Experiences with the Fourth Hurdle – The relative importance of clinical and economic components

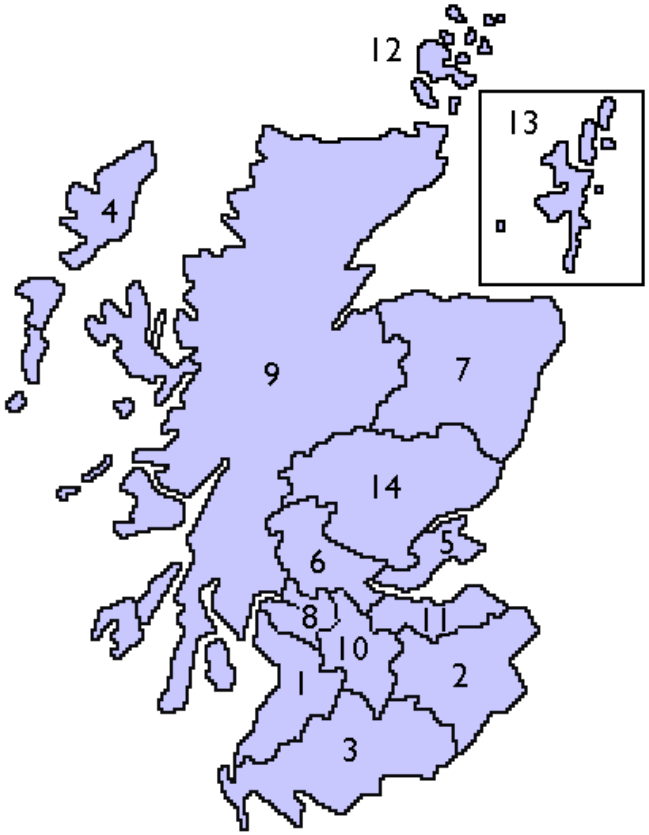
Jan Jones

Scottish Medicine Consortium

Overview

- Scottish healthcare system
- Scottish HTA process
- Evolution over time
- Why does SMC say no?
- Sharing challenging experiences
- Key points …

Scotland



- Population of 5 million
- National Health Service
  - funded from taxation
- Branded drug prices set by the Pharmaceutical Price Regulation Scheme (PPRS)
- Full cost of medicines reimbursed by the NHS
- Value for money assessed by HTA organisation – SMC
- SMC issues ‘advice’
- Health Boards (n=14) process advice and issue local recommendations for use

Scottish Medicines Consortium

- Provides advice to Scottish NHS Boards on comparative clinical and cost-effectiveness of:

  New active substances

  New formulations of medicines

  New indications for medicines

  - 80 products (approx.) per annum

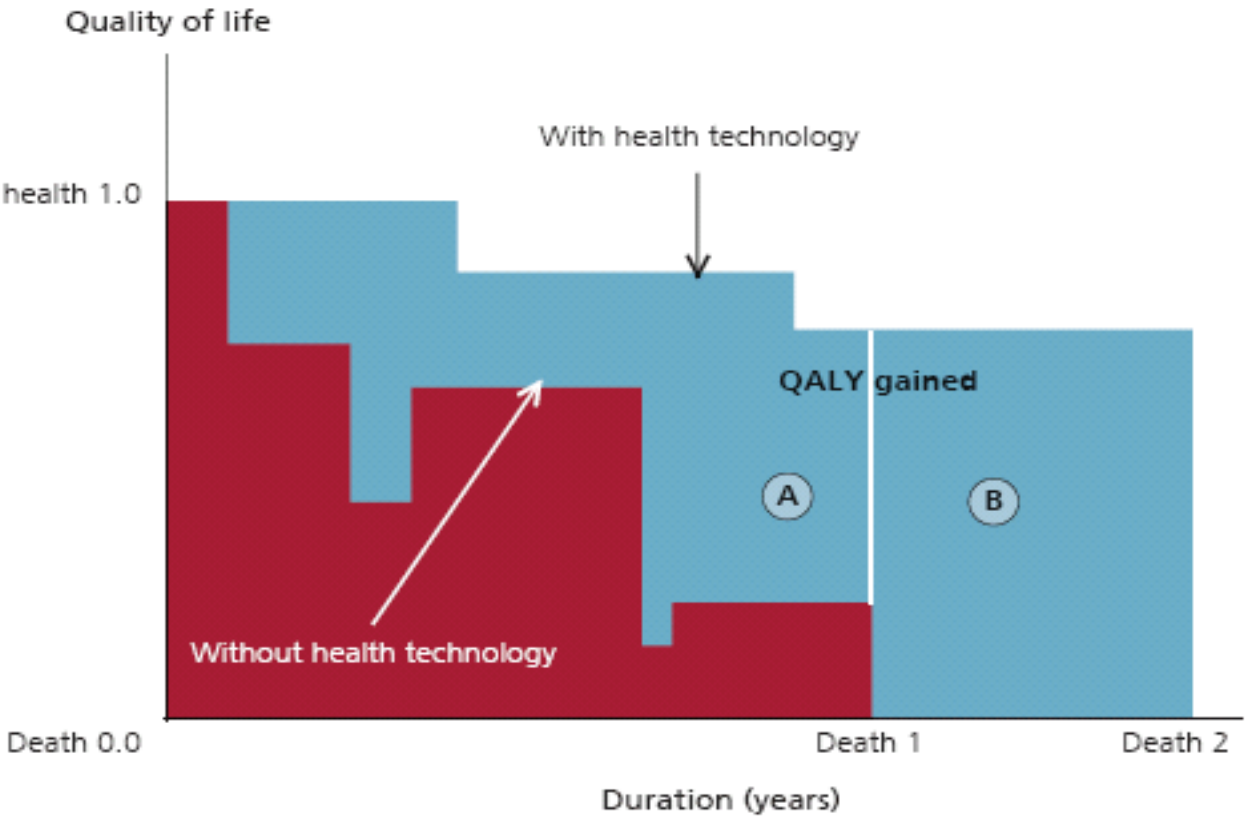
- Provide advice as close to product launch as possible (within 3-6 months)

  - “shape practice, not change practice!”
  - Manufacturers must submit to SMC
  - www.scottishmedicines.org.uk

Cost-effectiveness

- SMC prefers cost utility analysis (QALYs)

Figure. Diagram of the concept of QALY (quality-adjusted life years)



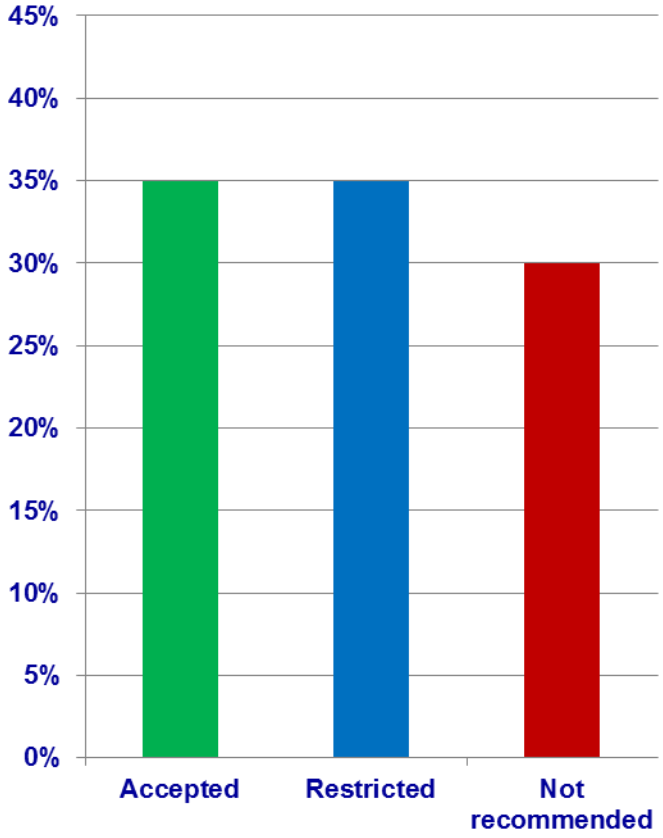
Thresholds for assessing value

- No cost per QALY threshold
  - <£20,000 is usually acceptable to NHS
  - >£30,000 must be justified

