



Australian Government

Department of Health

Therapeutic Goods Administration

# Can we make better use of monographs to abridge OTC medicine evaluation?

## The experience in Australia

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**TGA** Health Safety  
Regulation

# OTC medicine monographs

- Introduced in 2013 following the introduction of a risk-based categorisation framework:
  - N1 Generic medicines (clones, flavour/fragrance/colour variants)
  - N2 Generic medicines (fully meets a specific OTC monograph)
  - N3 Generic medicines (only quality data)
  - N4 Generic medicines (safety and/or efficacy data)
  - N5 New medicines that are not generics



# OTC medicine monographs

- Introduced as an initial 12 month trial in Australia to determine:
  - the effectiveness of the process
  - uptake by applicants
- Monographs developed for selected established and well categorised active ingredients



## Criteria for a monograph candidate

- There is a high level of knowledge and experience within the TGA with the active ingredient
- Frequency of generic applications
- Evaluation of bioavailability, bioequivalence, or other clinical data is not required
- A relevant BP or US Pharmacopoeia product monograph exists
- The quality aspects can be sufficiently assured through sponsor assessment and assurance



## Monograph details are based on:

- TGA records of previous evaluations
- Relevant Australian guidelines and standards (ARGOM & RASML)
- Guidance information endorsed by other comparable regulatory agencies
- Relevant BP/USP pharmacopoeia monographs and requirements
- Literature searches



# The monograph specifies requirements in relation to:

- Active ingredient and strength
- Dosage form
- Indications and claims
- Directions for use
- Labelling & advisory statements
- Quality standards



# Example of an OTC monograph: Bromhexine

## Introduction

This OTC Medicine Monograph outlines the requirements for Australian market authorisation of preparations containing bromhexine hydrochloride as a single active ingredient when applied for as an OTC new medicine N2 application. Proposed medicines 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 medicine N2 applications](#).

## Active substance

This monograph only applies to preparations that contain bromhexine hydrochloride (CAS no. 611-75-6) as the only active ingredient and excludes preparations containing any other salts and derivatives of bromhexine.

## Dosage forms and strengths

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

Active substance	Dosage strengths	Dosage forms
Bromhexine hydrochloride	0.8 mg/mL, and 1.6 mg/mL	Oral liquid
	8 mg	Tablets (conventional immediate release tablets and soluble tablets only)

## Indications

### Therapeutic indications for inclusion in the Australian Register of Therapeutic Goods (ARTG)

Mucolytic. Breaks down mucus and helps clear chest congestion.

### Label indications

Required label indication is 'Helps clear chest congestion'.

Further description of the relief of chest congestion may be included by selecting one or more of the following:

- Thins/loosens/breaks down mucus to help clear the chest
- Mucolytic
- Helps clear stubborn chest congestion
- Chesty cough



## Directions for use

Directions must be as shown in the table below, as relevant.

Dosage strength	Age*	Single dose	Dose interval	Maximum daily dose
0.8 mg/mL oral liquid	Adults and children 12 years and over	10-20 mL (8-16 mg)	Every 8 hours as necessary	3 doses
	Children 6-11 years (only on the advice of a doctor, pharmacist or nurse practitioner)*	10 mL (8 mg)	Every 8 hours as necessary	3 doses
	Do not use in children under 6 years of age.			
1.6 mg/mL oral liquid	Adults and children 12 years and over	5-10 mL (8-16 mg)	Every 8 hours as necessary	3 doses
	Children 6-11 years (only on the advice of a doctor, pharmacist or nurse practitioner)*	5 mL (8 mg)	Every 8 hours as necessary	3 doses
	Do not use in children under 6 years of age.			
8 mg tablet	Adults and children 12 years and over	1 to 2 tablets (8-16 mg)	Every 8 hours as necessary	3 doses
	Children 6-11 years (only on the advice of a doctor, pharmacist or nurse practitioner)*	1 tablet (8 mg)	Every 8 hours as necessary	3 doses
	Do not use in children under 6 years of age.			

