Making a good case for cost-effectiveness

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Working with the process

AWMSG Process guidance

- Clinical and cost-effective evidence
- Decision-making framework
- Rules and policies (cost-effectiveness thresholds, end-of-life, orphan)
- Value judgements

Company submission

- Content
- Evidence presentation
- Transparency
- Plausibility

AWMSG Process Guidance

All Wales Medicines Strategy Group
Grŵp Strategaeth Meddyginiaethau Cymru Gyfan

Search
Home | About us | Contact us

About AWMSG **Appraisals** **Medicines management**

Pharmaceutical industry

Appraisal information

- About
- Appraisal process
- Wales Patient Access Scheme
- AWMSG in relation to NICE
- Orphan, ultra-orphan and rare diseases
- All appraisal documents

All appraisal documents

ABPI and AWTTC confidentiality agreement
Appraisal FAQs
Appraisal principles and process flowchart
Appraisal process flow diagram & timeline
AWTTC Budget Impact template (Excel 2003)
AWTTC Budget Impact template (Excel 2007)
Clinical expert questionnaire and declarations of interest form
Clinician and Patient Involvement Group (CAPIG) Information
Clinician and Patient Involvement Group (CAPIG) Terms of reference
Decision process for full & limited submissions
Exclusion criteria
Form A
Form A guidance notes
Form B
Form B guidance notes
Form C
Form C guidance notes
Independent review process
Industry engagement
Information for companies attending AWMSG appraisal meetings
Letter to companies following a NICE negative
Life-extending, end of life medicines
Orphan, ultra orphan and rare disease medicines
Recommendation wording
Summary guidelines for appraising medicines
Summary information for patients to be completed by the company
Therapeutic Development Assessment (TDA) Partnership Group
Template for raising an issue during an appraisal
Welsh Health Circular (2017) 001 The new treatment fund - Access to medicines recommended by NICE and AWMSG

Defining the scope of the submission

P	Patients	Is the licensed indication representative of the eligible population in Wales How does the modelled population reflect the trial population and the Welsh population?
I	Intervention	Positioning in care pathway - representative of care in Wales Align with the licensed indication (full vs. restricted) Are there sub-groups that may be more relevant?
C	Comparators	Have relevant comparators been considered based on standard of care in Wales? What is going to be displaced in routine practice – licensed and unlicensed – several? Seek Welsh clinical opinion
O	Outcomes	Efficacy, Costs, QALYs,
S	Study design	CUA preferred

Modelling approach

- Reflect the decision problem at hand

- Base case:
  - **perspective** of NHS in Wales and personal social services
  - **robust, plausible** assumptions and estimates
  - **most relevant analysis** to address decision problem (PICOS)

- a **range of alternatives** (combinations of sensitivity and scenario analyses)

CUA vs CMA

- **CUA is preferred approach**, cost per QALY gained

- CMA ***only*** acceptable when no clinically meaningful differences in the distribution of effects between the medicine and its comparator(s).
  - include **all dimensions of health**
  - Well designed **equivalence trials** for the evaluation of efficacy and evidence of close comparability of other effects
  - Non-inferiority ≠ equivalence

Comparative effectiveness

- Well designed head to head RCTs
- Conduct indirect treatment comparisons *only* if there are no direct trials of the relevant comparator
  - Follow **best practice**:
  - full details of SR, reasons for inclusion/exclusion, tests for heterogeneity, (in)consistency, etc.

Utilities

- **EQ-5D** is the preferred measure of HRQL in adults, other methods accepted
  - SF-36, CHU9D, HUI, disease-specific utilities etc
- Use **primary QoL data** from trial where possible
  - Avoid unnecessary mapping
- Consider a separate TTO study if there are no utility data whatsoever
- **Check plausibility**
  - Utilities (disease state) vs. previously used values vs. population average

Resource use

- Identified, measured and valued within a Welsh context
  - based on **trial data**
  - using **Welsh data** on resource utilisation and unit costs
    - *Patient Episode Database for Wales* (PEDW) http://www.wales.nhs.uk/statisticsanddata/sourcesofdata
    - *SAIL Databank* https://saildatabank.com/
    - Opinion from Wales
- **If not,** comment on the validity of using resource data from outside Wales, and make reference to any relevant differences in the healthcare environments
- Data from any other UK country, or elsewhere, **will not be accepted** where Wales-specific data is available

Costs

- List price, not discounted (unless part of agreed PAS/WPAS)
- Relevant to Wales where possible
- Drug costs
  - BNF
  - Prescription Cost Analysis Data
- Healthcare Service Use costs
  - NHS Reference Costs
  - National Tariff
  - PSSRU