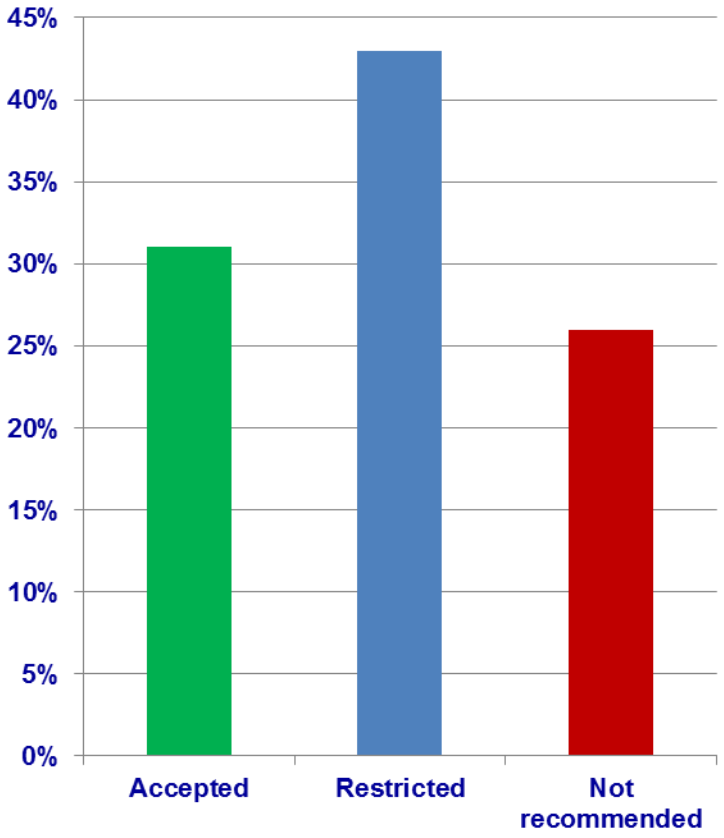
- Level of certainty is important
- Not just cost/QALY point estimate

Outcome of assessments to Oct 2012

All submission types (n=803)



Full submissions (n=516)



‘*The SMC has been in Scotland now for 10 years, and it is hugely and substantially admired because of its independence and thoroughness…….*’

Mr Alex Salmond, Scotland’s First Minister, March 2012

Clinical engagement

- Key to the success of SMC

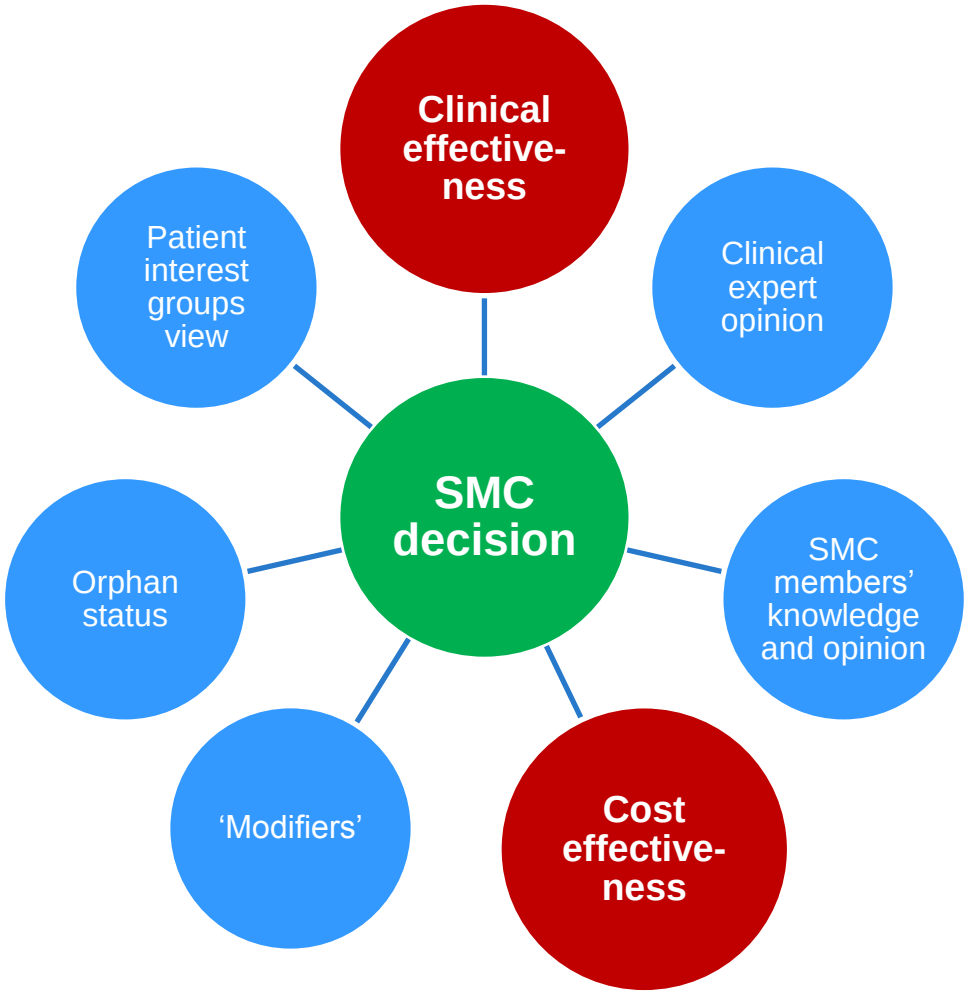
- SMC membership
  - 25/38 clinicians
  - Good critical appraisal skills
  - Awareness of what drives economic models
  - Able to query and test assumptions
  - Link clinical and cost-effectiveness data and service implications

