Preparing for market access in the new millennium
Time to face new world reality?

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Presentation outline

- Background – experience with pharmaceuticals
- Current situation in the major markets (US and EU top 5)
  - What are governments & payers doing to meet the challenges
- Introduction to HTA and economic evaluation as an aid to decision-making
  - A few recent examples
- What can and should the industry do to meet these challenges
  - Some recommendations

Background

While there is an infinite demand for health care, there is and always will be a finite supply of resources

- Demand for health care is on the rise
  - New technologies
  - Ageing population
- Supply is getting tighter
  - Industry productivity is falling
  - New technologies have higher unit prices
- Affordability is getting worse
  - Competing government priorities
  - Worsening government fiscal situation

Who are payers?

- Those charged with the responsibility of making decisions or recommendations on the reimbursement and pricing of new health care technologies
  - Strictly speaking they are not payers
  - Whilst the ultimate decision maker is usually an elected official, such decisions are complex and require technical advice
  - Technical advice is provided by an agency (i.e. NICE-UK) or an independent expert committee (PBAC-Australia)
  - Same or different agencies/expert committees for different health care technologies
  - The agency/expert committee is comprised of individuals with a variety of backgrounds

The emerging importance of payers

- For a new health care technology, regulatory approval is no longer a guarantee for its commercial success
  - Commercial success now requires a favourable pricing and reimbursement outcome
- Payers have a different perspective to the regulators and they ask different questions
  - Regulators are more concerned about absolute efficacy & safety (i.e. placebo-controlled trials). This is changing in Europe.
  - Payers are more concerned about comparative efficacy and safety (i.e. active-controlled trials)

Payers' decision-making frameworks

- Traditional criteria
  - Clinical need (public health policy)
  - Clinical benefit (evidence-base medicine)
  - Value for money (economic evaluation)
  - Affordability (budget impact analysis)
- Other criteria (less amenable to quantification)
  - Rarity of the disease/condition
  - Disease/condition severity
  - Availability and affordability of alternatives

Current situation in the US

- Complex health care system with multiple payers (public and private)
- Medicare Prescription Drug, Improvement and Modernization Act of 2003 (MMA)
  - Lead to the introduction of an entitlement for prescription drugs for those aged 65 and older through tax breaks and subsidies via Medicare part D
  - The MMA establishes a standard drug benefit that private Part D plans must offer
  - The MMA stipulates which drugs/drug classes should be included in Part D plans
- Patient Protection and Affordable Care Act of 2010 (PPACA)
  - Kick started the Comparative Effectiveness Research (CER) movement
  - Federal government agencies (i.e. CMS) are prevented from using cost as a decision-making criterion
  - Recent report from the Institute of Medicine says cost must be considered in determining a package of "essential health benefits" to be provided under the PPACA. The report does not list the specific benefits to be covered.
- Several large private plans (e.g. WellPoint, Humana) use the results from value for money assessments to inform their coverage decisions
  - Academy of Managed Care Pharmacy (AMCP) guidelines

Current situation in the UK

- National Institute for Clinical Excellence (NICE)
  - NICE was set up on 1 April 1999 to ensure everyone has equal access to medical treatments and high quality care from the NHS - regardless of where they live in England and Wales.
  - Role expanded to include public health issues in 2005; National Institute for Health and Clinical Excellence
  - Appraises all types of health care interventions
  - Not all new health care technologies are appraised
- Introduction of value-based pricing for all new medicines in 2014
  - New medicines will be priced according to the expected benefits
  - Department of Health currently working on how it be operationalised. The role of NICE is yet to be finalized.

