Australian Government
Department of Health
Therapeutic Goods Administration

Updates from the Therapeutic Goods Administration

For medicine sponsors

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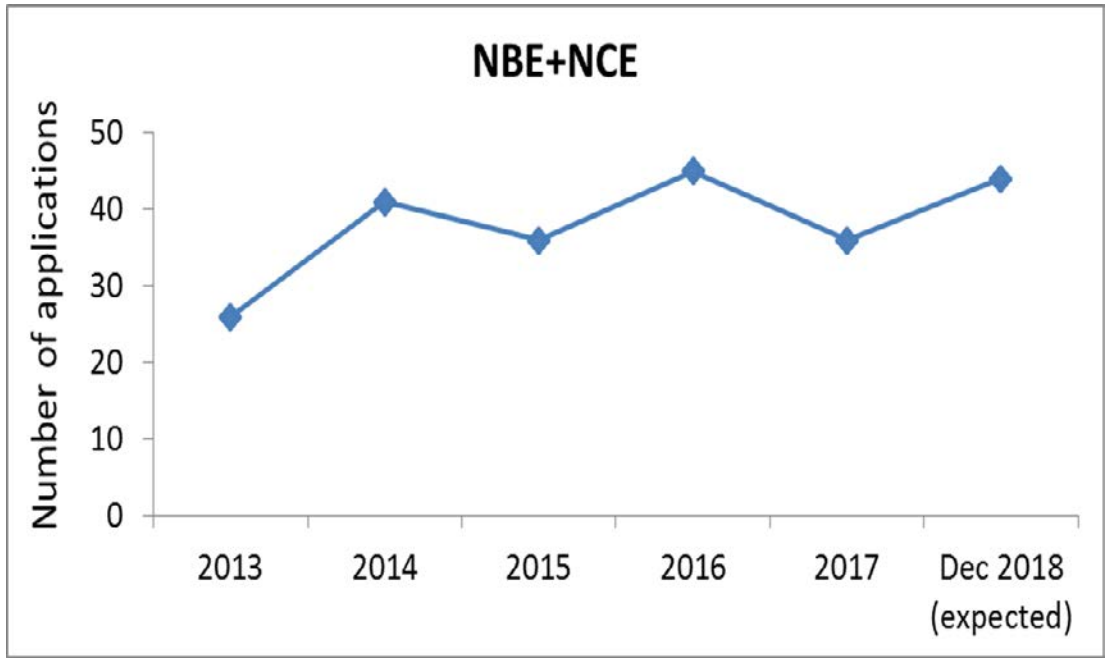
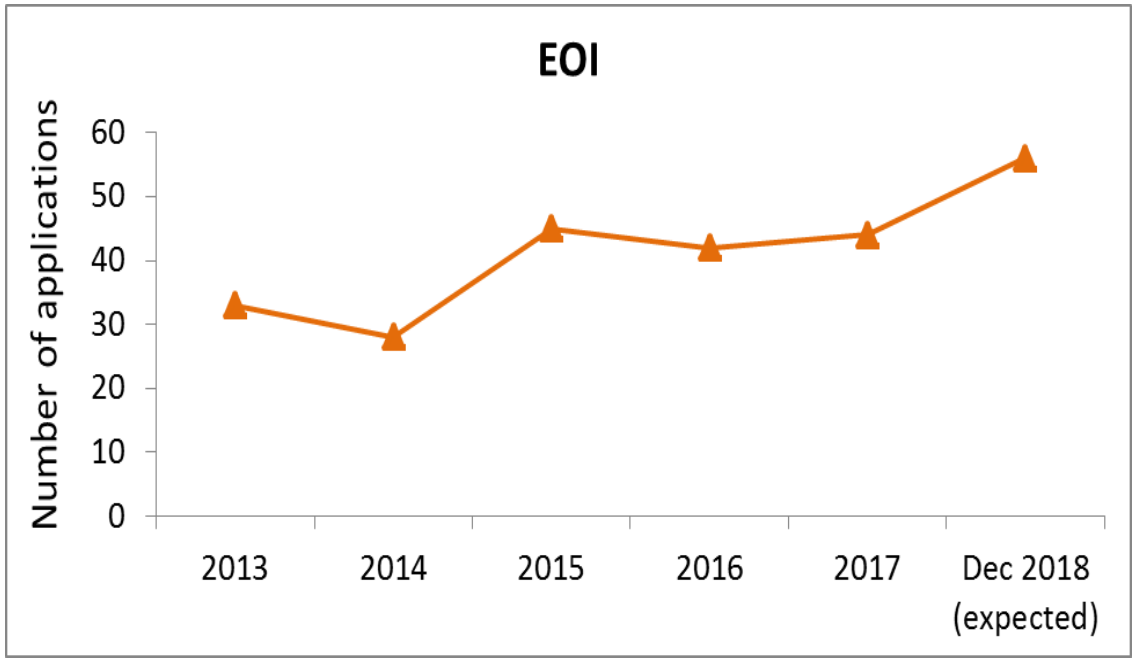
Therapeutic Goods Administration

