Australian Government

Department of Health
Therapeutic Goods Administration

Instrument of Approval

Approved form for product information in relation to medicine under subsection 7D(1) of the *Therapeutic Goods Act 1989*

I, Larry Kelly, First Assistant Secretary of the Medicines Regulation Division and delegate of the Secretary of the Department of Health for the purposes of section 7D of the *Therapeutic Goods Act 1989* ("the Act"):

REVOKE any previous approvals made under subsection 7D(1) of the Act; and

APPROVE under subsection 7D(1) of the Act, in relation to medicine, the form in Schedule 1 to this instrument to be the form in which product information must be given to the Secretary with:

(a) an application for the registration of a restricted medicine in accordance with paragraph 23B(2)(e) of the Act;

(b) an application for the registration of any other medicine for which the Secretary has given notice that product information is to be provided in accordance with subparagraph 25(1)(da)(ii) of the Act;

(c) a response to a written notice of the Secretary requiring product information to be given under subsection 25AA(1B) of the Act; and

(d) a request to vary an entry in the Register under section 9D of the Act, in relation to a medicine, which would result in a variation to approved product information in accordance with paragraph 25AA(4)(c) of the Act.

COMMENCEMENT

This approval commences on 9 March 2018 ("the commencement").

TRANSITIONAL ARRANGEMENTS

This approval is subject to the following arrangements.

In this instrument –

an earlier approved form, in relation to product information, means a form approved in an instrument of approval made under subsection 7D(1) of the Act, including those approved on 12 May 2011 and 8 November 2017, as in force before the commencement of this instrument.

restricted medicine means the classes of medicines mentioned in Schedule 1 to the *Restricted Medicine Specification 2011*.

transition period means the period beginning on the commencement of this instrument and ending on 31 December 2020.

For the duration of the transition period, product information accompanying a request to vary an entry in the Register mentioned in paragraph (c) of this instrument, which is given to the Secretary in accordance with an earlier approved form, is taken to have been given in accordance with the approved form in Schedule 1 to this instrument.

INTERPRETATION

In this instrument and the approved form in Schedule 1 to this instrument –

ARTG is taken to mean the Register as defined in section 3 of the Act.

Australian Approved Name, in relation to a therapeutically active ingredient, means the name of that ingredient in the *Australian Approved Names List* – being a document defined in section 2 of the *Therapeutic Goods Regulations 1990* entitled Australian Approved Names List for Therapeutic Substances, as in force from time to time, and published by the Therapeutic Goods Administration.

date of first approval is taken to mean the date on which the Secretary included the medicine in the Register in accordance with paragraph 25AB(1)(e) of the Act.

date of revision is taken to mean, in relation to a medicine, the date on which the Secretary:

(a) provides notice to a person under subsection 25AA(4) of the Act that it is appropriate to vary the product information approved in relation to that medicine as a result of a variation to the relevant entry under section 9D of the Act; or

(b) approves product information under subsection 25AA(1) of the Act following a decision to register that medicine under subsection 25(3) of the Act, where the medicine is part of an existing gazetted therapeutic goods group determined by the Secretary under subsection 16(2) of the Act.

excipient has the same meaning as given in the *Therapeutic Goods Order No. 91 – Standard for labels of prescription and related medicines.*

gazetted therapeutic goods group has the same meaning as given in section 3 of the Act.

Poisons Standard is taken to mean the current Poisons Standard as defined in section 3 of the Act.

therapeutic indications is taken to mean indications as defined in section 3 of the Act.

Note A number of expressions used in this instrument and the approved form in Schedule 1 to this instrument are defined in the Act, including the following:

(a) container;

(b) dosage form;

(c) indications;

(d) medicine;

(e) presentation;

(f) product information;

(g) Register;

(h) restricted medicine;

(i) sponsor; and

(j) standard.

All headings, and information of the kind specified as mandatory standard text, in the approved form in Schedule 1 to this instrument must be included in product information unless indicated otherwise in the approved form.

To avoid any doubt, the information provided in the substantive dot points and the notes to the approved form in Schedule 1 to this instrument is provided to assist with the interpretation of the approved form, and is not intended to be reproduced in product information unless otherwise indicated.

