Australian Government
Department of Health and Ageing
Therapeutic Goods Administration

OTC medicine monograph: Ibuprofen for oral use

Version 1.0, June 2013

TGA Health Safety Regulation

About the Therapeutic Goods Administration (TGA)

- The Therapeutic Goods Administration (TGA) is part of the Australian Government Department of Health and Ageing, and is responsible for regulating medicines and medical devices.
- The TGA administers the *Therapeutic Goods Act 1989* (the Act), applying a risk management approach designed to ensure therapeutic goods supplied in Australia meet acceptable standards of quality, safety and efficacy (performance), when necessary.
- The work of the TGA is based on applying scientific and clinical expertise to decision-making, to ensure that the benefits to consumers outweigh any risks associated with the use of medicines and medical devices.
- The TGA relies on the public, healthcare professionals and industry to report problems with medicines or medical devices. TGA investigates reports received by it to determine any necessary regulatory action.
- To report a problem with a medicine or medical device, please see the information on the TGA website <www.tga.gov.au>.

Confidentiality
All submissions received will be placed on the TGA's Internet site, unless marked confidential. Any confidential material contained within your submission should be provided under a separate cover and clearly marked "IN CONFIDENCE". Reasons for a claim to confidentiality must be included in the space provided on the TGA submission coversheet. For submission made by individuals, all personal details, other than your name, will be removed from your submission before it is published on the TGA's Internet site. In addition, a list of parties making submissions will be published. If you do not wish to be identified with your submission you must specifically request this in the space provided on the submission coversheet.

Version history

Version	Description of change	Author	Effective date
V1.0	Original Publication	OTC Medicines Evaluation /OMA	18/06/13

Contents

Introduction 5

Active substance, dosage forms and strengths 5

Active substance 5

Dosage forms and strengths 5

Indications 6

Required therapeutic indications for inclusion in the Australian Register of Therapeutic Goods 6

Label indications 6

Directions for use 7

Adults and children 7 years and over (solid dose oral preparations) 7

Children 3 months to 12 years (oral liquid suspension) 7

Labelling 10

Quality requirements 10

Active premixes 10

Finished product specifications 10

Coated tablets 10

Orally disintegrating tablets (uncoated) 11

Oral suspensions 11

Container/measuring device 12

Introduction

This OTC Medicine Monograph outlines the requirements for Australian market authorisation of oral medicines containing ibuprofen as a single active ingredient when applied for as an OTC New Product N2 application. Proposed products must comply with all aspects of the monograph relevant to their strength and dosage form to qualify for evaluation as an N2 application.

This monograph should be read in conjunction with the document Requirements for OTC new product N2 applications.

Active substance, dosage forms and strengths

Active substance

This monograph only applies to ibuprofen (CAS no. 15687-27-1) and excludes preparations containing any salts and derivatives of ibuprofen.

Dosage forms and strengths

Acceptable dosage forms and strengths are shown in the table below.

Active substance	Dosage strengths	Dosage forms (excludes modified release dosage forms)
Ibuprofen	200 mg	Coated tablets
	200 mg	Orally disintegrating tablets
	20 mg/mL (100 mg/5 mL)	Suspension, liquids
	40 mg/mL (200 mg/5 mL)	Suspension, liquids

Indications

Required therapeutic indications for inclusion in the Australian Register of Therapeutic Goods

Temporary relief of pain and/or inflammation associated with headache, migraine headache, tension headache, sinus pain, toothache, dental procedures, backache, muscular aches and pains, arthritis, osteoarthritis, rheumatic pain, period pain, fibrositis, neuralgia, sore throat, tennis elbow, and colds and flu. Reduces fever.

For paediatric formulations, in addition to any of the indications above that are appropriate to the age group, the following indications would be acceptable: relief of pain associated with teething, earache and/or immunisation.

Label indications

All or some of the indications listed above may be included as label claims, as appropriate, depending on the intended age group. Terms should be exactly as specified above and qualified by the words "temporary relief of pain [and/or inflammation] associated with...".

Directions for use

Adults and children 7 years and over (solid dose oral preparations).

Dosages must be as shown in the table below.

