Australian Government
Department of Health

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Global Cancer Clinical Research, Drug Development and Therapeutic Accessibility Workshop
April 2018

The Role of Health Authority Insurance on Access

Pharmaceutical Benefits Authority Committee (Australia)

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Overview

- Funding of cancer medications
- Process and criteria for reimbursement
  - Pharmaceutical Benefits Advisory Committee
- Challenges with a focus on cancer medications

Pharmaceutical funding in Australia

- Pharmaceutical Benefits Scheme (PBS)
  - Primary subsidy program
  - All Australian permanent residents are eligible
  - Patients pay co-payment ($39.50 or $6.40)
  - Includes a number of discrete programs
    - Eg. Section 100 Chemotherapy Cancer Drugs Program for infused or injected drugs to enable reimbursement of the most efficient combination of vial
- Public hospitals for inpatients
  - Variable access
- Private health insurance
  - Limited

PBS and Cancer medicines

- Total PBS spend (2015-16): $11 billion
- Cancer medicines: $1.9 billion
- Increasing spend on cancer medicines, 1999-2000 vs 2011-2012
  - 133% increase for cancer medicines
  - 37% increase for non-cancer medicines
  - Driven by increasing number of patients, increasing number of treatments and cost of drugs

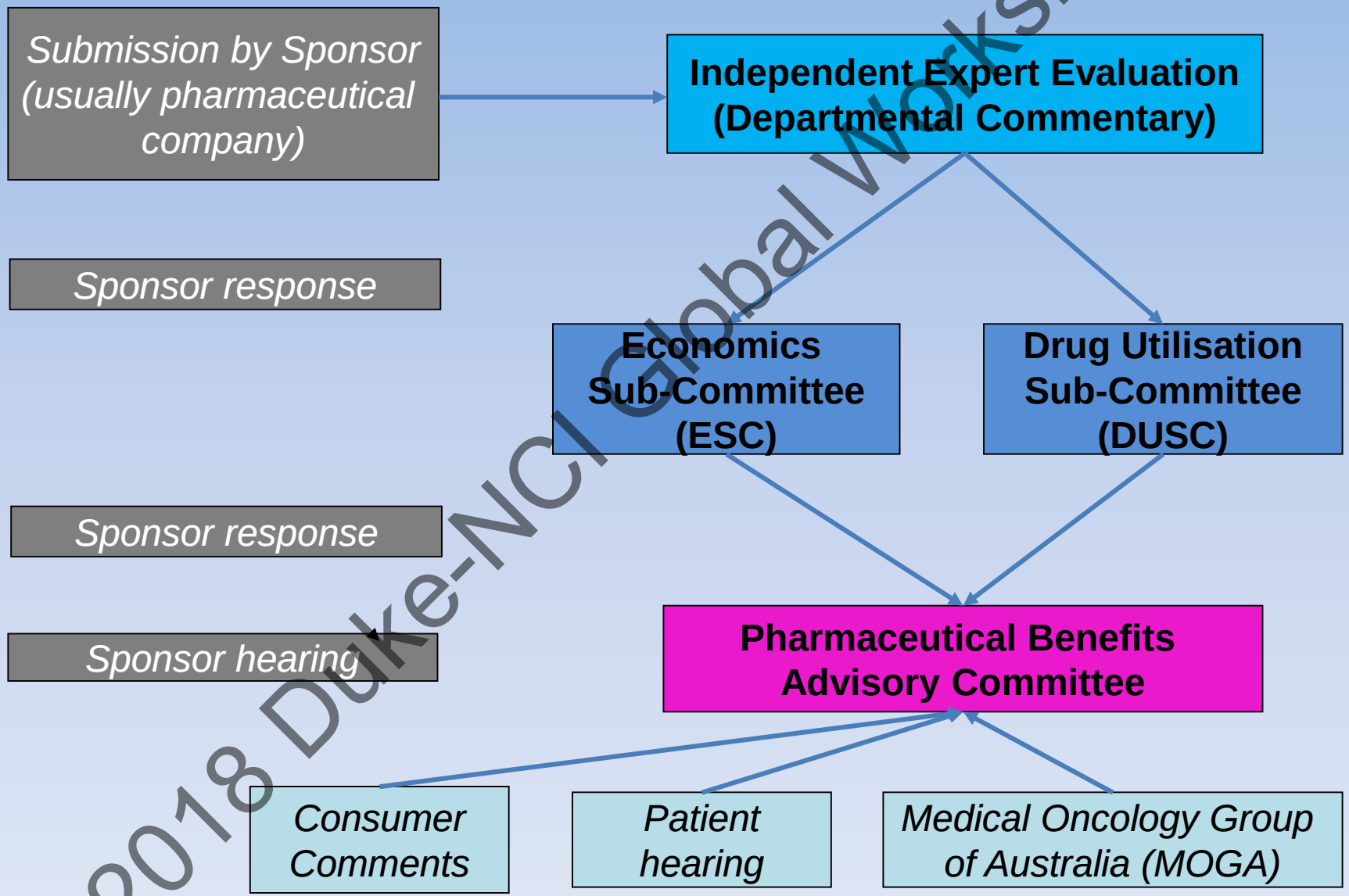
Reimbursement process

- Prerequisite: registered drug (Therapeutic Goods Administration - TGA)
  - Assesses efficacy, safety, quality
- Pharmaceutical Benefits Advisory Committee (PBAC) "recommends"
  - Assesses comparative effectiveness, comparative safety, comparative costs (cost-effectiveness)
- Health Minister "declares"
  - Accepts/rejects recommendation
  - Government provides the funding (Cabinet >$20M)

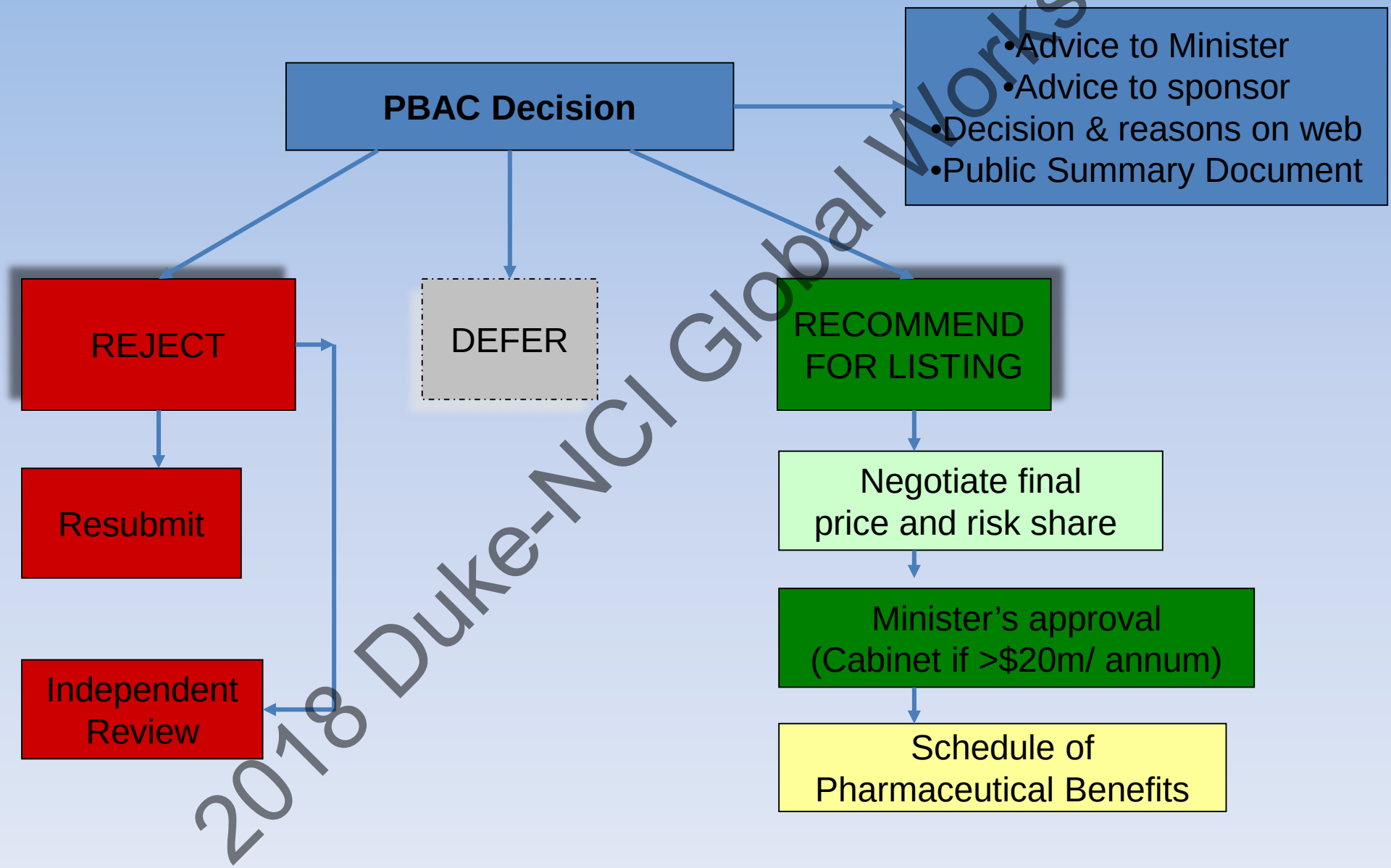
Major PBAC submissions – Nov 17, Mar 18, July 18

