CODEINE INDUSTRY FORUM

Regulatory options for up-scheduling

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11 May 2017
Codeine Industry Forum Agenda

1. Introduction to the Forum

2. Introduction to Prescription Medicines Authorisation Branch (PMAB) and Scientific Evaluation Branch (SEB)

3. TGA application processes & data requirements
   (a) Converting existing S2/S3 medicines to S4:
      - Process for varying existing medicines
      - Data requirements for existing medicines (converted to S4)
   (b) New applications for codeine containing medicines submitted prior to 1 Feb 2018 and those submitted on or after 1 Feb 2018
      - Process and data requirements

4. Supply of remaining S2 & S3 stock after 31 January 2018
   - Labelling
   - Advertising
   - RASML update (Effective 1 July 2017)

5. Management of ARTG entries
   - ARTG scheduling status on 1 February 2018
   - Annual fees
   - Cancelled Products
Prescription Medicines Authorisation Branch Introduction

Regulatory options for up-scheduling

Dr Felicity Jameson
Prescription Medicines Authorisation Branch
Medicines Authorisation Division
Prescription Medicines Registration

Medicines Regulation Division

Scientific Evaluation Branch

Pharmaceutical Benefits Division

Prescription Medicines Authorisation Branch

PM Registration Processes

Pharmacovigilance and Special Access Branch

Medical Devices Product Quality Division

Laboratories Branch

Manufacturing Quality Branch
## Prescription Medicines Authorisation Branch Structure

The Prescription Medicines Authorisation Branch is comprised of 5 Clinical Evaluation Units (CEU).

Each unit is responsible for assessing prescription medicines applications within particular therapeutic areas.

<table>
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<tr>
<th>CEU 1</th>
<th>CEU 2</th>
<th>CEU 3</th>
<th>CEU 4</th>
<th>CEU 5</th>
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| • Analgesia  
• Neurological disorders  
• Psychiatric/Psychological /Behavioural disorders  
• Anaesthesia  
• Gastrointestinal disorders  
• Nutrition  
• Disorders of the mouth  
• Disorders of the skin  
• Disorders of the ear | • Infectious diseases  
• Vaccination against infectious disease  
• Immunological disorders  
• Other  
  • radiological agents (e.g. contrast media)  
  • adjuncts to radiopharmaceuticals and contrast media use  
  • diagnostic tests for infections  
  • allergens (diagnostic or therapeutic)  
  • antivenenes  
  • radiopharmaceuticals for cancer (diagnostic) | • Cardiac disorders  
• Lipid disorders  
• Inherited metabolic disorders  
• Vascular disorders  
• Disorders of the male reproductive system  
• Poisoning | • Neoplastic disorders  
• Haematological disorders  
• Other  
  • radiopharmaceuticals for cancer (therapeutic) | • Contraception  
• Infertility  
• Obesity  
• Endocrine disorders  
• Disorders of the female reproductive system  
• Pregnancy and labour  
• Fluid & electrolyte disorders  
• Disorders of the eye  
• Respiratory disorders  
• Disorders of the nose, paranasal sinuses & upper airway  
• Renal & urinary tract disorders  
• Bone disorders |

Further information can be found in Guidance 4 of the Australian Guidelines for Prescription Medicines (ARGPM)
Branch Overview: Sections

Application Management and Exports
Application Entry Team
application.entry.team@health.gov.au
Application Support Team
application.support.team@health.gov.au
Exports
FOI requests

Business Review and Reporting
Retrospective performance reporting
Key Performance Indicate reporting for prescription medicines
Half Yearly Performance Reports
Weekly workload management reporting for Section Heads
Sponsor Pipeline Reporting (Forecasting)

Policy and Reform Facilitation
Implementation of the recommendations of the MMDR
Associated legislative and guidance change
Change management

Evaluation Management
Case Management
External evaluator procurement
Evaluation Support Unit eCTD
Pre-submission meetings
streamlinedsubmission@health.gov.au

Transparency and Advisory Management
AusPAR preparation and publication
Secretary of Advisory Committee for Medicines
Media and ministerial enquiries
Minor Variations for Prescription Medicines

