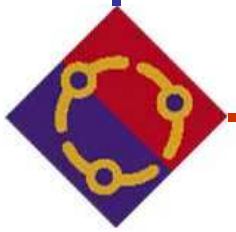
Approval, reimbursement and pricing of high cost cancer medicines in Australia

Dr Agnes Vitry

University of South Australia



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Media

Revolutionary medicine !

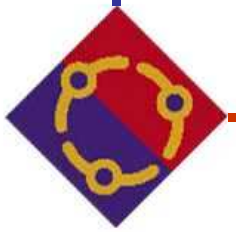
Value novelty and tend to emphasize clinical benefits rather than expressing uncertainties or discussing the potential harms

HOLY GRAIL OF CANCER MEDICINES !

Major breakthrough!

Herald Sun May 04 2014

Thirty-six wonder drugs could extend or save the lives of cancer sufferers, but our leaders just need to fund them



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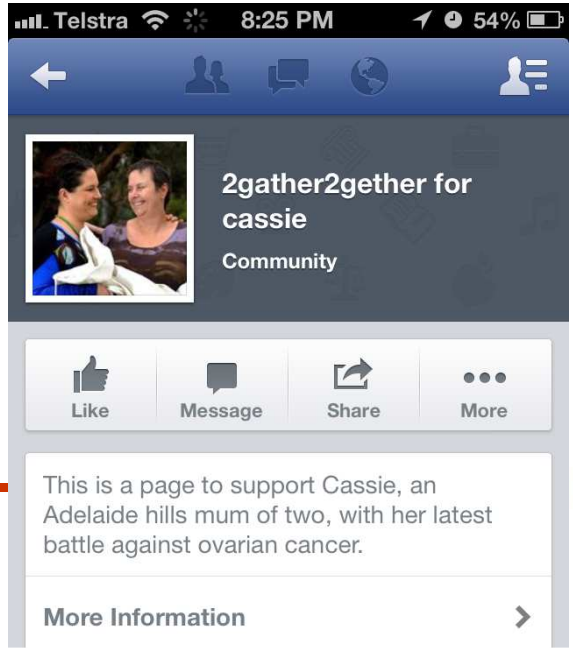
Consumers

- Strong beliefs in the therapeutic value of new medicines
- Savvy consumers
  - Internet, social media and consumer networks
  - Media
- **Cancer is a war and new (= breakthrough) medicines are the weapons**
  - 'To give it your best shot'
- Lobby of governments
- Private fundraising

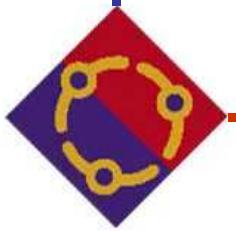


Pharmaceutical industry

- Media campaigns
  - Oncology Industry Taskforce (http://medicinesaustralia.com.au/issues-information/oncology-industry-taskforce/)
  - the Cancer Drugs Alliance (http://www.cancerdrugsalliance.org.au/)
  - Complains that funding of new cancer medicines on the PBS is too low
  - Calls for reforms of the current funding processes and fast-track access like the UK cancer drug fund

Background

- Annual cost of cancer care to Australian government between $4 billion and $5 billion
- Government expenditure on cancer medicines
  - one third of cancer funding
  - $1.5 billion in 2013-2014
  - increasing faster than any other area of health care
    - average annual growth rate of 63% from 2009-10 to 2013-14



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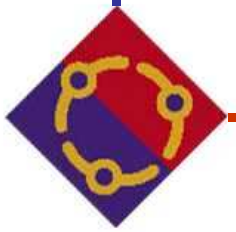
National Medicines Policy

- **Timely access to the medicines that Australians need, at a cost individuals and the community can afford**
- Medicines meeting appropriate standards of quality, safety and efficacy
- Quality use of medicines
- Maintaining a responsible and viable medicines industry