Reference: www.nice.org.uk

Current situation in Germany

- Institute for Quality and Efficiency in Health Care (IQWiG)
  - An independent scientific institute that investigates the benefits and harms of medical interventions for patients
  - Not all new health care technologies are appraised
  - Insistence on evidence from RCTs
- Major reform in 2010 (AMNOG) has signaled the end of free pricing for new medicines
  - Sponsor to prepare a value dossier with a detailed description of a new medicines' incremental clinical benefits are now mandatory. Dossier to be provided to the Federal Joint Committee (GBA).
  - GBA will either review the dossier or will commission independent review by IQWiG or another agency
  - Mandatory price decreases

Reference: www.iqwig.de

Current situation in France

National Authority for Health (HAS)

- Established in August 2004 to bring together under a single roof a number of activities designed to improve the quality of patient care and to guarantee equity within the national health care system
- They range from assessment of drugs, medical devices, and procedures (Commission de la Transparence) to the publication of clinical guidelines, the accreditation of health care organizations and the certification of doctors
- The CT uses its own rating system (ASMR) to determine the level of clinical benefit of a new medicine
- Recent reforms of note
  - Creation of an economic evaluation committee (CEESP)
  - Economic evaluation of some existing drug classes

What are payers doing to meet the challenges?

- Even greater scrutiny of health care budgets and expenditure
  - Budgets often determined by elected officials
  - Greater use of risk-sharing agreements (mostly financial-based)
- Greater use of health technology assessment (HTA) methods and procedures to improve their decision-making
  - +/- Economic evaluation (i.e. 'value for money' assessments and determinations)
- Increasing their transparency (decisions and processes)
- Introducing/improving their appeal processes

What is HTA?

- HTA is a field of scientific research to inform policy and clinical decision-making around the introduction and diffusion of health technologies
- HTA is a multidisciplinary field that addresses the health impacts of technology, considering its specific healthcare context as well as available alternatives. Contextual factors addressed by HTA include economic, organizational, social, and ethical impacts. The scope and methods of HTA may be adapted to respond to the policy needs of a particular health system.

Reference: Health Technology Assessment International (HTAi)

Methods of economic evaluation

There are 4 established methods of full/complete economic evaluation:

- Cost-effectiveness analysis (CEA)
- Cost-minimisation analysis (CMA)
- Cost-benefit analysis (CBA)
- Cost-utility analysis (CUA)

Reference: Drummond M, *et al*. Methods for the Economic Evaluation of Health Care Programmes. Third edition. Oxford University Press.

What is utility?

- A relative measure of satisfaction from consuming a good or service
  - Takes account of personal preferences
- Not the same as health related quality of life (HRQoL)
  - Traditional generic (i.e. SF-36) and disease-specific (SGRQ) HRQoL instruments do not take personal preference into account
- Measured on an interval scale
  - Prefect or full health = 1, death = 0
- Utility can be measured quickly using a multi-attribute utility assessment instrument (MAUI)
  - Examples are the EQ-5D, HUI and AQoL

What is a QALY?

- The quality-adjusted life year (QALY) is a measure of disease burden that seeks to includes both the quality and the quantity of life lived
  - Some interventions improve survival with or without an effect on HRQoL/utility
  - Some interventions improve HRQoL/utility but do not improve survival
- A QALY is based on the number of years of life that would be added by the intervention.
  - A full year in perfect health = 1 QALY, 2 years of impaired health (utility of 0.5) = 1 QALY
- A metric that facilitates meaningful comparisons across diseases/conditions and interventions
  - Improves decision-making

What is a cost-effectiveness ratio?