8th Annual EyeforPharma Conference

TGA Health Safety Regulation

TGA: Major applications 2013-2018





TGA: options for new medicines

Approval on basis of substantial evidence

- Standard approval pathway

Approval on basis of substantial evidence (with faster review)

- Priority review pathway
- Comparable Overseas Regulator (COR) process
- Work-sharing (pilot)

Approval on basis of earlier data (available years earlier)

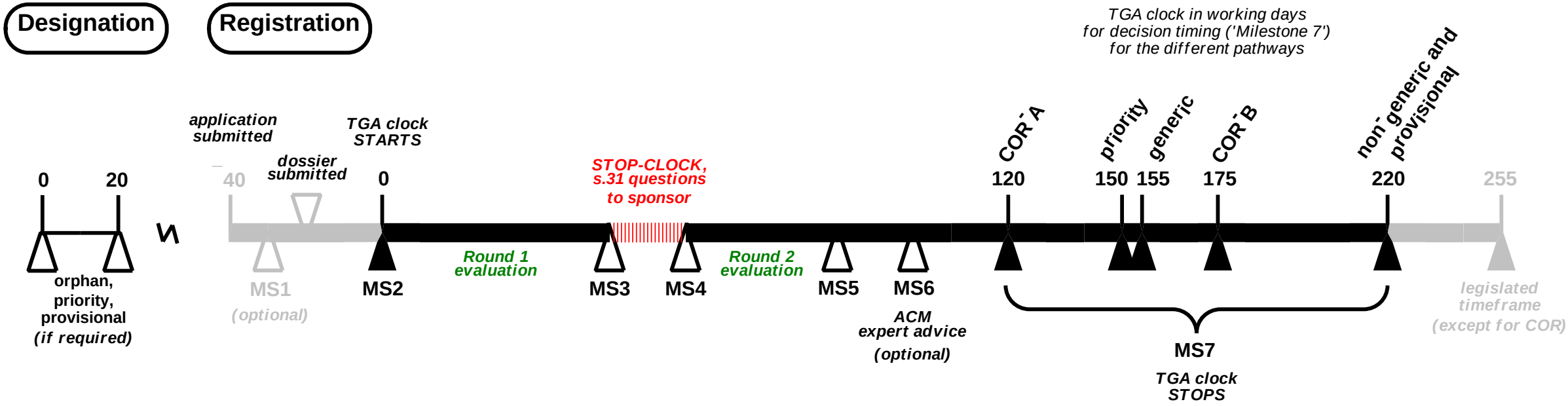
- Provisional approval pathway

Orphan Drug Program

Incentive for rare disease

- 100% fee waiver for registration