Converting from Schedule 2 or 3 to Schedule 4

- New Registrations:
  - Application form to register or vary the registration of prescription medicines (Category 1 application)
  - Section 23 Category 3 application that creates a separate and distinct good
  - Section 23 Self-assessable request (SAR) that creates a separate and distinct good
  - Additional trade name

- Variations:
  - Application form to register or vary the registration of prescription medicines (Category 1 application)
    - 9D(1) Request to correct an ARTG entry
    - 9D(2) Safety-related request (SRR) to vary an ARTG entry
    - 9D(3) Category 3 application to vary an ARTG entry
    - 9D(3) Self-assessable request (SAR) to vary an ARTG entry or minor editorial change to the PI

- Further information on minor variations applications for prescription medicines can be found at:
M1 – Changes to medicines and poisons scheduling

Specific conditions

- The change in scheduling is from a Schedule 2 or 3 medicine to a Schedule 4 or 8, or from a Schedule 4 to a Schedule 8 medicine, or
- The medicine has been rescheduled from Schedule 4 or 8 to Schedule 2 or 3, but continues to be regulated as a prescription medicine (see Part 1 of Schedule 10 of the Regulations).

Required information

- Relevant evidence of the change, such as a copy of the final Advisory Committee on Medicines Scheduling decision
- A copy of the revised labels
- A clean and marked-up copy of the proposed Product Information document.

45 working day timeframe

Labels: Pharmaceutical Chemistry Section within SEB
Product Information: Clinical Evaluation Unit 1 within PMAB

Approval letter will reflect timing of conversion from S3 to S4.
Available regulatory options

- **s23 New Register Entry**
  - e.g. Major variation for new strength

- **Schedule 3 with an existing PI**
  - 9D(3) M1 change
    - Reschedule

  - May include **9D(2) SRR**
    - Vary the entry to reduce the class of persons for whom the goods are suitable

- **Schedule 4 with a PI**
  - 9D(3) M1 change
    - Reschedule
  - **s28 Condition of Registration**
    - New PI for product required

- **Schedule 2 without a PI**

**Department of Health**

**Therapeutic Goods Administration**
New Applications for Codeine Containing Medicines

Regulatory options for up-scheduling

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Scientific Evaluation Branch
Medicines Authorisation Division
Over-the-counter medicines

Australian regulatory guidelines for OTC medicines (ARGOM)

- N1 Generic medicines (clones or flavour etc variants)
- N2 Generic medicines that fully meet a specific OTC monograph
- N3 Generic medicines that are not an N1, N2 or N4 level application (N3 applications require CTD Modules 1 and 3)
- N4 Generic medicines that are one or more of the following:
  - require supporting safety and/or efficacy data
  - have not been previously registered as an OTC medicine following down-scheduling
- N5 New medicines that are not generics
Processes for NEW medicine applications

New OTC applications for codeine replacement (codeine-free) products

- Application to be submitted to OTC and evaluated as usual (according to standard OTC procedures)

Applications to register new OTC codeine containing products received before 1 February, 2018

- Application is to be submitted via the OTC ePortal (OTC data requirements apply).
- PI required for both S2 and S3 products.

Applications for new S4 codeine-containing products received on or after 1 February, 2018

- Application to be submitted to PMAB and evaluated according to PMAB/SEB standard procedures.
- A sponsor may be able to submit an application based only on in vitro dissolution data given that codeine is likely to be highly permeable and soluble (BCS Class I: JPharmSci 103: p1592 2014)
The Registration Process

A submission to register a new prescription medicine is supported by:

1. **Quality data**: for both the drug substances (drug master files etc) and for the dosage form
2. **Nonclinical data** (if required)
3. **Clinical data**: might be evidence of bioavailability (i.e. the extent and rate of release from the dosage form: *in vivo* or sometime *in vitro*)


Evidence of Good Manufacturing Practice is required.
Changes to Registered Medicines:
Label requirements

For S4 medicines

• **Therapeutic Goods Order No. 69** - General requirements for labels for medicines

• **Therapeutic Goods Order No. 91** - Standard for labels of prescription and related medicines (TGO 91)
  from 1 September 2020 Medicine labels: Guidance on TGO 91 and TGO 92
Label approval

• To allow you to use up existing pre variation stock, the date of effect of this approval, and the date from which the varied product may be supplied, is that date on which all pre variation stock:
  – which is currently in storage in Australia, and
  – for which you have placed orders prior to the date of this letter has been supplied.