Time horizon

- **Long enough** to capture all important differential effects on health outcomes and costs

- Lifetime horizon
  - Chronic conditions
  - Differential mortality

- **Explore alternative** if model is sensitive to
  - Time frame
  - Approach used to extrapolate trial data over time

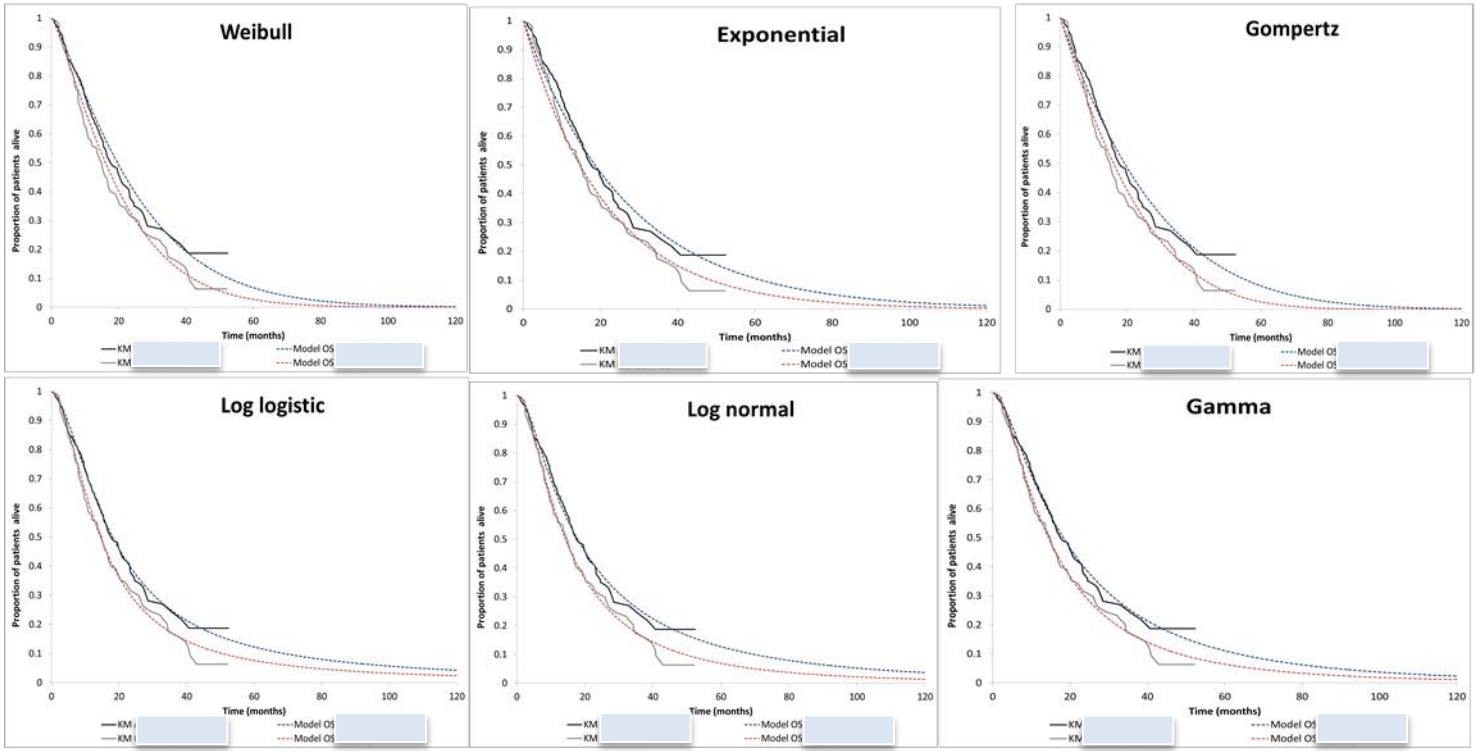
Extrapolation

- Don’t choose parametric function based on one that makes ICER look lowest
  - **Based on fit to the observed data**
  - Diagnostics, visual inspection
- Duration of treatment benefit in extrapolated phase
  - Nil
  - Same as treatment phase and continues at the same level
  - Diminishes in the long term

- **Plausibility**
  - 12 week trial => lifetime benefit?
  - **Expert clinical opinion** on plausibility