Dosage form and strength	Age	Single dose	Dose interval	Maximum daily dose
200 mg tablet	7 -12 years	1 tablet	Every 6-8 hours when necessary	4 tablets in 24 hours
200 mg tablet	Adults and children 12 years and over	1 – 2 tablets	Every 4-6 hours when necessary	6 tablets in 24 hours

Children 3 months to 12 years (oral liquid suspension)

Dosages for ibuprofen oral liquid suspension in children 3 months to 12 years must be consistent with those shown in the 'Recommended dosages' table below or, alternatively, with those shown in the 'Alternative acceptable dosages' table below.

Recommended dosages:

Age	Average body weight (kg)	Dose (mg)	Dose (mL) from 20 mg/mL suspension	Dose (mL) from 40 mg/mL suspension
3 – 6 months	6 – 8 kg	40 – 60 mg	2 – 3 mL	1 – 1.5 mL
6 – 12 months	8 – 10 kg	60 – 80 mg	3 – 4 mL	1.5 – 2 mL
1 – 2 years	10 – 12 kg	80 – 100 mg	4 – 5 mL	2 – 2.5 mL
2 – 3 years	12 – 14 kg	100 – 120 mg	5 – 6 mL	2.5 – 3 mL
3 – 4 years	14 – 16 kg	120 – 140 mg	6 – 7 mL	3 – 3.5 mL
4 – 5 years	16 – 18 kg	140 mg	7 mL	3.5 mL
5 – 6 years	18 – 20 kg	140 – 160 mg	7 – 8 mL	3.5 – 4 mL
6 – 7 years	20 – 22 kg	160 – 180 mg	8 – 9 mL	4 – 4.5 mL
7 – 8 years	22 – 25 kg	180 – 200 mg	9 – 10 mL	4.5 – 5 mL
8 – 9 years	25 – 28 kg	200 – 220 mg	10 – 11 mL	5 – 5.5 mL
9 – 10 years	28 – 32 kg	220 – 240 mg	11 – 12 mL	5.5 – 6 mL
10 – 11 years	32 – 36 kg	240 – 280 mg	12 – 14 mL	6 – 7 mL
11 – 12 years	36 – 41 kg	280 – 300 mg	14 – 15 mL	7 – 7.5 mL

Doses should be given every 6-8 hours as necessary, with no more than four doses in 24 hours.

Wider age ranges than those listed above could be specified for children aged 1 year and over. Age ranges of "1-3 years" or "2-4 years" would be acceptable, but "1-4 years" or "2-5 years" would not be acceptable. Beyond 3 years of age, age groupings of 2 or 3 years would be acceptable (eg. 2-4 years, 4-6 years... or 3-6 years, 6-9 years...). Doses must still be consistent with the above table. For children under 12 months, age ranges must be specified as shown in the table.

Alternative acceptable dosages:

Age	Average body weight (kg)	Dose (mg)	Dose (mL) from 20 mg/mL suspension	Dose (mL) from 40 mg/mL suspension
3 – 6 months	6 – 8 kg	60 – 80 mg	3-4 mL	1.5 – 2.0 mL
6 – 12 months	8 – 10 kg	80 – 100 mg	4-5 mL	2.0 – 2.5 mL
1 – 3 years	10 – 14 kg	100 – 140 mg	5-7 mL	2.5 – 3.5 mL
3 – 5 years	14 – 18 kg	140 – 180 mg	7-9 mL	3.5 – 4.5 mL
5 – 7 years	18 – 22 kg	180 – 220 mg	9 – 11 mL	4.5 – 5.5 mL
7 – 9 years	22 – 28 kg	220 – 280 mg	11 – 14 mL	5.5 – 7.0 mL
9 – 12 years	28 – 40 kg	280 – 400 mg	14 – 20 mL	7.0 – 10 mL

Doses should be given every 6-8 hours as necessary, up to 3 times a day

A product label could include only a subset of the age groups – for example, 7-10 years and 10-12 years only.

Doses must be presented on the labels with ages (in months or years), weights (kg) and volumes (mL). Dosage instructions must also include advice consistent with the following:

- If you know that your child's weight is less than the weight corresponding to their age in the table, choose the dose for their weight.

Labels must state the maximum daily dose. For liquid preparations that include doses for more than one age group, this should be stated as: *Do not give more than 4 doses in 24 hours* (or *3 doses in 24 hours*, depending on the doses specified).

Where dosage instructions for children under 12 months of age are included on the labels, the dosage instructions must include statements advising that:

- the product should not be given to infants under 3 months, and
- the product should only be given to infants aged 3-12 months following medical advice.

