Managing uncertainty in reimbursement decision making:
PBAC/ESC perspective

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Don’t mention the U word!

- Uncertainty is a fact of life in HTA
  - Particularly for the ICER (outcomes are in the denominator)
  - Also for utilisation and costs
- No confirmation of the rumour that evaluators run a search and replace on that word.....but......
  - Knowing something is uncertain is not usually helpful
  - Uncertain or unknown or unknowable?
  - What direction and why?
  - Can it be managed and how?
Are we becoming more uncertain?

These new Guidelines sought to reduce the uncertainty for the PBAC. The results show that the “average” number of times that the words, “uncertain/uncertainties/uncertainty”, appeared per PSD page was significantly higher after the new PBAC guidelines introduction.

The introduction of version 4 of the PBAC Guidelines in 2008 might have led to an increase in the complexity and, thus, uncertainty faced by PBAC during their deliberations around reimbursement of pharmaceuticals in Australia. There was a significant 25% increase in the number of times that the words, “uncertain/uncertainties/uncertainty”, were found per PSD page compared with the period prior to the introduction of the version 4 of the Guidelines (2003-2008).

Source:
Chollet, Lindsay and Gonzalo
Complexity increases uncertainty: The impact of PBAC Guidelines (version 4) on PBAC decision making
4th Asia-Pacific ISPOR Meeting
Do they have a point? Is there a Section C effect?

• Made explicit gaps between clinical evidence available and economic evidence required
• Identified methods to address these gaps
• Methods have increased in sophistication
• The uncertainty is inherent in the clinical data, but can be exaggerated by the economic claim
• No pre-modelling techniques that can substitute for lack of data
• Take home message: don’t blame the guidelines!
Other factors at play

- Parallel process
- CED as an emerging international trend
- High cost drugs as an emerging trend
- Rare conditions, new more tailored treatments
- New agents: more options in the treatment algorithm, more options for place in treatment
- Shifting comparators
- Pharmacogenomics (co-dependents, sub-groups)
When does uncertainty matter most?

- Unclear data on quantifiable treatment effect (cross-over, surrogate outcomes, small numbers, trial designs)
- No/limited data to inform transitions in model
- Lack of information on patient relevant outcomes (impact on QOL, survival)
- Trials that are not applicable to the Australian clinical context
- Models that do not calibrate with Aust’n utilisation and costs
- Wildly varying ICERs
- Utilisation and costs (potential for leakage, initiation and stopping criteria, overall costs)
What SA are informative?

• If a model relies on a particular statistical analysis, present alternatives
• If extrapolation is necessary, different methods, different starting points
• If QOL drives QALYs test the impact of the weights, the method, the instrument
• One way deterministic SA are useful to identify the key sources, directions and range
• Multi-way important for obvious reasons
• PSA/CEAC are useful, but not to replace these
You cannot “manage” uncertainty with…..

• Bold assertion/Robust rhetoric
• More data, but from the wrong trials
• Statistical analyses as a substitute for more data when the data are the problem
• New techniques/methods without assessment of their impact (ie without SA to these methods)
How does the PBAC deal with uncertainty?

- **Reject** – when the clinical data or the model cannot be relied on for DM
- **Defer** – when there are potential (and imminent) answers/solutions to the unknowns
- **Risk share** (including caps and rebates)
- **Indicate** a lower price is the most acceptable way forward
- **Managed entry** – an option but not an easy solution
Role of post-market reviews

- Neither the ICER nor costs and outcomes are predictable in practice
- DUSC utilisation and PBAC reviews focus attention on VFM in practice
  - Impact of new therapies on cost-effectiveness
  - Shifts in clinical practice over time that impact on utilisation, costs, cost-effectiveness
  - How often does treatment occur, in whom?
  - Are cost-savings realised in practice?
  - Are stopping rules applied as at time of listing?
- Challenge of how to manage this to maintain sustainable PBS system
Some thoughts on managed entry

• The data to address the gaps must be obtainable
  – forthcoming trial or a feasible study that will specifically address the missing info
  – an appropriate timeframe
  – a predictable landscape for the condition and treatment

• Managed entry must incorporate some form of feasible managed exit (via price, or change in restriction)

• The price must address the risks to the funder

• The value proposition must be clear from the outset