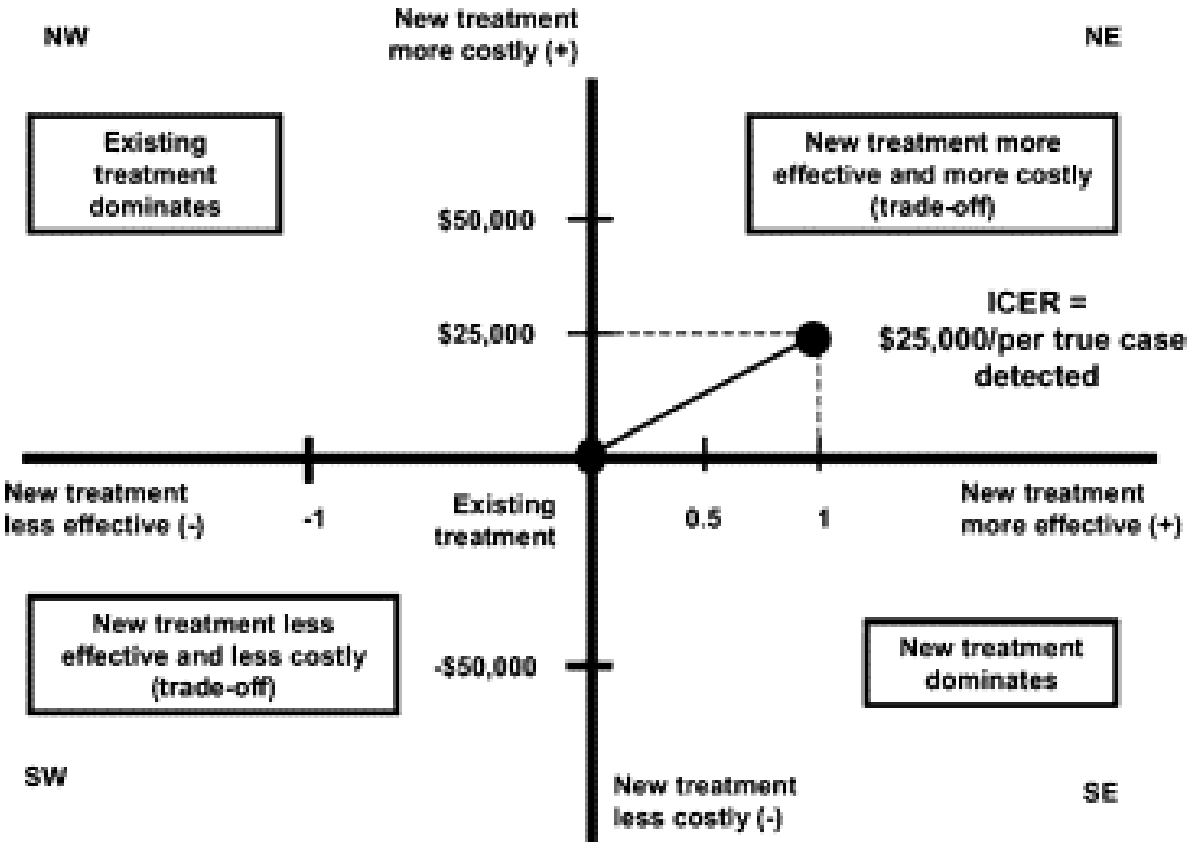
- The ratio of the cost of the intervention (numerator) to a relevant measure of its effect (denominator)

  $CE = (C_2 - C_1)/(E_2 - E_1)$

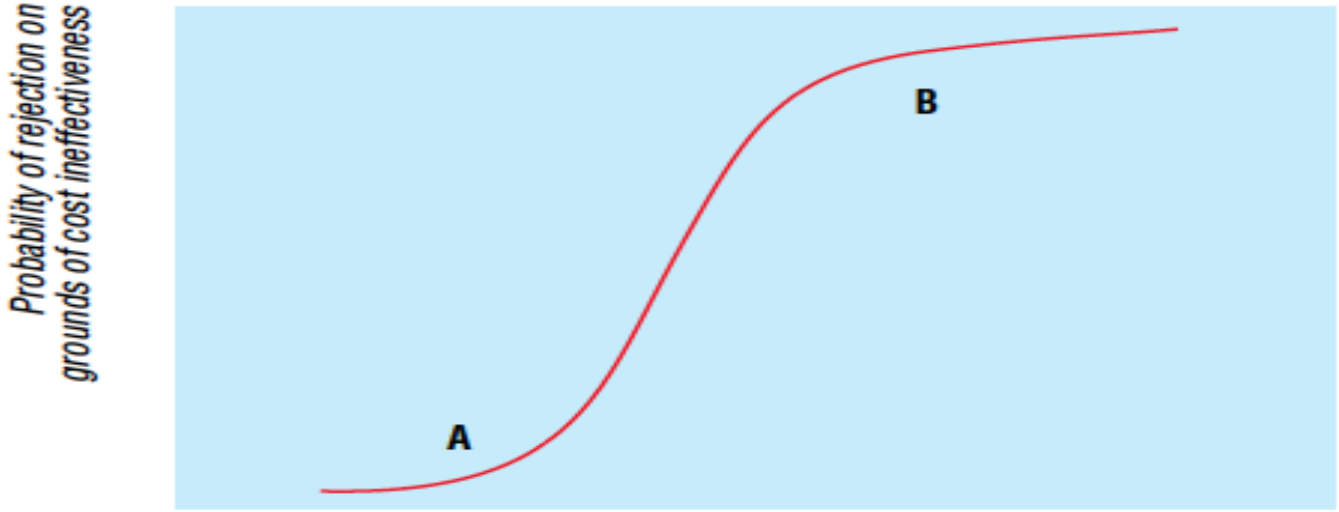
  - Costs expressed in local monetary units ($)
  - Effects expressed in either
    - Local monetary units (CBA)
    - Natural units (CEA, CMA)
    - Utility (CUA)

