs and symptoms of the disease. It can be used alone or in combination with other disease-modifying antirheumatic drugs. This medicinal ingredient should be used in patients only after diagnosis and appropriate assessment by a physician. Appropriate follow up is required because use of anakinra has been associated with an increased incidence of serious infections.

3. **Atipamezole and its salts** - an alpha-2 adrenergic receptor antagonist. This medicinal ingredient is used to reverse the effects of alpha-2 adrenergic receptor agonists which are sedative agents for minor surgical or medical procedures or used as pre-anaesthetic agents. Atipamezole should only be administered under the direct supervision of a practitioner.
4. **Bimatoprost and its derivatives** - a medicinal ingredient to reduce elevated pressure within the eye. Bimatoprost is used to treat patients who have elevated pressure within the eye, including glaucoma. It is for use in patients who cannot be treated with other pressure lowering medication due to intolerance or insufficient response. Patients using bimatoprost require diagnosis and regular monitoring by a physician. Glaucoma is a major cause of blindness if not diagnosed and treated properly.
5. **Carprofen and its salts and derivatives** - a non-steroidal anti-inflammatory drug (NSAID). Carprofen is indicated for use in dogs for the relief of pain and inflammation associated with osteoarthritis. Professional veterinary expertise is required to diagnose osteoarthritis in dogs. Carprofen can cause severe (life-threatening) adverse effects at normal therapeutic dosage levels in dogs. Professional veterinary expertise is required to monitor treated dogs for signs of adverse reactions.
6. **Ganirelix and its salts and derivatives** - a gonadotropin-releasing hormone (GnRH) antagonist. Ganirelix is used as part of the treatment for assisted reproduction techniques including in-vitro fertilization (IVF - fertilization of an egg in a test tube). Ganirelix allows the release of an egg to be controlled so that it occurs at an optimal time for pregnancy to occur. Although the product may be self-administered by the patient, ganirelix requires direct physician supervision and continuous laboratory monitoring.
7. **Glimepiride** - an oral hypoglycemic agent. Glimepiride is used to lower the blood glucose of patients with type 2 diabetes whose high blood glucose levels cannot be controlled by diet and exercise alone. The safe use of glimepiride requires initial physician diagnosis and assessment followed by

regular monitoring of the product's effectiveness and side effects.

8. **Medetomidine and its salts** - a alpha-2 adrenergic receptor agonist. Medetomidine is used in animals as a sedative agent for minor surgical or medical procedures or a pre-anaesthetic agent. This medicinal ingredient should only be administered under the direct supervision of a veterinarian. Medetomidine possesses the potential for undesirable or severe side effects at normal therapeutic dosage levels.
9. **Moxidectin and its derivatives** - Moxidectin is used as an antiparasitic for the prevention of heartworm in dogs. The safe use of moxidectin involves testing for existing heartworm infection by a licenced veterinarian before administration of the product.
10. **Orbifloxacin and its salts and derivatives** - a synthetic broad spectrum antibacterial agent. Orbifloxacin is used for the treatment of skin and soft tissue infections in dogs and cats and for the treatment of urinary tract infections in dogs. Professional veterinary expertise is required to diagnose and treat infections in these animals.
11. **Palivizumab** - a humanized monoclonal antibody produced by recombinant DNA technology. This medicinal ingredient is administered by monthly intramuscular injections to high-risk children for the prevention of serious lower respiratory tract disease caused by respiratory syncytial virus. The safe and effective use of palivizumab requires initial diagnosis by a physician and monitoring for side effects.
12. **Romifidine and its salts** - a potent alpha-2 adrenergic receptor agonist. Romifidine is used in animals as a sedative agent and for pain relief during minor surgical or medical procedures or as a pre-anaesthetic agent. This medicinal ingredient should only be administered under the direct supervision of a veterinarian. Romifidine possesses the potential for undesirable or severe side effects at normal therapeutic dosage levels.
13. **Tegaserod and its salts** - a 5-HT₄ receptor partial agonist. Tegaserod is used to treat the symptoms of irritable bowel syndrome with constipation in female patients whose main symptoms are constipation and abdominal pain and/or discomfort. A physician's diagnosis and supervision is necessary to ensure that the appropriate individuals receive tegaserod for the appropriate period of time. A physician must monitor the duration and severity of the side effects that may be associated with the use of the medicinal ingredient and take corrective action if necessary.

14. **Thyrotropin alfa** -human thyroid stimulating hormone produced by recombinant DNA technology. Thyrotropin alfa is a diagnostic tool used in conjunction with other tests in the follow-up of patients with certain kinds of thyroid cancer. The use of thyrotropin alfa should be directed by physicians knowledgeable in the management of patients with thyroid cancer.
15. **Tiotropium bromide** - anticholinergic agent. Tiotropium bromide is a bronchodilator for the treatment of chronic obstructive pulmonary disease including chronic bronchitis and emphysema. The safe and effective use of tiotropium bromide requires initial diagnosis by a physician followed by continued supervision to assess effectiveness and monitor for side effects.
16. **Tolfenamic acid and its salts and derivatives** - a non-steroidal anti-inflammatory drug (NSAID). Tolfenamic acid is used to alleviate inflammation and pain associated with osteoarthritis in dogs with hip dysplasia. It is also used as an aid in the treatment of upper respiratory diseases and as symptomatic treatment of fever in cats. Tolfenamic acid was approved for use without prescription in dogs in 1997 and cats in 1999. Some adverse reactions with serious consequences have been reported following use in these animals. Changes in product labelling are being required to address target species safety concerns. In addition, Veterinary Drugs Directorate is recommending that tolfenamic acid be added to Schedule F. Professional veterinary expertise is required for appropriate use of this medicinal ingredient and to monitor treated animals for signs of adverse reactions.
17. **Unoprostone and its salts and derivatives** - a medicinal ingredient to reduce elevated pressure within the eye. Unoprostone is used to treat patients who have elevated pressure within the eye, including glaucoma. It is for use in patients who cannot be treated with other pressure lowering medication due to intolerance or insufficient response. Patients using unoprostone require diagnosis and regular monitoring by a physician. Glaucoma is a major cause of blindness if not diagnosed and treated properly.
18. **Valdecoxib and its salts** - a nonsteroidal anti-inflammatory drug (NSAID). Valdecoxib is used to treat the signs and symptoms of osteoarthritis and rheumatoid arthritis in adults. It is also indicated for the relief of menstrual pain. The safe and effective use of valdecoxib requires the supervision of a physician to monitor for side effects and adverse reactions.