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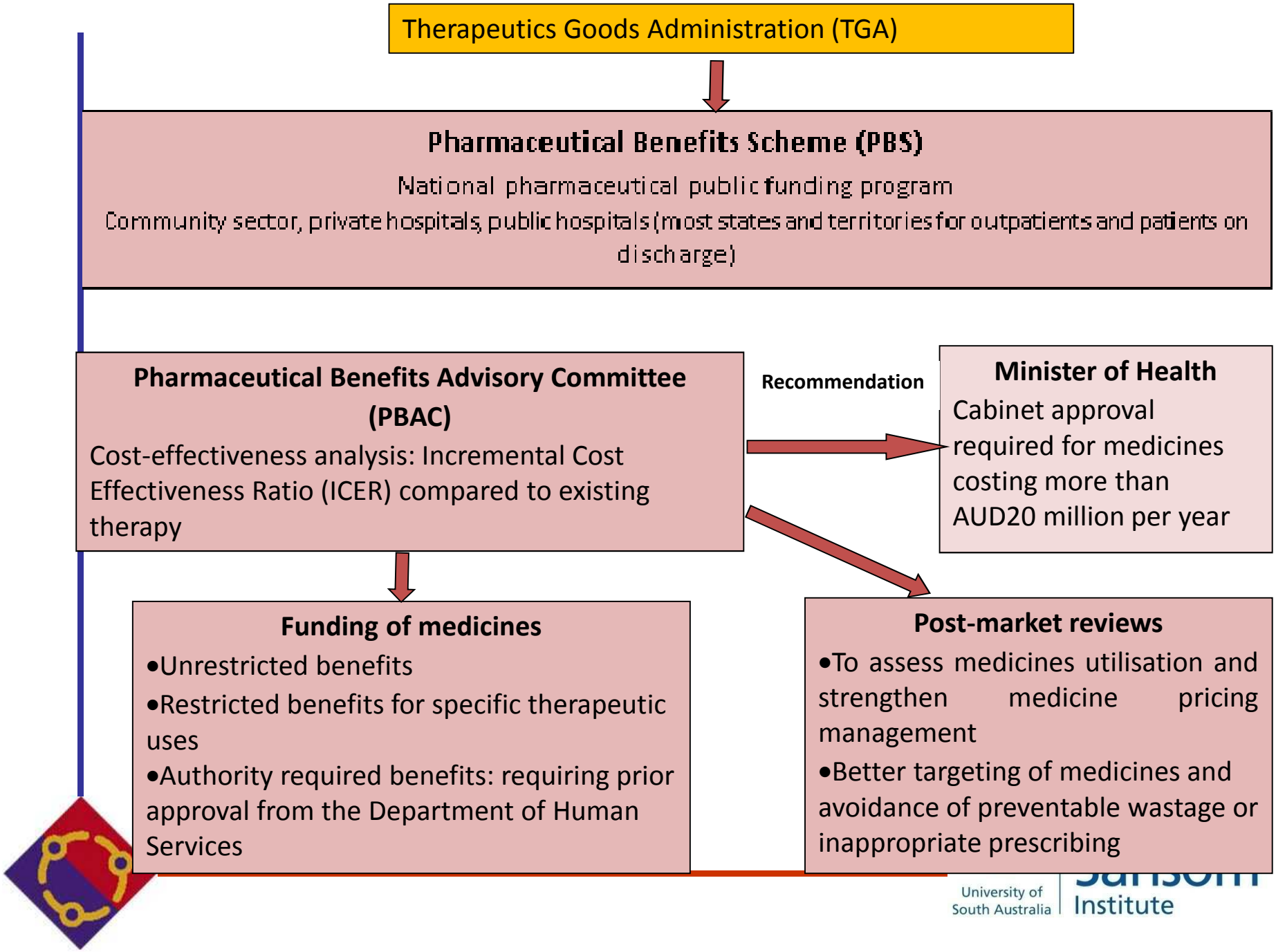
Therapeutics Goods Administration (TGA)
Pharmaceutical Benefits Scheme (PBS)
National pharmaceutical public funding program
Community sector, private hospitals, public hospitals (most states and territories for outpatients and patients on discharge)
Pharmaceutical Benefits Advisory Committee (PBAC)
Cost-effectiveness analysis: Incremental Cost Effectiveness Ratio (ICER) compared to existing therapy
Recommendation
Minister of Health
Cabinet approval required for medicines costing more than AUD20 million per year
Funding of medicines
•Unrestricted benefits
•Restricted benefits for specific therapeutic uses
•Authority required benefits: requiring prior approval from the Department of Human Services
Post-market reviews
•To assess medicines utilisation and strengthen medicine pricing management
•Better targeting of medicines and avoidance of preventable wastage or inappropriate prescribing
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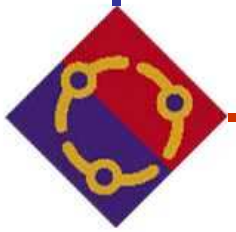
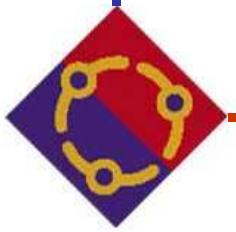
Background