Requirements for measuring devices are included under Container/measuring device.

Labelling

Labelling must comply with all relevant Australian regulatory requirements, as detailed in the document Requirements for OTC new product N2 applications, including all required warning statements.

Quality requirements

In addition to the quality requirements outlined in the document Requirements for OTC new product N2 applications, the following specific requirements apply to ibuprofen monograph products:

Active premixes

Where ibuprofen is sourced by the finished product manufacturer as part of an active premix, the finished product manufacturer must, as a minimum, control the premix for appearance/description, identification (one chromatographic and one non-chromatographic test), assay, related substances, residue on ignition or sulfated ash, and heavy metals. The limits applied should be taken from either the BP or USP monograph for ibuprofen (with all limits to be taken from the same monograph), adjusted where necessary to account for the presence of excipients in the mixture (for example, assay). Additional requirements in relation to active premixes are specified in the document Requirements for OTC new product N2 applications.

Finished product specifications

In addition to other requirements specified in the document Requirements for OTC new product N2 applications, the finished product specifications must comply, at a minimum, with one of the sets of requirements below, as relevant. The requirements below include all relevant BP general monograph/USP General Chapter requirements and TGO78 requirements. Further reference to these is not required.

Coated tablets

The tests and limits in the BP monograph **Ibuprofen Tablets** with the addition of:

- tablet appearance
- dissolution (900 mL phosphate buffer pH 7.2, paddle at 50 rpm, 80% *(Q)* after 60 minutes)[1];
- uniformity of dosage units (BP);
- content of 4'-isobutylacetophenone[2] (NMT 0.3% wrt ibuprofen);

[1] from *Ibuprofen Tablets USP*

- test and limits for microbiological quality, in compliance with TGO 77.

Orally disintegrating tablets (uncoated)

The tests and limits in the USP monograph **Ibuprofen Tablets** with the addition of:

- tablet appearance
- tighter limits for ibuprofen content of 92.5-107.5% (in accordance with TGO78)
- BP/Ph. Eur test and limit (within 3 min) for disintegration, using *water R* at 15-25°C.
- test and limits for individual unspecified impurities (0.3%) and total impurities (0.7%)[3];
- test and limits for microbiological quality, in compliance with TGO 77.

Oral suspensions

The tests and limits in the BP monograph **Ibuprofen Oral Suspension** with the addition of:

- suspension appearance
- dissolution (900 mL phosphate buffer pH 7.2, paddle at 50 rpm, 80% *(Q)* after 60 minutes)[4];
- content of any preservatives included in the formulation;
- suitable test and limits for pH;
- suitable test and limits for viscosity;
- test and limits for individual unspecified impurities (0.3%) and total impurities (0.7%)[3];
- test and limits for microbiological quality, in compliance with TGO 77,

or

The tests and limits in the USP monograph **Ibuprofen Oral Suspension** with the addition of:

- suspension appearance
- content of any preservatives included in the formulation;
- suitable test and limits for viscosity;
- test and limits for individual unspecified impurities (0.3%) and total impurities (0.7%)[3].
- test and limits for microbiological quality, in compliance with TGO 77.

[2] Assay method specified for *Ibuprofen Oral Suspension BP* or *Ibuprofen Tablets USP* would be relevant. Alternative equivalent or superior method could be used if appropriately validated.
[3] Assay method specified for *Ibuprofen Tablets BP* would be relevant. Alternative equivalent or superior method could be used if appropriately validated.
[4] from *Ibuprofen Oral Suspension, USP*

Container/measuring device

- Ibuprofen products must be sold in containers that comply with Therapeutic Goods Order No 80, Child Resistant Packaging Requirements for Medicines.
- If a measuring device is to be supplied with the product, calibrations must be exclusively in metric units and must allow all the doses shown on the labels to be measured accurately. Details of the calibrations on the measuring device must be provided with the submission (a sample may also be requested). Further considerations and requirements regarding measuring devices are detailed in *ARGOM Appendix 2: Guidelines on quality aspects of OTC applications, 8. Finished product container*.

Therapeutic Goods Administration

PO Box 100 Woden ACT 2606 Australia
Email: info@tga.gov.au Phone: 1800 020 653 Fax: 02 6232 8605
www.tga.gov.au