

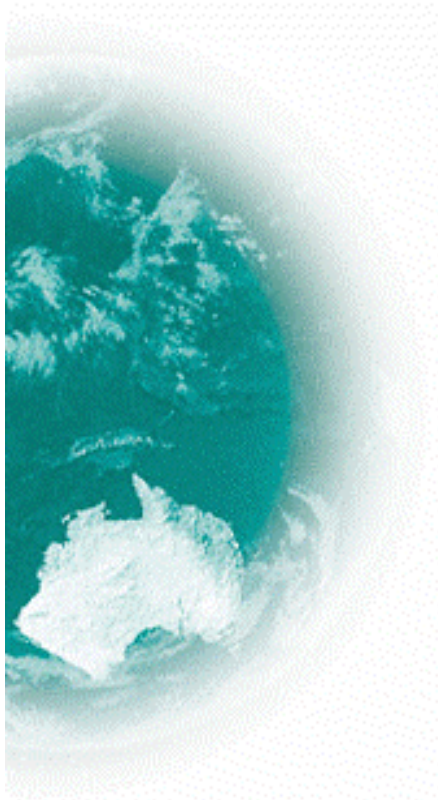


**Australian Government**  

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**Department of Health and Ageing**  
**Therapeutic Goods Administration**

# **Australian Regulatory Guidelines for Prescription Medicines**



***June 2004***

## APPENDIX 8: PRODUCT INFORMATION

### 1. *Introduction*

The product information (PI) is regarded as a document that contains information sufficient to ensure safe and effective use of the medicine under nearly all circumstances. It is to present a scientific, objective account of the medicine's usefulness and limitations as shown by the data supporting the application. It is to be devoid of promotional material.

It is a condition of registration under Section 28 of the *Therapeutic Goods Act 1989* (the Act) that a PI be provided for each registered product. After registration, the PI must not be changed without TGA approval, except in the case of:

- safety related changes, which should be notified to the TGA under the conditions set out in Section 4.4.5.1 of the *Australian Regulatory Guidelines for Prescription Medicines* (ARGPM).

Section 9D(2) of the Act refers to Safety Related notifications (SRN). To be acceptable an SRN application must reduce the class of persons for whom the goods are suitable or add a warning, or precaution, that does not include any comparison of the goods with any other therapeutic goods by reference to quality, safety or efficacy. Review is limited to checking that the proposed SRN meets the above criteria. The acceptance letter sent to the sponsor after receipt of an SRN specifies that the TGA has not approved the entire PI, only the specified change.

- self-assessable changes to the quality aspects of the PI (Self-Assessable Notification, SAN) which are discussed in Section 4.4.5.2 and Appendix 12 of the the *Australian Regulatory Guidelines for Prescription Medicines* (ARGPM).
- some editorial changes, which should be notified to the TGA under the conditions set out in section 4.4.5.3 of the ARGPM.

Section 9D(3) of the Act refers to Minor Editorial Changes. To be acceptable an application for Minor Editorial Change must not be a SRN and the variation requested must not indicate any reduction in the quality, safety or efficacy of the goods for the purposes for which they are to be used. Review is limited to checking that the proposed Minor Editorial Change meets the criteria for Minor Editorial Change.

The PI should be supplied as a package inset for products for parenteral use. For self-administered parenterals, the Consumer Medicine Information (CMI) may be included as the package insert as well as, or in addition to, the PI.

The PI on radiopharmaceuticals should advise users to observe the National Health and Medical Research Council (NHMRC) *National guidelines for waste management in the health industry* (1999)<sup>1</sup>.

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<sup>1</sup> <http://www.nhmrc.gov.au/publications/pdf/eh11.pdf>

## 2. Contents

The PI should contain information under the following headings:

- i) Name of the medicine
  - The non-proprietary name of the substance, or in the case of a mixture of substances, of each therapeutically active ingredient;
  - The chemical structure should be included except in the case of inorganic salts and simple organic compounds (where a molecular formula may suffice), complex biological molecules such as large peptides and proteins (where a simpler schematic presentation of the structure may suffice), and substances where the structure is not defined;
  - CAS number
- ii) Description
  - A description of relevant physical and chemical characteristics of the medicine and its formulations. Australian Approved Names should be used;
  - Excipients should be listed for new product registrations (but may be included under (xi) Presentation). Inclusion of excipients is recommended for PI updates.
- iii) Pharmacology
  - The pharmacology, including pharmacokinetics and pharmacological actions, especially in humans.
- iv) Clinical trials
  - The Clinical Trials section should describe trials supportive of the indications;
  - If the product has been registered prior to 1991 and there have been no applications requiring ADEC advice since then it is unlikely that a suitable clinical trial will be available. In that case the Clinical Trials section shouldn't be added.
- v) Indications
  - The therapeutic applications of the medicine, clearly stating whether the treatment is curative, palliative, adjunctive, and including any conditions imposed by TGA.
- vi) Contraindications
  - Situations where patients should never or generally not be treated with the medicine. In rare cases where the medicine should never be given, this must be specifically outlined.
- vii) Precautions
  - Include information under the following sub-headings:

- Describe the circumstances where caution is required (for example, describe particular populations or clinical situations where dosage reduction is required);
- Describe the actions the health care professional should take (for example, specify particular investigations that may need to be carried out);
- Effects on fertility;
- Use in pregnancy.  
Include a proposed or approved Australian Pregnancy Categorisation, any relevant standard text and other information consistent with this categorisation. Also include effects on labour and delivery;
- Use in lactation;
- Paediatric use;
- Use in the elderly;
- Carcinogenicity;
- Genotoxicity;
- Interactions with other medicines.  
Include known clinically relevant interactions and other potentially serious interactions based on the pharmacology of the medicine. It is useful to group interactions according to outcome (for example, potentiation or reduction of effect) and to explain the mechanism of action where this is known;
- Effect on laboratory tests;

vii) Adverse effects

- An indication of severity, clinical importance and frequency should be given. This section of the PI should be written in CIOMS (Council for International Organizations of Medical Sciences) format.

viii) Dosage and administration

Include information on:

- dosage (dose and interval);
- dosage adjustment in:
  - renal insufficiency;
  - hepatic insufficiency;
  - dialysis;
  - concomitant disease;
- maximum tolerated daily dose and the maximum dose for an entire course of therapy;
- monitoring advice;
- other pertinent information such as relationship to meals and compatibility with other drugs and fluids.

ix) Overdosage

- The symptoms, signs and recommended treatment of overdosage or accidental poisoning;
- ADEC had made the following recommendations for the Overdosage section:

*Syrup of Ipecac and gastric lavage.* These are no longer considered to be standard therapy for gut decontamination. Reference to these interventions should be excluded from the PI.

*Activated charcoal.* If activated charcoal is considered to be potentially useful in the management of overdose of the drug, then a suitable statement for inclusion in the PI would be:

*Activated charcoal may reduce absorption of the drug if given within one or two hours after ingestion. In patients who are not fully conscious or have impaired gag reflex, consideration should be given to administering activated charcoal via a nasogastric tube, once the airway is protected.*

*Whole bowel irrigation.* Whole bowel irrigation may be useful in the management of overdose of slow release preparations with significant toxicity (eg. slow release calcium channel blockers) or drugs not absorbed by charcoal (eg. iron, lithium). If whole bowel irrigation is considered to be potentially useful in the management of overdose of the drug, then a suitable statement for inclusion in the PI would be:

*Whole bowel irrigation (eg. 1 or 2 litres of polyethylene glycol solution orally per hour until rectal effluent is clear) may be useful for gut decontamination.*

For all overdoses, the mainstay of treatment is supportive and symptomatic care. This should be emphasised before discussion of specific antidotes. Information on serious toxicity,  $T_{max}$ , elimination half-life (in the setting of overdose) and the effectiveness of haemodialysis and repeated doses of activated charcoal in removing the drug are very useful in the management of overdose. Any available information on these issues, including animal data, should be included. It is generally inappropriate to include  $LD_{50}$  values from the animal studies.

- x) Presentation and storage conditions
  - The presentation, including dosage form and quantity, proportion or strength of each therapeutically active ingredient;
  - The container type and pack sizes.
- xi) Name and address of the sponsor.
- xii) Poison schedule of the medicine
- xiii) Date of approval
  - Following approval for registration, the date of approval is to be given in the PI;
  - If the PI is changed at some time after approval, the PI must show the date of approval of the changed PI, except where notification or self-assessment is involved. In these cases, where the PI change does not require approval, the PI must show the date of the last TGA approval (if applicable) and the date of the most recent notification or self-

assessment which resulted in the change, as *Date of most recent amendment*.