Submission Pathways – Overview



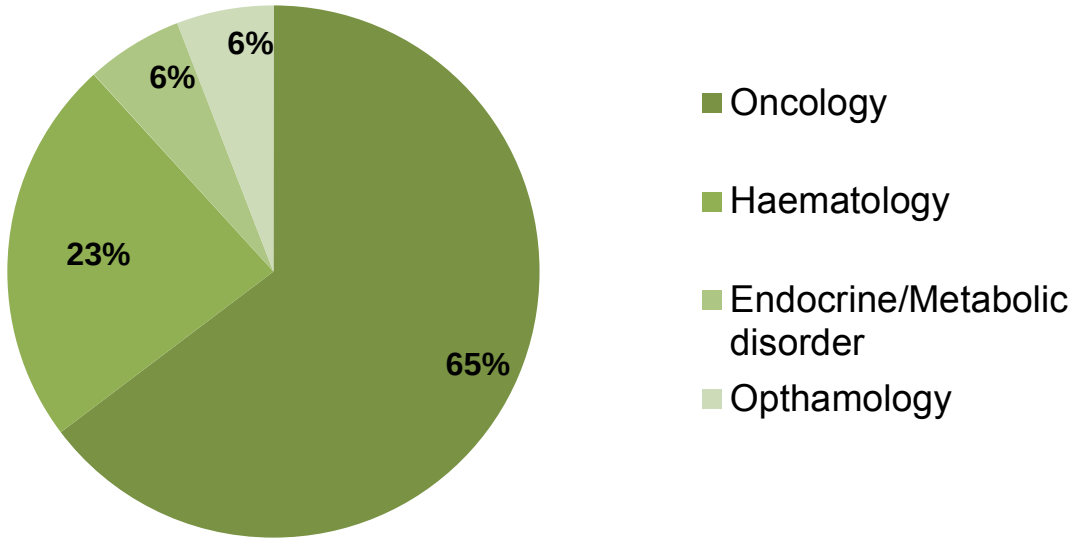
- Multiple submission pathways ranging from 120-220 target days to grant market approvals
- Evaluation questions to sponsors occur at different time points depending on the pathway
- Orphan designation applicable to all 5 pathways (standard, priority, provisional, COR A & B)
- International collaboration applicable to most pathways (excepting provisional approval)

Priority review: Implemented 1 July 2017

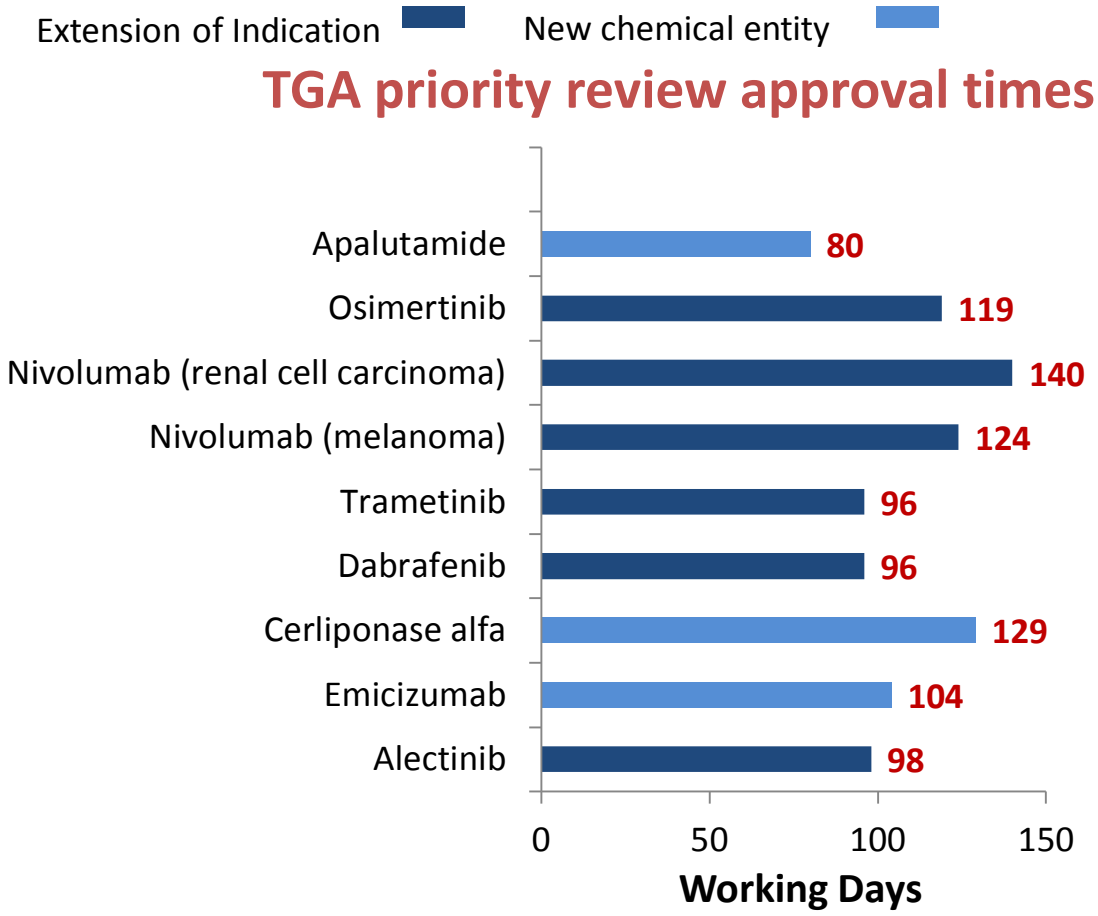
Priority determination applications by status:
1 July 2017-30 September 2018