LARRY KELLY
Delegate of the Secretary
8 March 2018

SCHEDULE 1 – Approved form for product information

The following form is approved for product information (PI) in relation to medicine under subsection 7D(1) of the *Therapeutic Goods Act 1989.*

AUSTRALIAN PRODUCT INFORMATION – TRADE NAME (ACTIVE INGREDIENT)

1 NAME OF THE MEDICINE

- The Australian Approved Name (AAN) of the therapeutically active ingredient or, in the case of a fixed dose combination or composite pack containing multiple therapeutically active ingredients, the AAN of each therapeutically active ingredient.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

- A description of the formulation(s) including quantity, proportion or strength of each therapeutically active ingredient.
- A description of clinically relevant physical and chemical characteristics of each therapeutically active ingredient.
- List of excipients with known effect, followed by the mandatory standard text 'For the full list of excipients, see Section 6.1 List of excipients.'

Note 1: For the purpose of this approved form, "quantitative composition" only relates to the quantity of the therapeutically active ingredient.

Note 2: Excipients with known effect are those listed in Schedule 1 to the *Therapeutic Goods Order No. 91 – Standard for labels of prescription and related medicines* and Schedule 1 to the *Therapeutic Goods Order No. 92 – Standard for labels of non-prescription medicines.*

Note 3: Australian Approved Names should be used for the excipients.

Note 4: For products registered prior to 1 January 2018, this section may be combined with section 3 under the heading '2 and 3 QUALITATIVE AND QUANTITATIVE COMPOSITION and PHARMACEUTICAL FORM'.

3 PHARMACEUTICAL FORM

- Presentation of the medicine, including information about:
    - dosage form; and
    - any other information relevant to the presentation or appearance of the medicine.

Note 5: The pharmaceutical form should be described by the AAN, together with a visual description of the appearance of the product (colour, markings, tablet scoring etc). In the case of products to be reconstituted before use, a reference to the appearance before reconstitution should be included.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

- The therapeutic indications of the medicine.

Note 6: The specific therapeutic uses should be stated clearly and concisely, and should define the target disease or condition, distinguishing between treatment (symptomatic, curative or modifying the evolution or progression of the disease), prevention (primary or secondary) and diagnostic indications. Mandatory conditions of product usage, where relevant, should also be included if not covered more appropriately in other parts of the PI.

4.2 DOSE AND METHOD OF ADMINISTRATION

- Dosage (dose and interval)
- Method of administration
- Dosage adjustment (if applicable) in:
    - renal impairment
    - hepatic impairment
    - dialysis
    - concomitant disease.
- If relevant, the maximum tolerated daily dose and the maximum dose for an entire course of therapy.
- Monitoring advice.
- Other relevant information such as relationship to meals and compatibility with other medicines and fluids.

4.3 CONTRAINDICATIONS

- A description of situations in which persons:
    - should never be treated with the medicine; and
    - should generally not be treated with the medicine.

Note 7: Situations where life threatening or fatal adverse reactions may occur can also be referred to.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Note 8: The circumstances where caution is required in relation to the medicine should be described. The actions the health care professional should take should also be described. Information on special warnings and precautions should include, but not be limited to, information of the kind listed below. Additional information can also be provided if appropriate.

Note 9: Examples of the circumstances where caution is required could be in relation to particular population groups or clinical situations where dosage adjustment is required.

Note 10: An example of the actions the health care professional should take could be to specify particular investigations that may need to be carried out.

Identified precautions

- Include identified precautions and special warnings specific to the use of the medicine under relevant subheadings.
- If not relevant, this subheading may be deleted from this section of the PI.

Note 11: Example subheadings include 'Hepatotoxicity', 'QT prolongation' etc. These should replace the term 'identified precautions' which is not intended as a subheading in the PI.

Use in hepatic impairment

- If relevant, include a precaution regarding use of the medicine in persons with hepatic impairment.
- If not relevant, this subheading may be deleted from this section of the PI.

