The Emergency Drug Release Program: regulatory aspects of new drug access in Canada

Ian Gilron, MD

La nécessité de traiter des maladies contre lesquelles aucun médicament commercialisé n'existe au Canada a donné lieu à la création du Programme de médicaments d'urgence (PMU), qui est fondé sur une stricte autorité législative et qui fonctionne selon des lignes directrices administratives particulières. Récemment, on a apporté des changements à la réglementation — la mise en oeuvre de protocoles de «traitement» et d'«accélération» de l'approbation des médicaments — pour permettre l'accès aux médicaments non commercialisés et réduire le volume des approbations de médicaments traitées par le PMU. De même, la réglementation du PMU est en cours de modification pour veiller à l'accès sécuritaire et rapide aux médicaments expérimentaux.

The Food and Drug Regulations[1] of Canada's Food and Drugs Act[2] were amended in 1954 to specifically address the sale and distribution of new drugs. The revised regulations required that (a) a submission for a new drug be filed before the drug was marketed and (b) before marketing approval the drug be studied by qualified investigators in approved clinical trials. Subsequently, the need arose to provide unmarketed drugs to treat illnesses for which no drug therapy existed in Canada and for which the enrolment into or the development of an investigational protocol was unfeasible. This led to further amendments to the Food and Drug Regulations to provide for the sale of new drugs for emergency treatment[3] and to the development of the Emergency Drug Release Program (EDRP), which is administered by the Health Protection Branch, Department of National Health and Welfare, Ottawa.[4]

Since its inception the EDRP has released over 600 essential drugs before their approval for sale in Canada, and approximately 900 Canadian physicians use the program in any given month. Over the past decade the Canadian drug regulatory process has undergone changes that have significantly affected the EDRP. As well, the Health Protection Branch recently proposed legislative revisions that may modify the program.[5] The purpose of this article is to review current legislation and procedures of the EDRP and to discuss proposed changes to the program.

Legislative authority and procedure

The legislative authority of the EDRP is outlined in Table 1.

Table 2 describes the administrative guidelines for obtaining approval from the EDRP to use an emergency drug. The EDRP is becoming a centralized program equipped to authorize the release of all classifications of human prescription drugs.

After the EDRP authorizes a drug's use the manufacturer has the legal right to provide or restrict access to the drug and to impose a fee. The emergency use of an investigational drug necessitates a judicious risk:benefit analysis in the context of the clinical situation. Factors to be considered include the patient's clinical condition and prognosis, the response to other therapies, and the safety and efficacy of the requested drug. Information in addition to the requirements outlined in Table 2 may be requested from the practitioner if a favourable risk:benefit profile is not evident.

EDRP authorization is given on an individual basis only, and the previous authorization of a drug does not imply automatic authorization in subsequent requests for the drug. As well, EDRP authorization does not imply Health Protection Branch

From the Bureau of Human Prescription Drugs, Health Protection Branch, Department of National Health and Welfare, Ottawa, Ont.

Reprint requests to: Dr. Ian Gilron, 5022 Jean-Brillant St., Montreal, PQ H3W 1T7

endorsement or approval of the drug — it simply allows legal access.

To comply with the emergency drug regulations physicians must provide written feedback on the patient's response to treatment, particularly any adverse reactions. The evaluation of submitted information establishes a basis for the continued release of a drug. This surveillance protects against health hazards through the discontinuation, when necessary, of the release of drugs that cause particularly severe or frequent adverse reactions that would implicate an unfavourable risk:benefit profile.

Regulatory changes

In 1988 the demands of the acquired immunodeficiency syndrome (AIDS) epidemic on the drug regulatory process gave rise to the implementation of "treatment," or "compassionate," protocols that allow physician-investigators to use unmarketed drugs to treat seriously ill patients.[6] These are less rigorous than the usual protocols for drugs under investigation and may be implemented more rapidly while substantial information on the drug's safety and efficacy is being gathered. As well, by forgoing strict entrance criteria the treatment protocols allow seriously ill patients who might otherwise be ineligible for a clinical trial to have access to the drug. Since their introduction such protocols have been used in the investigation of several illnesses other than AIDS.