	Number (%)
Applications lodged	28
Approved	17 (60.7%)
Rejected	9 (32.1%)

Approved priority determinations by therapeutic area:
1 July 2017- 30 September 2018



Priority medicines approved: as at 30 September 2018



- 9 priority medicines approved
  - 3 new chemical entities, 6 extension of indication
  - 7/9 indications in Oncology
- We are faster than our target timeframes
- Apalutamide also a work-sharing pilot with Health Canada

Priority review pathway: key issues

Priority review eligibility criteria
New prescription or new indications medicine
Seriously debilitating or life-threatening condition
Comparison against registered therapeutic goods (*excludes provisional registration and off-label use, considers alternate treatment and clinical significance)*
Major therapeutic advance (*the magnitude of the effect is, or is expected to be well beyond minimum requirement for clinical significance, major impact on patient outcomes…*)

- Justification for the 'major' in major therapeutic advance

  Provide justification of why the supporting evidence is substantial: e.g. progression free survival vs overall survival

- Comparison
  - Compare against all relevant registered goods
  - Compare against standard care if there is no registered treatment
- Separate determination applications for each active ingredient if not a fixed dose

Provisional approval: Implemented March 2018

- Expedited through accepting early data where the benefit of availability outweighs the risk
- Confirmatory safety and efficacy data required
- Up to 6 years to apply for transition to full registration
- Like other regulators the pathway provides

  "Early access to certain prescription medicines"

FDA

Fast Track

CMA Conditional Marketing Authorisation
How early access to medicines has helped patients from 2006 to 2016

Provisional approval eligibility criteria
New prescription or new indications medicine
Seriously debilitating or life-threatening condition
Comparison against registered therapeutic goods (*excludes provisional registration and off-label use, considers alternate treatment and clinical significance)*
Major therapeutic advance (*the magnitude of the effect is, or is expected to be well beyond minimum requirement for clinical significance, major impact on patient outcomes…*)
Clinical study plan *(evidence to submit comprehensive data before the end of 6 years)*

Provisional approval pathway

All positive determinations and designations are published on the TGA website

Pfizer Australia Pty Ltd

Medicine Name: lorlatinib

Therapeutic area: Oncology

Designation/determination: Provisional approval
Effective Date: 27/09/2018
Lapse Date: 27/03/2019

Celgene Pty Ltd

Medicine Name: enasidenib

Therapeutic area: Haematology

Designation/determination: Provisional approval
Effective Date: 27/09/2018
Lapse Date: 27/03/2019