Use in renal impairment

- If relevant, include a precaution regarding use of the medicine in persons with renal impairment.
- If not relevant, this subheading may be deleted from this section of the PI.

Use in the elderly

- This subheading is mandatory standard text. If no data are available, then a cross-reference to another relevant section or the following optional standard text may be included: 'No data available'.

Paediatric use

- This subheading is mandatory standard text. If no data are available, then a cross-reference to another relevant section or the following optional standard text may be included: 'No data available'.

Effects on laboratory tests

- This subheading is mandatory standard text. If no data are available, then a cross-reference to another relevant section or the following optional standard text may be included: 'No data available'.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

Note 12: In relation to interactions with other medicines or other forms of interaction (such as with food), include known clinically relevant interactions and other potentially serious interactions. Interactions should be grouped according to outcome, for example, potentiation or reduction of effect, and the mechanism of action should also be explained where this is known.

Note 13: If relevant, a cross-reference to 'Section 6.2 – Incompatibilities' may be included.

4.6 FERTILITY, PREGNANCY AND LACTATION

Note 14: The following subheadings are mandatory standard text. If no data are available, then the following optional standard text may be included: 'No data available'.

Effects on fertility

Use in pregnancy

Note 15: Include a proposed or approved Australian Pregnancy Categorisation, any relevant standard text for the class of medicine and other information consistent with this categorisation, as well as effects on labour and delivery.

Use in lactation

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

- Extent to which the medicine influences the ability of persons to drive or use machines.

Note 16: Medicines listed in Appendix K to the current Poisons Standard should include a sedation warning in this section.

Note 17: If the medicine was registered prior to 1 January 2018 and there is currently no statement regarding effects of ability to drive and use machines, then the following optional standard text may be included: 'The effects of this medicine on a person's ability to drive and use machines were not assessed as part of its registration'.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

- Severity, clinical importance and frequency of adverse effects.

Note 18: For clarity and consistency, the following format is preferred:

A table of adverse events (not adverse reactions) at a cut-off of, for example, 1% comparing the frequency of adverse events (n(%) or (%)) on drug with placebo/active comparator (if studies support this comparison) (usually very common and common);

A line listing of adverse reactions that fall below the cut-off by System Organ Classes (SOC) using CIOMS[1] frequencies (usually uncommon, rare); and

A post-marketing section of adverse reactions by system organ class using CIOMS frequencies (usually rare or very rare).

Reporting suspected adverse effects

- Information on how to report adverse events.

Note 19: This subheading is mandatory standard text, and the following mandatory standard text must be included in this section:

'Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at www.tga.gov.au/reporting-problems.'

[1] Council for International Organizations of Medical Sciences.

4.9 OVERDOSE

- Symptoms, signs and recommended treatment of overdose or accidental poisoning.

Note 20: The following mandatory standard text must be included under this heading:

For information on the management of overdose, contact the Poisons Information Centre on 131126 (Australia).

Note 21: 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 medicine are very useful in the management of overdose. Any available information on these issues, including animal data, should be considered for inclusion.

Note 22: If activated charcoal is considered to be potentially useful in the management of overdose of the medicine, then a suitable statement for inclusion would be:

'Activated charcoal may reduce absorption of the medicine 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.'

Note 23: 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 medicine not absorbed by charcoal (eg. iron, lithium). If whole bowel irrigation is considered to be potentially useful in the management of overdose of the medicine, then a suitable statement for inclusion 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.'

Note 24: Syrup of Ipecac and gastric lavage are no longer considered to be standard therapy for gut decontamination. Reference to these interventions therefore need not routinely be included.

Note 25: It is generally inappropriate to include LD_{50} values from any animal studies.

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Note 26: The following subheadings are mandatory standard text.

Mechanism of action

- The pharmacology and pharmacological actions of the medicine, especially in humans.

Clinical trials

- Clinical trials related to the indications, both positive and negative.

Note 27: If the medicine was registered prior to 1991 and there have been no applications to the Therapeutic Goods Administration requiring the advice of either the Australian Drug Evaluation Committee (ADEC) or the Advisory Committee on Prescription Medicines (ACPM) since then, it is unlikely that suitable clinical trial data will be available. In that case, the Clinical Trials section may include the optional standard text 'No data available'.