Type of submission	Number
Total major submissions	95
Cost-effectiveness analysis	64 (67%)
Parallel process (concurrent regulatory application)	39 (41%)
Cancer medication	38 (40%)
PD1/PDL1 inhibitor	11 (12%)

Process for listing 1: 17-week cycle



Process for listing 2: post-PBAC



Co-dependent technologies

- The patient health outcomes related to the use of one health technology (eg a medicine) are improved by the use of another health technology (eg a pathology test)
- Most common is medicine-test combination with pathology test determining eligibility for medicine
  - Pembrolizumab for NSCLC patients with high PD-L1 expression
  - Osimertinib for NSCLC patients with EGFR T790M mutation
- Pathology tests are reimbursed through the Medical Benefits Scheme
- Considered by PBAC and Medical Services Advisory Committee (MSAC)

Informative Patient and Consumer Inputs

- Expectations of treatment benefits and harms
- Better understanding of how the benefits or harms influence patient quality of life
- Benefits versus harms trade offs
- Broader impacts of medicine availability
- Societal values and perspectives on costs and benefits

Key factors influencing decision making by the PBAC

Quantifiable

- Comparative health gain
- Comparative cost-effectiveness (no ICER threshold)
- Patient affordability in the absence of PBS subsidy
- Predicted use in practice and total financial implications for the PBS and Government health budgets

Less Quantifiable

- Overall confidence in the evidence and assumptions in submission
- Equity
- Presence of effective alternatives
- Severity of the medical condition treated
- Ability to target therapy with the proposed medicine precisely and effectively to patients likely to benefit most

Rule of rescue

- When all four factors apply - influential in favour of listing:
  1. No alternative nonpharmacological or pharmacological interventions for these patients
  2. The medical condition is severe, progressive and expected to lead to premature death
  3. The medical condition applies to only a very small number of patients
  4. The proposed medicine provides a worthwhile clinical improvement sufficient to qualify as a rescue from the medical condition
- Effect is to allow PBAC to recommend at higher ICER

Managed entry programs (2012-May 2016)