- Over 100 cancer medicines on the Pharmaceutical Benefits Scheme (PBS)
  - Australian patients pay no more than co-payment ($36.9 and $6.00 for general and concessional beneficiaries respectively for chemotherapy treatment)
  - Between 2-3% of the total cost of cancer medicines funded by patient co-payment versus 15% for non-cancer medicines
  - Risk of 'financial toxicity' for Australian patients minimal except for unfunded medicines



Background

- Funding decisions on new, high cost cancer medicines are challenging
  - insufficient evidence on benefits and risks
  - high prices requested by pharmaceutical companies

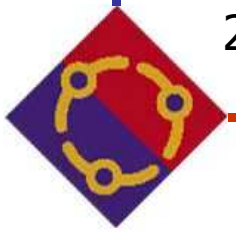


Retrospective analysis of submissions for cancer medicines considered by the PBAC between 2005 and 2012

- On average, one in every two major submissions had a significant problem with the supporting evidence

Problem area	Specific problem	No. (%) of all problems
Choice of comparator	Choice of main comparator	53 (20)
Estimate of comparative clinical efficacy	Availability of randomized clinical trial evidence	18 (7)
	Poor-quality evidence	16 (6)
	Analysis of interpretation of clinical evidence	140 (54)
	Determination of therapeutic noninferiority	34 (13)

Wonder M, Value in Health 2015; 18: 467-476



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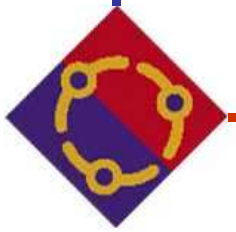
Funding of cancer medicines

- Similar decision criteria for cancer and non-cancer drugs
- Acceptable Incremental Cost Effectiveness Ratio (ICER) compared to existing therapy
- No fixed ICER threshold
  - Unlikely to be listed when ICER > $75 000 per QALY

Mauskopf J, Int J Technol Assess Health Care 2013; 29: 92-100



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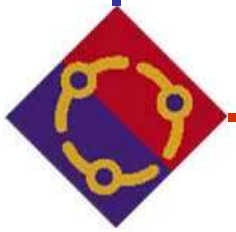
Funding of cancer medicines

- Cancer drug submissions tend to have a modelled economic evaluation and have a higher cost per QALY than non-cancer drugs
  - 29% vs 15% of cancer and non-cancer drugs respectively had a reported modelled cost per QALY of more than Australian dollars 45 000 ($p < 0.001$)

Chim, L. Pharmacoeconomics 2010; 28: 463-475



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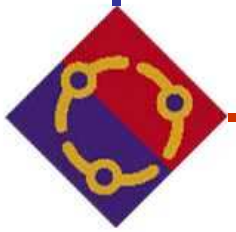
Pricing of cancer medicines

- Value-based pricing in Australia

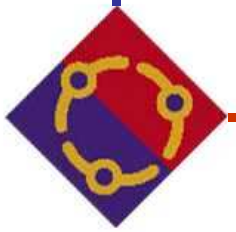
  versus

- US prices of cancer medicines
  - Not explained by the importance of benefits
  - Remain high despite the marketing of competitive products
  - Launch prices adjusted for inflation and survival have increased substantially overtime



Comparison of marketing authorisation and funding approval of cancer medicines in Australia, Europe, US

- Between 2010 and 2013
  - 92 indications authorised for 65 cancer medicines in at least one of the three regions Australia, Europe and the US.
    - 50% new active substances
    - 50% new indications for existing active substances.