\* If the medicine is not to be indicated for children below 'x' years of age (where 'x' is any age between 6 and 12 years of age), then the label must contain the statement "Do not give to children under 'x' years of age" as required by the Required Advisory Statements for Medicine Labels).

## Advisory statement

The following advisory statement is also required:

*If symptoms persist, consult your doctor or pharmacist.*





## Labelling

Labelling must comply with all relevant Australian requirements, as detailed in the document [Requirements for OTC new medicine N2 applications](#), including all required warning statements.

## Quality requirements

In addition to the quality requirements outlined in the document [Requirements for OTC new medicine N2 applications](#), the following specific requirements apply to bromhexine hydrochloride monograph medicine.

## Finished product specifications

In addition to other requirements specified in the document [Requirements for OTC new medicine N2 applications](#), the finished product specifications must comply, at a minimum, with the relevant set of requirements below.

For tablets, the following tests and limits:

- tablet appearance
- identity of bromhexine hydrochloride
- for soluble tablets only: disintegration (disintegrate within 3 minutes, using water at 15-25°C as the liquid medium)
- uniformity of dosage units (BP)
- dissolution (a suitable test and limit for dissolution that demonstrates the appropriate release of the active ingredient)
- bromhexine hydrochloride content of 92.5 – 107.5%
- individual unspecified impurity (not more than 1.0%) and total impurities (not more than 3.0%)
- microbiological quality in compliance with [Therapeutic Goods Order No. 77 – Microbiological Standards for Medicines](#),

For oral liquids, the following tests and limits:

- organoleptic properties (such as appearance, smell, taste etc)
- pH
- identity of bromhexine hydrochloride
- bromhexine hydrochloride content of 90.0 – 110.0%
- individual unspecified impurity (not more than 1.0%) and total impurities (not more than 3.0%)
- content of any preservatives included in the formulation
- microbiological quality in compliance with [Therapeutic Goods Order No. 77 – Microbiological Standards for Medicines](#).

## Container/measuring device

Bromhexine hydrochloride medicines 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 medicine, 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](#).



# Requirements for monograph applications

- Applications are submitted with a [list of assurances](#) confirming that the medicine meets the specified requirements (in lieu of providing full supporting data)
- Full compliance with the monograph and with [associated general requirements](#)
- Copy of the label(s) and product specifications submitted with the application
- Full data package must be held by the sponsor (selective post-market monitoring to establish compliance with requirements)



# Process

- Labelling and product specifications reviewed against the monograph
- Significantly shorter timeframe
- Lower fees



## So far...

- 14 monographs developed for single active ingredients:
  - common analgesics
  - cough & cold ingredients
  - topical antifungals
  - topical nasal decongestants
- Available monographs:
  - aspirin
  - bromhexine
  - dextromethorphan
  - guaifenesin
  - hand sanitisers
  - ibuprofen
  - laxatives
  - loperamide
  - mebendazole
  - paracetamol
  - pholcodine
  - ranitidine
  - topical imidazole antifungals
  - topical nasal decongestants



## To date...

- Low uptake by industry
  - only around 20 applications submitted (in 4 years)



# Feedback from industry

- N1 application level (clones) is more attractive
- Monograph details are perceived as restrictive
- Combination products (vs single ingredient products) may be of some interest



# Possible future approaches

- Hybrid applications
  - Higher application levels (N3, N4 & N5), only data supporting aspects outside the monograph are submitted and evaluated
- Development of monographs for common medicines containing fixed-combinations
- Development of monographs for S3 medicines which would include the development of standard Product Information (PI) documents



# Possible future approaches

- Labelling-only monographs for medicines requiring quality assessment
- Labelling
  - Medicine-specific Critical Health Information (CHI) panel (medicine info panel) development to be part of the monograph
- **But first, level of interest of the OTC medicines industry to be explored**





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