- One-third of new listings, more common for cancer medicines
- Financial (81%)
  - Discount on published price (Special Pricing Arrangement)
  - Rebate if exceed cap (use, expenditure), for additional administration or tests, when used in combination
  - Price-volume agreement
- Financial + information (14%)
  - Rebate based on lack of response, amount of treatment, other resource use
  - Treatment ceased if lack of response (continuation rules)
- Outcome (5%)
  - Data collected for subsidised patients
  - Follow-up data from trial provided

M. Robinson et al, International Journal of Technology Assessment in Health Care, 34:1 (2018), 46–55.

International reference pricing

- Prices often set based on markets that do not use HTA processes
- Sponsors constrained by international reference pricing
- PBAC constrained by legislation
- Use of special pricing arrangements in Australia an many other jurisdictions
- Can delay access in Australia

Process changes

- Regulatory (TGA) process changes
  - Priority review (commenced July 17)
    - Faster assessment of vital and life-saving medicines
    - Target: 150 working days (30 weeks; 12 weeks quicker)
  - Provisional review (to commence April 2018)
    - Enable certain promising medicines to become available up to two years earlier on the basis of early clinical data on efficacy and safety
    - Time limited registration
    - Implications for data available for PBAC consideration
- PBAC processes under review

Challenges – cancer medications

- Uncertain extent of gain in overall survival
  - Cross-over from control group to new medication in trial
    - Example: osimertinib, submission based economic model on single arm comparisons
  - Difference in trial not being statistically significant
    - Example: palbociclib and ribociclib; Is the gain in progression free survival at the expense of reduced time post-progression?
  - Trial results extrapolated over long-period
    - Example: daratumumab for multiple myeloma, in trials ~15% of dara treated patients had died
    - PBAC: Greater confidence in establishing cost effectiveness will be derived by limiting the time horizon to 10 years

Challenges – cancer medications

- Modest and/or uncertain comparative benefits and toxicity
  - Will the modest benefits observed in the trial setting be observed in clinical practice?
  - Unclear benefit vs alternative therapies
  - What is the impact on patient QoL?
  - Price reduction may be required to be considered cost-effective
    - Optimistic assumptions in economic evaluation
  - March 18 meeting
    - Cetuximab for head & neck cancer
    - Ramucirumab for gastric cancer
    - Regorafenib for liver cancer
    - Nanoliposomal irinotecan for pancreatic cancer

Challenges – cancer medications

- Combination therapies, example carfilzomib for multiple myeloma (MM)
  - Registered for use as Cd and CLd
  - Reimbursed for Cd only
    - ICER for Cd vs Bd: $45-75k per QALY (submission estimate; Nov 16 & Jul 17)
    - ICER for CLd vs Ld: $105-200k per QALY (submission estimate excluding cost of lenalidomide); >$200k per QALY including lenalidomide (Nov 16)
  - Stakeholder meeting planned for May 2018 to discuss discrepancies between PBS listings for MM treatments and guidelines, and barriers to availability of combination therapies

Challenges – cancer medicines

- Use of molecular markers to target patients
  - Easier when absolute and drug only works when specific target receptor or marker present
  - Often depends on degree of expression of biomarker
  - Detection may be test and/or sample specific
  - Can create apparent inequity of access

Challenges – cancer medicines

- Possible pan tumour (multiple tumours) listing for PDL1 cancer immunotherapies
  - Health Minister requested PBAC consider options
  - To be considered at August 2018 PBAC meeting
  - Treatment responses to PDL1s are not uniform across different types of cancers, different ages and different patient populations
  - Inconsistent results as to whether it is necessary to classify patients by PDL1 tumour marker expression for effective treatment
  - In most cases, results from trials still early in terms of estimating overall and comparative benefits

Conclusions

- PBAC consider comparative benefits and harms and cost-effectiveness
- Complexity of submissions is increasing
- Complexity of decisions is increasing
- Risk sharing arrangements important for many new listings
- PBAC processes continue to evolve and are currently being reviewed