Recently procedures were proposed to allow for the "fast-tracking" of submissions for new drugs intended for the treatment of acute life-threatening illnesses and other serious diseases for which no comparable drug is marketed in Canada.[7]

In addition to the EDRP these regulatory changes demonstrate alternative ways for the Canadian public to have safe and timely access to new drugs.

On Aug. 8, 1991, a Health Protection Branch information letter[5] was distributed to Canadian drug manufacturers and health care professionals for their comments on proposed regulatory changes to the EDRP. At the time of writing, the proposed regulations had received public comment and were to be appropriately revised for publication in Part I of the *Canada Gazette*. Once the revised regulations have

Table 1: Legislative authority of the Emergency Drug Release Program (EDRP) for the sale of new drugs for emergency treatment

Section C.08.010

(1) The Director may issue a letter of authorization authorizing the sale of a quantity of a new drug for human or veterinary use to a practitioner named in the letter of authorization for use in the emergency treatment of a patient under the care of that practitioner, if
  (a) the practitioner has supplied to the Director information concerning
    (i) the medical emergency for which the drug is required,
    (ii) the data in the possession of the practitioner with respect to the use, safety and efficacy of that drug,
    (iii) the names of all institutions in which the drug is to be used, and
    (iv) such other data as the Director may require; and
  (b) the practitioner has agreed to
    (i) report to the manufacturer of the new drug and to the Director on the results of the use of the drug in the medical emergency, including information respecting any adverse reactions encountered, and
    (ii) account to the Director on request for all quantities of the drug received by him.

(2) The Director shall, in any letter of authorization issued pursuant to subsection (1), state
  (a) the name of the practitioner to whom the new drug may be sold;
  (b) the medical emergency in respect of which the new drug may be sold; and
  (c) the quantity of the new drug that may be sold to that practitioner for that emergency.

Section C.08.011

(1) Notwithstanding section C.08.002, a manufacturer may sell to a practitioner named in a letter of authorization issued pursuant to section C.08.010, a quantity of the new drug named in that letter that does not exceed the quantity specified in the letter.

(2) A sale of a new drug made in accordance with subsection (1) is exempt from the provisions of the Act and these Regulations.

Table 2: Administrative guidelines for obtaining approval from the EDRP to use an emergency drug

The physician or a delegated representative (e.g., nurse, pharmacist or medical resident) can make the initial request either in writing or, if urgent, by telephone or facsimile between the hours of 0830 and 1630 Eastern Time; tel. (613) 993-3105, after hours (613) 991-0123; fax (613) 993-1350.

The request should include the following.
  (i) Physician's name and telephone number
  (ii) Address of physician's office or hospital pharmacy where the drug is to be distributed
  (iii) Drug name and dosage form (e.g., tablet, capsule)
  (iv) Manufacturer's name
  (v) Total quantity of drug requested
  (vi) Intended dosage
  (vii) Patient's initials, age, sex and condition

Once the request is approved the drug manufacturer will be contacted promptly by telephone and given authorization to release the drug. An official authorization letter will be sent later and a copy forwarded to the attending physician.

Under urgent circumstances most North American pharmaceutical companies can ship the drug within 24 hours after a request, depending on the destination.

been published, additional comments will be accepted for 60 days before the recommendations are submitted to the Governor in Council. The final regulations will then be published in Part II of the *Canada Gazette*.

A key element of the proposed regulations is a procedure to release an emergency drug in a block. This procedure will allow a drug manufacturer to apply for a certificate that authorizes the sale of an emergency drug to several practitioners for a particular medical emergency. The regulations define "emergency drug" and "medical emergency" and expand the Conditions of Issuance for authorization. They also stipulate that the Health Protection Branch can refuse to authorize the sale of a drug if the Conditions of Issuance are not satisfied and may require the manufacturer to submit samples of the drug.

A recent report[8] made several recommendations on the future of the EDRP. One stated that the EDRP should become a strictly administrative procedure, because "safety is the responsibility of the attending physician who makes the risk:benefit decision."[9] This report also emphasized the continuing need for the EDRP and its accessibility to all Canadian physicians. The upcoming changes to the EDRP should be followed to understand and maximally benefit from this vital program.

References

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