19. **Valganciclovir and its salts and derivatives** - an antiviral agent. Valganciclovir is used to treat inflammation of the retina of the eye caused by cytomegalovirus (CMV) in patients with acquired immunodeficiency syndrome (AIDS). Specialized ophthalmology equipment and knowledge are required to make the diagnosis of CMV retinitis. There is a narrow margin of safety between therapeutic and toxic doses of this medicinal ingredient. Close monitoring of blood counts while on therapy is important.

Revised listings

The listings of 5 medicinal ingredients presently included in Schedule F are being revised:

Amfebutamone

"Amfebutamone and its salts" is being removed from Part I of Schedule F and replaced with "Bupropion and its salts". International Nonproprietary Names (INN) are assigned by the World Health Organization and are the only internationally accepted generic names for medicinal ingredients. When available, the INN is used exclusively in identifying medicinal ingredients on Schedule F. Amfebutamone was the INN assigned in 1973 for the medicinal ingredient also known as bupropion. In 2001 bupropion was adopted as the INN for this medicinal ingredient to replace amfebutamone. To be consistent, Health Canada is amending Part I of Schedule F to reflect this change.

Melarsomine

As no human use has been identified for this medicinal ingredient, the listing of Melarsomine is being amended to exclude human use on Part I of Schedule F. Therefore, the amended description will now be:

Melarsomine and its salts, when sold for the treatment of heartworm in dogs.

Mélarso mine et ses sels, s'ils sont vendus pour le traitement du ver du coeur chez le chien

Omeprazole

Omeprazole is being amended in Part I of Schedule F to include its salts:

Omeprazole and its salts

Oméprazole et ses sels

Praziquantel

Praziquantel currently is listed in Part I of Schedule F without any qualifications or exceptions. That means a prescription is required for all human and veterinary uses. Praziquantel is used as an antiparasitic. The indications for

use of this medicinal ingredient have been extended to include treatment of horses infected with the tapeworm, *Anoplocephala perfoliata*. This use is not considered to require veterinary supervision. Therefore, this use in horses is being excluded from Part I of Schedule F. The revised wording is:

Praziquantel, except when sold for the treatment of the tapeworm *Anoplocephala perfoliata* in horses
Praziquantel, s'il est vendu pour le traitement du ver solitaire Anoplocephala perfoliata chez les chevaux

Ivermectin

Ivermectin currently is listed in Part II of Schedule F as:

Ivermectin, except when sold or recommended for intramuscular injection into horses or for administration to dogs.

Ivermectine, sauf si elle est vendue ou recommandée pour injection intramusculaire aux chevaux ou pour administration aux chiens

The listing in Part II of Schedule F is being moved to Part I while keeping the same status regarding its use in horses and dogs. This is in keeping with an ongoing clean-up of Schedule F to eliminate inconsistencies and to remove potentially confusing 'exception listings' from Part II.

In addition, the listing in Part I is being amended to include the derivatives of ivermectin and to add a restriction regarding veterinary use in cats. The new listing is:

Ivermectin and its derivatives, for human use or for veterinary use when sold for intramuscular injection into horses or for oral administration to dogs and cats.

Ivermectine et ses dérivés, destinés à l'usage humain ou à l'usage vétérinaire s'ils sont vendus pour injection intramusculaire aux chevaux ou pour administration par voie orale aux chiens et aux chats

Alternatives

The recommended 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 medicinal ingredients 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 drug.

Any alternatives to the degree of regulatory control recommended in this initiative would have to be established

through additional scientific information and clinical experience.

No other alternatives were considered.

Benefits and Costs

The amendment impacts on the following sectors:

- **Public**

Prescription access to the medicinal ingredients affected by Project 1329 benefits Canadians by decreasing the opportunities for improper use, and by ensuring professional guidance and care.

- **The Pharmaceutical Industry**

The industry is permitted to market new medicinal ingredients with appropriate supervision.

- **Health Insurance Plans**

These medicinal ingredients, 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 services that may result from improper use of the medicinal ingredients. The overall additional costs for health care services should therefore be minimal.

Consultation

The manufacturers affected by this proposed amendment were informed of the intent to recommend these medicinal ingredients for inclusion on Schedule F at the time of market approval of the drugs.

Direct notice of this regulatory proposal was provided to the Provincial Ministries of Health, medical and pharmacy licensing bodies, and industry associations on July 10, 2003 with a 30-day comment period. This initiative was also posted on the Therapeutic Products Directorate Website. No comments from external stakeholders were received.

The proposed amendment was then published in the *Canada Gazette*, Part I on October 11, 2003, with a 75 day comment period. The proposal was posted on the Therapeutic Products Directorate Website. One supportive response was received.

Compliance and Enforcement

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

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