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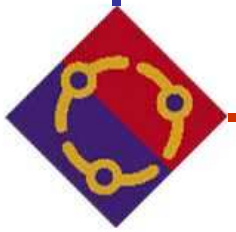
Marketing authorisation and funding approval of cancer medicines

Regulatory Bodies	Number of Indication Approved (n,%)
TGA	54 (59%)
EMA	72 (78%)
FDA	68 (74%)

- Lower percentage of indications approved by TGA is mainly caused by a delay in approval
  - EMA authorised 177 days earlier
  - FDA authorised 249 days earlier
- Delay in approval mostly explained by delay in submission by pharmaceutical companies
  - Lodgement to the TGA 266 days after lodgement to FDA and EMA (Department of Health 2015)



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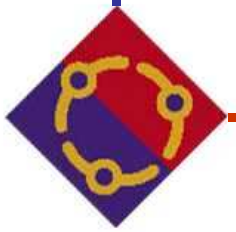
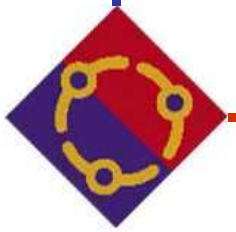
Marketing authorisation and funding approval of cancer medicines

- By June 2014
  - 24 (44%) of the 56 authorised indications had received a positive funding recommendation from the PBAC
    - 10 submissions received positive recommendation after the first PBAC assessment
    - 12 submissions after two assessments
    - 2 submissions after 3 and 4 assessments.



Marketing authorisation and funding approval of cancer medicines

- Average time between the TGA authorisation and the PBAC positive recommendation: 343 days
- Average time between the TGA authorisation and PBS actual listing: 641 days
  - 297 days in the parallel funding and approval process introduced in 2011



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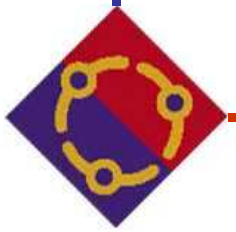
Marketing authorisation and funding approval of cancer medicines

Public funding	No of indications funded
PBS (Australia)	21 (39%)
NICE (UK)	14 (19%)



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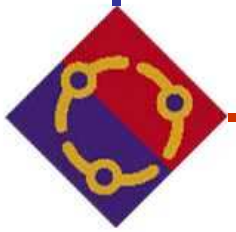
Comparison of funding decisions for cancer medicines

- Over 20 years: 1994-2014
- UK/Australia/Canada (pCODR)
- Proportion of positive funding decisions similar
- Reimbursement recommendations for cancer medicines with the highest cost-effectiveness ratios were the most inconsistent

Cressman S. The oncologist. 2015; 20: 729-736



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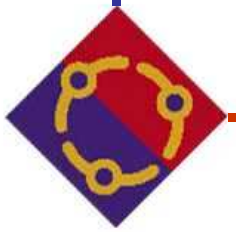
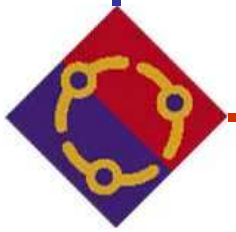
Special pricing arrangements

- Price-volume agreements, discounts
- 21 cancer medicines in May 2015
  - Abiraterone, bevacizumab, bortezomib, brentuximab, cabazitazel, cetuximab, dafrafenib, dasatinib, docetaxel, eribulin, enzalutamide, everolimus, fludarabine, imatinib, ipilimumab, ofatumumab pazopanib, panitumumab, rituximab, sorafenib, sunitinib



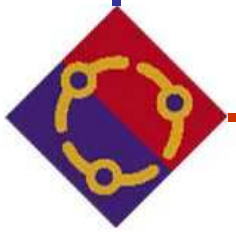
Managed access programmes

- Since 2010, a new type of managed entry agreement: 'Managed Entry Scheme'
- Provisional funding of new medicines conditional on the later provision of favourable scientific evidence
  - Medicine with high and urgent unmet clinical need,
  - Would not otherwise be funded because of high clinical uncertainty and/or high cost
  - There is evidence that can reliably be reported and evaluated within a reasonable timeframe which the PBAC is satisfied would resolve the identified area of uncertainty



Managed access programmes

- Ipilimumab (advanced melanoma)
  - ‘implementation of a mechanism to verify the anticipated overall survival benefits of ipilimumab in real world clinical practice in Australia... The sponsor would be expected to rebate the cost of difference in performance between observed versus predicted benefits of ipilimumab’ (PBAC 2012)’
- Prembrolizumab (advanced melanoma)
  - ‘pembrolizumab appears to be more effective than ipilimumab, but the magnitude of this benefit is uncertain, particularly for overall survival…the modelled economic evaluation could not be relied upon to estimate the incremental cost-effectiveness of pembrolizumab with sufficient confidence to determine the basis for any price advantage over ipilimumab.’ (PBAC 2015)