- Clinical expert panel
  - 500+ clinicians
  - Consulted as part of the review process
  - Keen to participate

- Gives credibility and ownership to SMC decisions
- Gains support from clinicians working in Health Boards

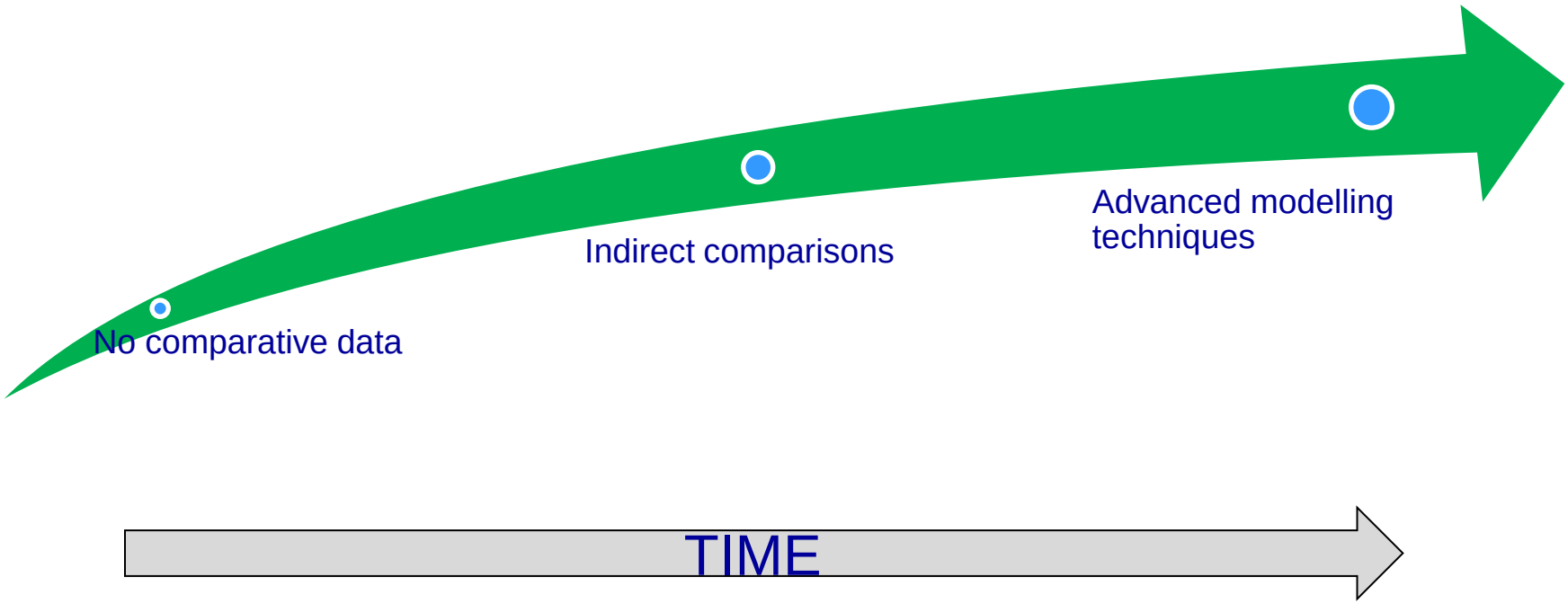
….and Pharma engagement….