Visual fits of the data

Parametric functions for OS compared with observations in the clinical study



Goodness of fit statistics

Summary of goodness of fit of parametric functions for OS

Parametric Model (OS)	Drug A		Drug B	
	AIC	BIC	AIC	BIC
Weibull	305.02	310.51	303.60	309.07
Exponential	307.07	309.82	308.09	310.83
Log Logistic	300.69	306.18	300.71	306.19
Log Normal	301.21	306.70	297.77	303.24
Gamma	302.79	311.02	299.72	307.93
Gompertz	308.55	314.04	307.83	313.30

Uncertainty

- **Structural uncertainty**
  - **Scenario analyses**
  - different care pathways, different health states
  - **If in doubt**, present the data for each and every scenario
- **Parameter uncertainty**
  - Sensitivity analyses on all key parameters
    - costs, utilities, estimates of relative effectiveness, extrapolation of survival curves
  - **One way sensitivity analyses**
    - Tornado diagrams, multi-way analyses
  - **Probabilistic Sensitivity Analysis**
    - C/E plane, % in each quadrant, CEACs
    - Probability C/E at thresholds of £20k and £30k per QALY

Budget impact

- Not considered by NMG, is considered by AWMSG
- *Is* important
- Needs to be as relevant and robust as the cost effectiveness model
  - Use AWTTC Budget Impact Template
  - Use Welsh data where possible
  - Costs are separated into medicines costs, and resource use costs
  - Justify assumptions
  - Model alternative scenarios

Beyond the submission

- Draft ASAR
  - Opportunity to comment
  - Address queries and concerns, clarify
  - Challenge interpretation
  - Not a chance to change mind and present different data!
- New Medicines Group meeting
- Public AWMSG meeting

Decision making

- **When the ICER < £20,000**
  - may not be recommended if AWMSG/NMG are not persuaded by the plausibility of the inputs and/or the certainty around the estimated ICER
- **When the ICER falls between £20,000-£30,000**
  - The degree of certainty surrounding the calculation of ICERs
  - The innovative nature of the medicine
  - The particular features of the condition and population receiving the medicine
  - Where appropriate, the broader societal impact
- **When the ICER is > £30,000**, the case for supporting the medicine has to be increasingly strong

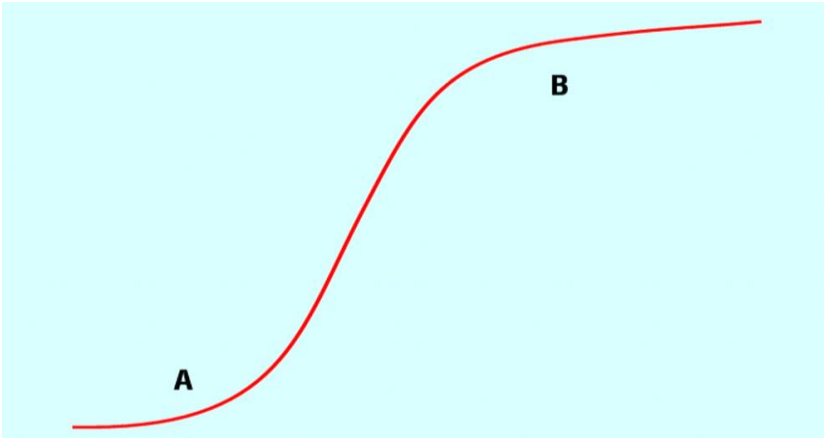
Cost-effectiveness judgements

- the strength of the supporting clinical effectiveness evidence
- the robustness and appropriateness of the structure and the uncertainties around the assumptions on which the model structure is based
- the plausibility of the inputs
- the range and plausibility of the incremental cost-effectiveness ratios (ICER)
- the likelihood of decision error and its consequences.

Cost-effectiveness threshold

A = <£20,000 per QALY gained
B = >£30,000 per QALY gained

Probability of rejection on grounds of cost infectiveness



Increasing cost/QALY (log scale)

Housekeeping

- **Align**
  - Form B Pharmacoeconomics and Resource Implications section
  - Cost-effectiveness model
  - Budget Impact model
- **Model**
  - Ensure transparency and robustness
  - Make sure the macros run
- **References**
  - Web links working

Key takeaways

- No magic formula
- Individual drugs appraised on individual basis using a common framework
- Best chance of successful submission is to present most:

plausible, transparent, robust case, using established best practices,

in line with the process guidance

Diolch yn fawr - Thank you

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PAMS Patient Access to Medicines Service
WNPU Welsh National Poisons Unit
WeMeReC Welsh Medicines Resource Centre
Yellowcard Centre Wales
WAPSU Welsh Analytical Prescribing Support Unit