Merck Sharp & Dohme (Australia) Pty Ltd

Medicine Name: pembrolizumab

Therapeutic area: Oncology

Designation/determination: Provisional approval
Effective Date: 02/08/2018
Lapse Date: 02/02/2019

Merck Sharp & Dohme (Australia) Pty Ltd

Medicine Name: pembrolizumab

Therapeutic area: Oncology

Designation/determination: Provisional approval
Effective Date: 16/05/2018
Lapse Date: 16/11/2018

Eli Lilly Australia Pty Ltd

Medicine Name: olaratumab (rmc)

Therapeutic area: Oncology

Designation/determination: Provisional approval
Effective Date: 12/04/2018
Lapse Date: 12/10/2018

Provisional approval pathway: some issues

How to judge when early data seems promising

Neurology. 2015 Jul 21;85(3):274-83. doi: 10.1212/WNL.0000000000001757. Epub 2015 Jun 24.

Improving early clinical trial phase identification of promising therapeutics.

Kent TA[1], Shah SD[2], Mandava P[2].

Use of Real- World data to supplement clinical trials

Am J Law Med. 2018 May;44(2-3):197-217. doi: 10.1177/0098858818789429.

Real-World Data Analytics Fit for Regulatory Decision-Making.

Schneeweiss S[1], Glynn RJ[1].

Emerging trends: expedited approval

Australian perspective

- Facilitate early access to medicines that address unmet needs
- Increase options for Australian patients
  - Benefit for extension of indication in addition to new chemical entities
- Maintain standards for safety, efficacy and quality.
- Minimise regulatory burden on sponsors and the regulator

- More products internationalised within the same time frame. Number of new active substances approved increased from 12 to 51 across 6 major regulators. Bujar M et al. 2018. R&D Briefing 67: New drug approvals in six major authorities 2008-2017: Focus on the availability of medicines and company size. CIRS

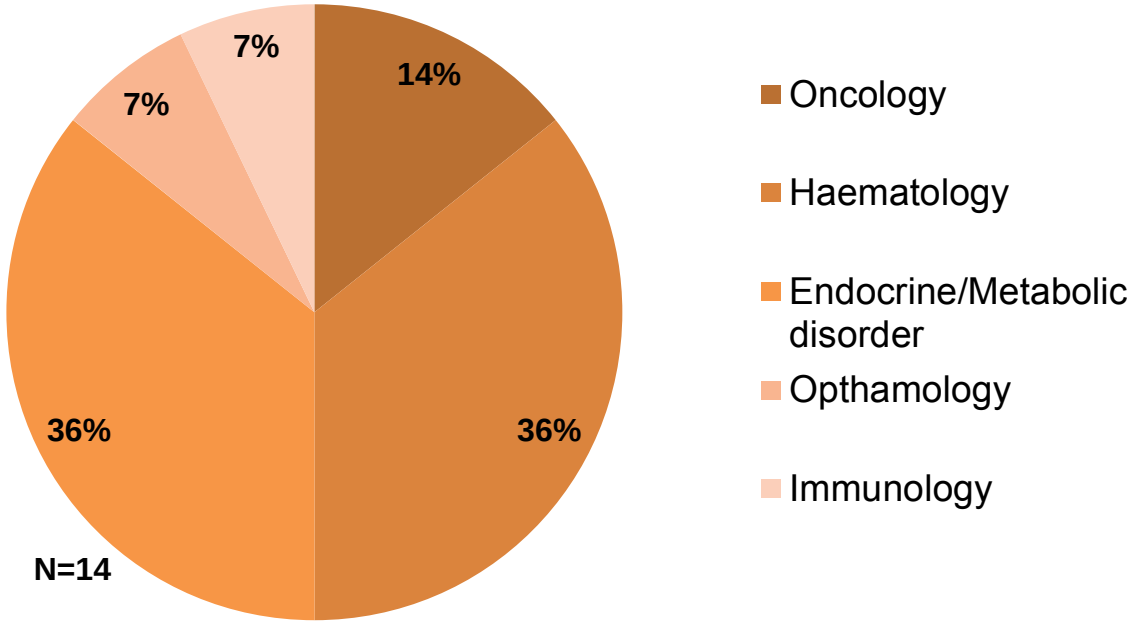
"Though some drugs associated with an expedited program may indeed provide noticeable clinical advances, this trend is being driven by drugs that are not first in class and thus potentially less innovative".