Note 28: For over the counter medicines not registered on the basis of clinical trial data, the Clinical Trials section may include the optional standard text 'No data available'.

5.2 PHARMACOKINETIC PROPERTIES

- Pharmacokinetics, especially in humans, with subheadings (if relevant) in the order shown below.

Absorption

Distribution

Metabolism

Excretion

5.3 PRECLINICAL SAFETY DATA

- Preclinical safety data with subheadings in the order shown below.

Genotoxicity

- This subheading is mandatory standard text. If no data are available, then the following optional standard text may be included: 'No data available'.

Carcinogenicity

- This subheading is mandatory standard text. If no data are available, then the following optional standard text may be included: 'No data available'.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

- Complete list of excipients, including those listed in section 2.

Note 29: Australian Approved Names should be used for the excipients.

Note 30: If the medicine was registered prior to 1 January 2018, the following optional standard text may be used in this section: 'Refer to Section 2 – Qualitative and quantitative composition.'

6.2 INCOMPATIBILITIES

- Information on physical and chemical incompatibilities of the medicine with other products with which it is likely to be mixed or co-administered.

Note 31: If the medicine was registered prior to 1 January 2018 and the approved PI did not require a statement on incompatibilities, then the following optional standard text may be used in this

section: 'Incompatibilities were either not assessed or not identified as part of the registration of this medicine.'

Note 32: If relevant, a cross-reference to 'Section 4.5 – Interactions with other medicines and other forms of interactions' may be included.

6.3 SHELF LIFE

- Duration of approved shelf-life

Note 33: The following optional standard text may be used in place of the shelf-life information in this section: 'In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.'

Note 34: If relevant, information on the in-use shelf life may be included in this section of the PI.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

- Storage conditions.

6.5 NATURE AND CONTENTS OF CONTAINER

- Container type.
- Pack sizes.

Note 35: Reference should be made to the immediate container for the medicine using the AAN and the material of construction of the immediate container (for example, "glass vials", "PVC/Aluminium blisters"). Any other component of the product should be listed (for example, needles, swabs, measuring spoons, syringes or inhaler devices). The container of any solvent provided with the medicine should also be described.

Note 36: All pack sizes should be listed. Pack sizes mentioned should include the number of units, total weight or volume of the immediate container (as appropriate) and the number of containers present in any outer carton.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

Note 37: If there are no special precautions for disposal, then one or other of the following optional standard text may be used in this section:

'In Australia, any unused medicine or waste material should be disposed of by taking to your local pharmacy.'

'In Australia, any unused medicine or waste material should be disposed of in accordance with local requirements.'

6.7 PHYSICOCHEMICAL PROPERTIES

Chemical structure

- The chemical structure of each therapeutically active ingredient, except in the case of therapeutically active ingredients that are:

- inorganic salts or simple organic compounds where a molecular formula may be included;
- complex biological molecules such as large peptides and proteins, where a simpler schematic presentation of the structure may be included; and
- substances where the structure is not defined.

CAS number

- The Chemical Abstracts Service (CAS) Registry Number of the medicine.

7 MEDICINE SCHEDULE (POISONS STANDARD)

- The schedule of the current Poisons Standard in which the medicine is included (if applicable).

8 SPONSOR

- Name, street address and contact details of the sponsor of the medicine.

Note 38: It is recommended that the PI include contact details such as an email address, phone number and/or website address for the sponsor.

Note 39: If the medicine was registered prior to 1 January 2018 and the approved PI did not include these details, then inclusion of the sponsor name and street address only is acceptable.

9 DATE OF FIRST APPROVAL

- Date of first inclusion in the Australian Register of Therapeutic Goods.

Note 40: To be completed when the medicine is included in the ARTG.

10 DATE OF REVISION

- Date of the most recent TGA approved changes to an approved PI.

Note 41: To be completed at the time of any approval of change(s) to the approved PI, including changes to tradenames or approval of additional tradenames.

Summary table of changes

Section changed	Summary of new information