- Greater focus on the incremental cost-effectiveness ratio (ICER)

Cost-effectiveness plane



Cost effectiveness threshold



Relation between likelihood of a technology being considered as cost ineffective plotted against the log of the incremental cost effectiveness ratio

Rawlins M, Culyer A. National Institute for Clinical Excellence and its value judgments. BMJ 2004; 329: 224-7.

Example 1 – new small molecule

Sitagliptin (Januvia) for type 2 diabetes mellitus (DPP IV inhibitor)

- Common, life threatening disease
- Many treatments (most are old and cheap)
- Available treatments have modest efficacy
- Price comparable to some treatments (glitazones)
- Evidence to support its market access came from large randomised, placebo and active controlled trials
- Relationship between surrogate outcome (HbA1c level) and final outcome (death) well established

Example 2 – new biological

Etanercept (Enbrel) for patients with rheumatoid arthritis (bDMARD)

- Relatively uncommon, non life threatening disease
- Many treatments (most are old and cheap)
- Available treatments have modest efficacy
- Substantial price premium over other treatments
- Evidence to support its market access came from large randomised, placebo-controlled trials
- Relationship between surrogate outcome (ACR response criteria) and final outcome (QALY?) not established

Example 3 – new orphan drug

Imatinib (Glivec) for chronic myeloid leukemia (tyrosine kinase inhibitor)

- Rare, life threatening disease
- Few treatments (interferon-alfa, hydroxyurea)
- Available treatments have modest efficacy
- Price premium over highest price treatment (interferon-alfa)
  - Comparator for second-line treatment was hydroxyurea
- Evidence to support its market access came from small, non-randomised and uncontrolled studies
- Relationship between surrogate outcome (major cytogenetic response) and final outcome (death) not established
  - Greater effect on major cytogenetic response
  - Limited data on its effect on survival

Recommendations for developers

- Acknowledge that new health care technologies should be developed to support market access
  - The evidence needs of payers can no longer be ignored or deferred
  - Clinical development paradigm change
- Recognise that HTA methods and procedures will be used more and more to support decision-making
  - Use by payers in more countries is inevitable
  - Wider scope to capture more new pharmaceuticals such as orphan drugs
  - Broader scope to capture new devices and procedures

Recommendations for developers

- Improve your understanding of the P&R systems of the major markets
  - Identify the decision-makers and study their decision-making criteria
- Improve your HTA knowledge and skills
  - Hire trained and experienced people
  - Personal professional development
- Study relevant recent P&R decisions for valuable insights
  - Learn from the experiences of others

Recommendations for developers

- Ensure payers' evidence needs are identified and considered for inclusion in the phase III clinical trials
  - Indirect – internal review of recent P&R decisions, external expert advice
  - Direct - scientific advice with payers (and regulators)

When should one start?

As soon as possible!