Managed access programmes

- Trametinib (advanced melanoma)
  - 'The initial price for the MES would be as requested in the submission. This is despite unresolved concerns that the ICER still favours trametinib. Instead of recommending trametinib at a price justified by the existing evidence (which would be lower), a rebate with interest would be put in place, thereby ensuring that the conditions of the MES framework are fulfilled. On submission of modelling based on more conclusive evidence of cost-effectiveness from COMBI-D and COMBI-V, there would be no option for an increase in the price of trametinib, as the higher price is being paid at entry into the PBS.' (PBAC 2014)
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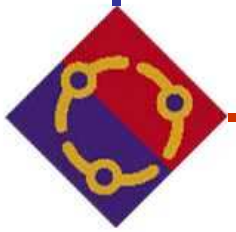
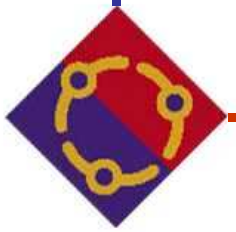


Managed access programmes

- Crizotinib (non-small cell lung cancer)
  - 'The initial entry price for the managed entry scheme (MES) would be as requested by the submission. The MES framework would include a mechanism for payment of a rebate with interest to the Commonwealth should crizotinib fail to deliver on its claimed benefits. On submission of new information as outlined below, there would be no option for an increase in price of crizotinib, as the higher price would already have been paid since entry onto the PBS.' (PBAC 2014)

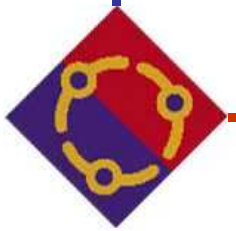


Conclusions

- Recommendations
  - Expert review of medicines and medical devices regulation
    - First report released 24 June 2015

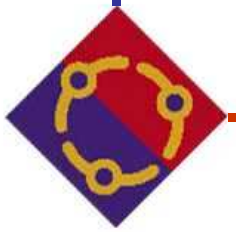
    https://www.tga.gov.au/media-release/expert-review-medicines-and-medical-devices-regulation
  - Australian Senate's inquiry on 'Availability of new, innovative and specialist cancer drugs in Australia'
    - Final report released 17 September 2015

    http://www.aph.gov.au/Parliamentary_Business/Committees/Senate/Community_Affairs/Cancer_Drugs



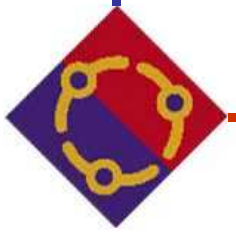
Conclusions

- Expand the TGA marketing approval pathways
  - Utilisation of assessments conducted by comparable overseas regulators
  - Expedited assessments in defined circumstances
- Expand role of consumers and clinicians in the PBAC assessment processes
- Improve monitoring and data collection
- Improve Managed Access Programmes



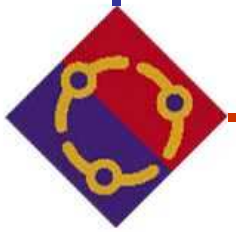
Conclusions

- Many difficulties ahead for successful implementation of managed access programmes
  - Choice of an appropriate study design
  - Feasibility of the research within a limited time frame
  - Interpretation of the results
- Confidentiality of risk sharing and managed entry agreements
  - Savings?
  - Real prices in other countries?
  - Difficulties for external pricing policies



Transparency of pricing and therapeutic value

- 'We cannot continue to accept novel therapeutics with very small benefits for exorbitant prices' (Lancet Oncology 2014)
- 'The pharmaceutical industry must be willing to show the public how it prices its drugs of face losing its trust' (Pharmafile 2014)



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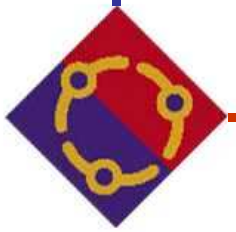
A better informed public debate

- How to obtain the best health outcomes for all within a financially sustainable insurance system?
  - More funding for end-of-life treatments and rare cancers ?
- More communication from the Australian Government
  - Detailed press releases to explain controversial decisions
  - Consumer-friendly documents
  - Consultation processes



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