SMC decision-making



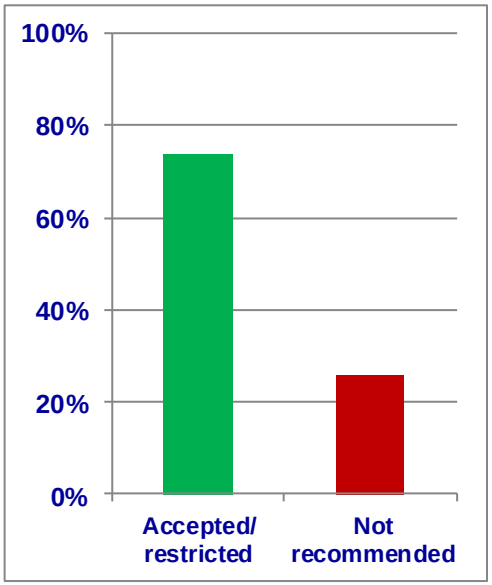
Evolution over time

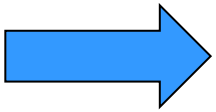
- Quality of submissions
- SMC statistical expertise

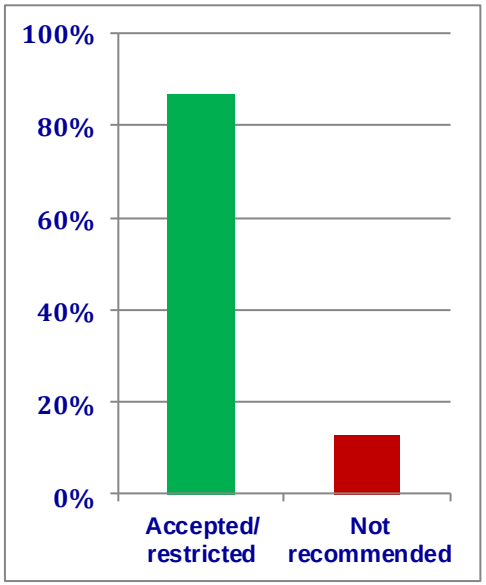


Why does SMC say no?

- Clinical reasons alone - 2%
- Economic reasons alone - 51%
- Both clinical and economic reasons – 47%
  - Value for money does matter







NHS SCOTLAND

Sharing challenging experiences…….

1. Licensing decisions

- Bibliographic applications
  - Well established medicinal use supported by bibliographic literature

  BUT…
  - Lack of clinical data on licensed formulation!

Advice: following a full submission

glucosamine (as hydrochloride) (Alateris®) is not recommended for use within NHS Scotland for relief of symptoms in mild to moderate osteoarthritis of the knee.

No direct clinical trial evidence of the efficacy and safety of this specific product is available. Randomised controlled trials of other formulations of glucosamine hydrochloride indicate little or no benefit over placebo in improving symptoms in patients with osteoarthritis of the knee.

In addition, the manufacturer did not present a sufficiently robust economic analysis to gain acceptance by SMC.

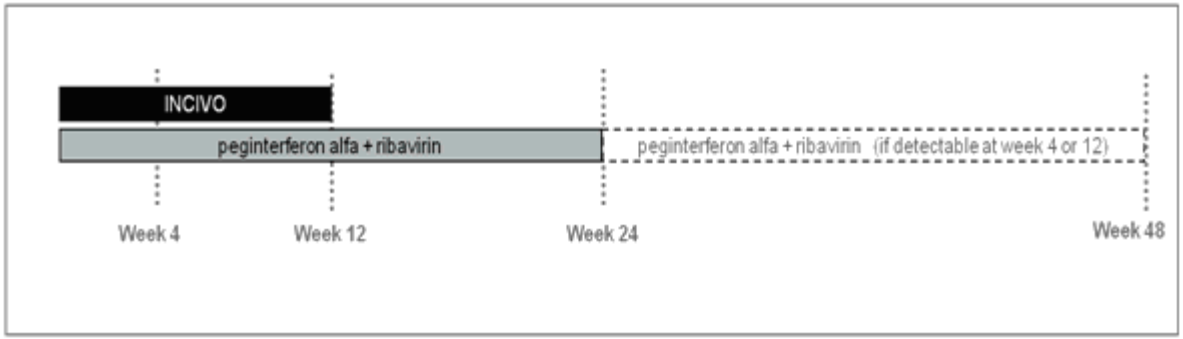
Licence not reflecting preferred practice

- Treatment schedule and duration
- Trastuzumab for the treatment of patients with HER2 +ve early breast cancer following surgery, chemotherapy/radiotherapy
  - Reduced disease progression alongside risk of cardiac toxicity
  - Licence -*'Patients should be treated for one year (or until disease recurrence)*' - based on HERA study

  However….
  - Similar benefit achieved with only nine weeks of concurrent adjuvant trastuzumab (FINHer study)
  - PBAC went to court over this
  - Is the licensed duration the optimal duration? Should treatment be sequential or concurrent?