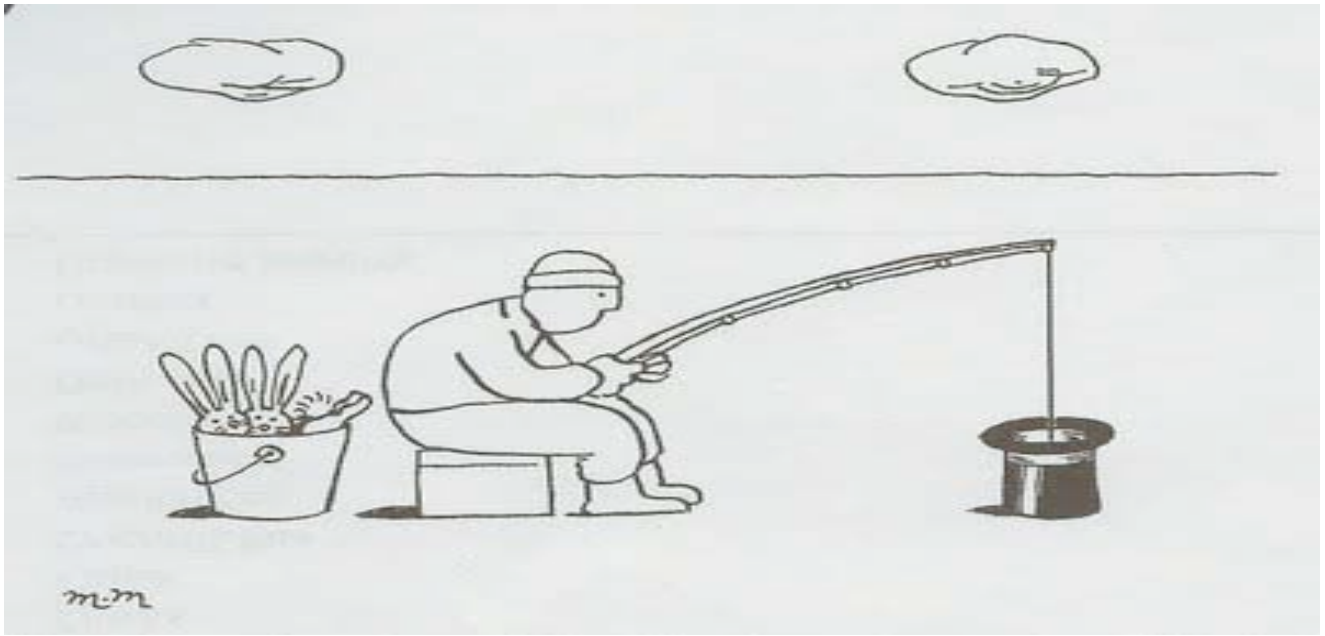
"It's never too early until it's too late" – Martin Backhouse

Use HTA methods in all stages of clinical development to inform internal investment decision-making

- Early phase – identification of candidates for further development
- Mid phase – priority setting, price setting, determination of commercial value
- Late phase – support P&R submissions in major markets

Health economists are not magicians

Most of the major market access problems relate to the strength and relevance of the clinical evidence.



What does the future hold?

- Regulators will become more interested in comparative efficacy (and perhaps effectiveness)
  - The EMA is currently looking to move into this space which is occupied by payers
  - This is not to suggest that the 2 parties should merge
- Regulators and payers will work more closely
  - Alignment of evidence requirements
  - Tripartite scientific advice meetings
- Payers will provide written guidance on their evidence needs
  - Guidelines only provide advice on how to compile P&R submissions using the realised evidence
- Developers will seek to produce ‘one dossier’

New world reality

"Pharma must wake up to the new price reality"

Shire CEO Angus Russell

Use HTA methods and tools to inform your decisions not just those of the payers!

Will real health care reform ever come to the US?

Need further information?

- Academia
  - Handbooks in Health Economic Evaluation, Oxford University Press
- Payer/Decision-maker
  - Rawlins M, Culyer A. National Institute for Clinical Excellence and its value judgments. BMJ 2004; 329: 224-7.
  - Rawlins M. *De testimonio*: on the evidence for decisions about the use of therapeutic interventions. Lancet 2008; 372 (9556): 2152-61.
- Regulator
  - Eichler HG, Bloechl-Daum B, Abadie E, Barnett D, König F, Pearson S. Relative efficacy of drugs: an emerging issue between regulatory agencies and third-party payers. Nature Rev Drug Discovery 2010; 9 (4): 277-91.
- Industry
  - Backhouse M, Wonder M, Hornby E, Kilburg A, Drummond M, Mayer FK. Early dialogue between the developers of new technologies and pricing and reimbursement agencies. A pilot study. Value in Health 2011; 14 (4): 608-15.

Thank you

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