• If these arrangements cause you difficulty, please nominate an alternative date of effect for the delegate's consideration (prior approval will be required for alternative arrangements).

• However the date of effect of this approval is no later than 31 January 2018.

• The conditions concerning date of effect and supply of post-variation stock are also decisions under subsection 28(3) of the Act.
Supply of remaining OTC stock after 31 January 2018
Management of ARTG entries
Regulatory options for up-scheduling

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Complementary & OTC Medicines Branch
Medicines Authorisation Division
Supply of remaining S2 & S3 stock after 31 January 2018

Labelling

1. Product already supplied and out of sponsor’s control (at retailers’ shelves)
   - OTC vs S4 labelling requirements
   - Role & responsibilities of TGA vs S&Ts
   - Subject to discussions with S&Ts: application of dispensing labels. Existing S2/S3 labelled retail stock can be supplied by pharmacies (as Prescription Only Medicine) with a dispensing label that is compliant with Appendix L of the SUSMP and with a sedation warning
   - Exemption from S&Ts if signal heading is not changed

2. Product has not been released for supply and/or is still the sponsor’s responsibility
   - must be re-packaged with Rx/ S4 labels (sponsors can’t release for supply products that don’t comply with S4 labelling requirements)
Supply of remaining S2 & S3 stock after 31 January 2018

RASML update (effective 1 July 2017)

- RASML 3 is being updated to remove new statement “If coughing persists …”

- No RASML-related changes required when RASML 3 is effective
Supply of remaining S2 & S3 stock after 31 January 2018

Advertising:

- Before 1 Feb 2018: pre-approval required (current process applies)
- Advertisement should not refer to impending changes in scheduling (could cause fear & distress .., TG Advertising Code refers)
- Can’t advertise after 31 Jan 2018
- Ensure no publication or broadcast, including on internet & social media. This also includes advertising in pharmacies
- Brand-based advertisement should be made specific to OTC medicines

See TGA website for recent publication: Changes to advertising for medicines containing codeine
Management of ARTG entries

ARTG scheduling status on 1 February 2018:

• Will change from S2/S3 to S4
• Area flag: will change from OTC to Rx
• Ingredient database: will be updated to reflect availability of codeine as a RX ingredient only
Management of ARTG entries

Annual fees

• Paid OTC annual charge for 2017-18 covers the full financial year

• Rx annual charge applies to 2018-19 financial year (due on 15 Sept 2018)

• Rx annual charge applies to a medicine kept on the ARTG but not supplied (unless had the ACE status before 1 Feb 2018)

• If already on ACE, ACE will be transferred, but you need to submit $0 turnover declaration for 2016-17 and 2017-18 by 22 July 2017 and 22 July 2018 respectively

• Cancelling a product latest by 30 June 2018: no annual charge for 2018-19

• Cancelling a product after 30 June 2018: Rx annual charge payable for 2018-19
  – Currently, OTC annual charge is $1,410, Rx annual charge is $3,180 (to be increased by 1.65% from 1 July 2017 subject to regulation amendment)
Management of ARTG entries

Cancelled products

• Sponsors & wholesalers will not be able to conduct further supply of cancelled products*
• Can’t advertise if not on the ARTG
• Already supplied and out of sponsor’s control (at retailers’ shelves):
  – Must dispense as Rx as of 1 Feb 2018
• Labelling: as under Labelling
• Sponsor’s responsibilities maintained for life of product, e.g. for pharmacovigilance activities, recall action, ongoing stability testing on retention samples as per GMP requirements, providing info to the TGA on request, etc.

* Supply of a cancelled product by retailers: the regulation of therapeutic goods is a co-regulatory scheme between the States and Territories. A person dealing with therapeutic goods must comply with all Commonwealth and State laws. You should review the relevant State laws regarding the supply therapeutic goods that are no longer included in the ARTG (cancelled products).