Positioning in treatment pathway

- Telaprevir in combination with peginterferon-ribavirin for the treatment of genotype 1 chronic hepatitis C
  - Increased sustained virological response alongside significant adverse event profile and risk of resistance mutations
  - Licence – treatment naïve and treatment experienced patients:



BUT…

  - UK consensus guidelines advise a 4 week lead-in with peginterferon-ribavirin prior to the initiation of PI triple therapy in treatment naïve patients and suggest the PI should not be added if rapid viral response achieved
  - Is the licensed strategy the optimal strategy?

Subgroup analysis

- Pemetrexed
  - Pem/cis first-line in metastatic NSCLC other than predominantly squamous cell histology
  - Non-squamous = 73% of study population (1252/1725)

- Gefitinib
  - Metastatic NSCLC with EGFR mutations
  - EGFR +ve = 21% of study population (261/1217)

- Studies not powered to show difference in subgroup
- Randomisation not stratified by EGFR mutation status
- Potential issue for personalised medicines in the future?

2. Complex economic models

- Continued validity of established health economic models
- Exenatide as adjunctive therapy to basal insulin in type 2 diabetes
  - Reduced HbA1c vs basal insulin alone at 30 weeks
  - CORE diabetes model based on UKPDS and Framingham studies
  - Validated model

  BUT…
  - Are assumptions still valid?

3. High cost per QALY

- Justification of cost in relation to health benefits not sufficient
- Orphan drugs and oncology agents
- Influenced by NICE (UK) ‘end-of-life’ criteria
- Patient Access Schemes offer a solution

Schemes proposed by a pharmaceutical company in order to improve the cost effectiveness of a medicine and enable patients to receive access to cost-effective innovative medicines

  - Simple discount schemes preferred
  - 23 schemes in place in Scotland (to Oct 2012)

The future and VBP?

- PPRS Dec 2013 will introduce value based pricing (VBP)
  - Aim:

To improve patient access to effective and innovative drugs by ensuring that they are available at a price that reflects the value they bring

  - To include societal benefits
  - To award severity of disease
  - To award innovation

Acceptance rate by cost per QALY to Sep 2012

SMC modifiers

- Allow SMC to accept medicines with a high cost per QALY if:
  - Evidence of substantial improvement in life expectancy (with sufficient quality of life)
  - Evidence of a substantial improvement in quality of life
  - Ability to target treatment at a subgroup who can benefit
  - Absence of other therapeutic options
  - Possible bridging to a definitive therapy
  - Emergence of a licensed alternative to an unlicensed therapy which is established practice in Scotland

- Allow SMC to accept more uncertainty in the economic case
  - Orphan medicines

Examples

- Lenalidomide for multiple myeloma (May 2010)
  - Median survival gain of 5.1 months vs. standard care in patients who had received 2 or more prior therapies
- Plerixafor for stem cell mobilisation (Jan 2010)
  - Increased collection of stem cells for autologous stem cell transplant vs placebo
  - Bridge to curative therapy
- Betaine anhydrous for homocysteinuria (Aug 2010)
  - Bibliographic data
  - Biochemical efficacy and symptom improvement vs historic controls
  - Licensed version of an established unlicensed therapy

Key points ……

- HTA for a health service operating within fixed resources requires consideration of cost effectiveness (value for money)
- Clinical engagement is essential to credibility of HTA decisions
- Clinical effectiveness is a key component of cost effectiveness
  - If a medicine is not clinically effective it can never be cost effective!
- Both factors are important to SMC decisions as part of a wider judgement on new medicines
- Relative importance depends on the quality of clinical and economic comparative data and relevance to the Scottish population
- Consideration of additional factors allows flexibility in decision-making


THIS IS FINE, I CAN SEE ALL THE EVIDENCE I NEED FROM HERE
COST-EFFECTIVENESS
EFFECTIVENESS
EFFICACY
COCHRANE LADDER of EVIDENCE