A S Kesselheim et al. Trends in utilization of FDA expedited drug development and approval programs, 1987-2014: cohort study. BMJ 2015;351:h4633

New Orphan Drug program: Implemented 1 July 2017

- To provide an incentive to sponsors to bring medicines for a small population to market and make medicines available that might otherwise not be registered
- New eligibility criteria
- End of transition from the previous program - 30 June 2018
- To be eligible for a fee waiver a related orphan designation must be in force when the relevant fee is payable

Approved orphan designations by therapeutic area: 1 July 2017 – 30 September 2018



"Will you receive the approval you hoped for?"

Where the nuance of wording helps define usage of a new medicine!

Case Study: Blincyto (blinatumomab)

Includes paediatrics

- Type C application:
  - To extend the approved indications to include treatment of paediatric patients with Philadelphia chromosome-negative relapsed or refractory B-cell precursor acute lymphoblastic leukamia (ALL)
- Approved indication at the time:
  - For the treatment of adults with Philadelphia chromosome-negative relapsed or refractory B-cell precursor acute lymphoblastic leukaemia (ALL)
- Australian Public Assessment Reports (AuSPARs) published
  - Search http://www.tga.gov.au/ws-auspar-index
- Sponsor's proposed new indication
  - Blincyto is indicated for the treatment of Philadelphia chromosome-negative relapsed or refractory B-precursor acute lymphoblastic leukaemia (ALL)
- Approved indication – post Advisory Committee on Medicines (ACM)
  - Blincyto is indicated for the treatment of Philadelphia chromosome-negative relapsed or refractory B-cell precursor acute lymphoblastic leukaemia (ALL).

Note to Indication: this indication is approved based on Phase II, non-randomised evidence. An improvement in clinical outcomes by direct prospective comparison in a randomised setting relative to other standard-of-care salvage therapies has not been established

- Indication amended to reflect the level of evidence that the submission relied on

Case Study: Opdivo(nivolumab)-priority review

- Type C application to extend indications in the setting of melanoma

- Indication proposed by sponsor in Type C application
  - Opdivo as monotherapy is indicated for the adjuvant treatment of patients with completely resected Stage III or Stage IV melanoma

- Type C approved indication –
  - Opdivo as monotherapy is indicated for the adjuvant treatment of patients with melanoma with involvement of lymph nodes or metastatic disease who have undergone complete resection.

- TGA reasons for change
  - reference to specific American Joint Committee on Cancer (AJCC) stages of disease, prefer to define the population without relying on third party staging definitions (AJCC in this case)
  - Third party staging subject to change and the indication would therefore change with third party changes to definitions.

Other updates

- Excluded goods
- Permitted indications for listed medicines
- Black Triangle Scheme
- SME Assist
- TGA Facebook and Twitter

Excluded goods: New determination effective 1 October 2018

Excluded goods for the purpose of the Therapeutic Goods Act 1989 (the Act)

Three key elements:

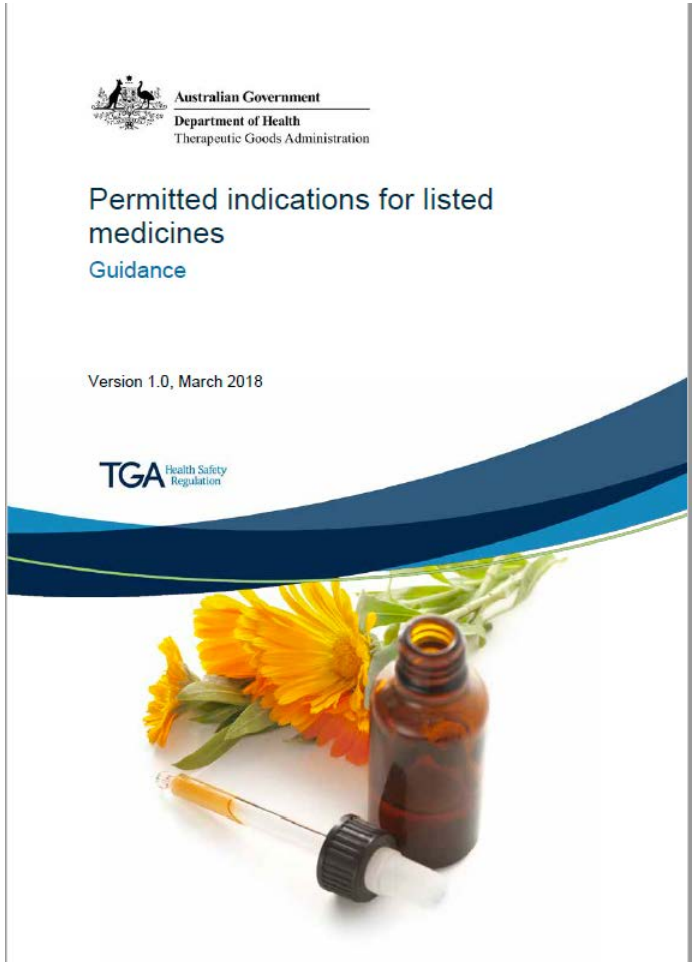
1. Antiperspirants and ear candles are now excluded from the operation of the Act
    - partial implementation of outcomes of options for 'future regulation of low risk products' https://www.tga.gov.au/future-regulation-low-risk-products

2. Therapeutic goods which are presently declared not therapeutic goods in the existing Therapeutic Goods (Excluded Goods) Order no. 1 of 2011 (EGO)
    - no impact on affected stakeholders

3. The requirements of the Cosmetics Standard 2007 (Cosmetics Standard) relating to a number of therapeutic goods have been reproduced directly in the new determination, rather than incorporating the Cosmetics Standard by reference as is currently the case in the EGO. Also no regulatory impact on stakeholders

Permitted indications for listed medicines

- New regulatory requirements effective 6 March 2018
  - 3 year transition period
- Guidance now available on TGA website
  - https://www.tga.gov.au/book-page/permitted-indications-listed-medicines
- Provides information for sponsor on:
  - What permitted indications are
  - Use of permitted indications
  - How to apply for inclusion of new indications on the permitted indications list



Black Triangle Scheme: Implemented 1 Jan 2018

- The Black Triangle Scheme provides a simple means for practitioners and patients to identify certain types of new prescription medicines, including those being used in new ways and to encourage the reporting of adverse events associated with their use.

- All provisionally approved medicines will be included in the Black Triangle Scheme
- Black Triangle displayed in Product Information (PI) and Consumer Medicines Information (CMI)
- Black Triangle also included in medicines information on MIMS online and Health Direct
- Search the Australian Register of Therapeutic goods (ARTG) under “advanced search”
  - 29 medicines as at 30 September 2018

SME Assist

SME Assist is a dedicated service to help small to medium enterprises (SMEs), researchers, start-ups and those unfamiliar with regulation understand their regulatory and legislative obligations.

- Guidance articles
- Educational workshops
- Interactive decision tools
- Subscription service
- Email + phone support

www.tga.gov.au/sme-assist

sme.assist@tga.gov.au

1800 020 653

Face book, Twitter and….Blogs

To improve communication to consumers & health professionals

"Some prescription medicines can now be approved faster"

"Report side effects to your health professional or call 1300 134 237"

"Not everything about a medicine is known when it is first approved"

"Some prescription medicines will be approved for a short period of time while more information about them is collected"

"We will watch medicines that have been approved for a short period of time more closely"

Australian Government

Department of Health

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