Economic evaluation of drugs for rare diseases

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Outline

• Economic rationale for orphan status
• Existing methods of evaluation and appraisal
• Evidence requirements
• Justification for special treatment
  – Cost of production
  – Valuation of benefits
    • Objective of health care
    • Measurement of health gain
    • Equity weights
• Conclusions
Economic rationale for orphan status?

• “Non commercial therapies”
  – Prevalence too low to provide an adequate return to R+D expenditure
  – Ability to pay (society) too low

• Support already provided
  – Direct research funding
  – Tax allowances
  – Lower evidential threshold at licence
  – Additional market exclusivity

• Justification?
  – Development of a promising drug is in the “public interest”
  – People with rare diseases have are entitled to same quality of treatment
Existing evaluation and appraisal

• Estimating costs and effects:
  – Synthesise evidence from a variety of sources
  – RCTs, observational studies and judgement
  – Reflect the uncertainty surrounding estimates
  – Combine in a formal decision framework
  – Estimate cost-effectiveness and the uncertainty surrounding the decision

• Is evidence sufficient to support decisions?
  – Assessment of the consequences of decision uncertainty
  – Formal valuation methods
  – Value of information and evidence requirements will be lower for a smaller patient population
  – Lower evidential standard (other things equal) for orphan drugs
Implications

• Existing methods and process:
  – Can estimate costs and effects using available evidence
  – Lower standards of evidence (more decision uncertainty) will be acceptable

• Orphan drug debate is about values not methods
  – Cost of production
    • Innovation and public interest
  – Valuation of benefits
    • Objective of health care
    • Equity weights
Cost of production

• Question?
  – Should society encourage the private sector to invest in the development of therapies where the cost of production exceeds the value we place on that health gain?

• But is there market failure?
  – Innovation now will lead to future valuable developments
    • Social time preference is less than private (public interest)
    • Property rights public good and free riding
  – Is there any evidence?
    • Directly fund the fundamental research – already done
    • Value and correct the externality – already done
    • Not specific to orphan status
Valuation of benefits

- Objective of health care and clinical “need”
  - Maximise health gain?
    - Capacity to benefit
  - Alternatives
    - Equality of health outcome
    - Equality of resource use
    - Severity of ill health
  - Implications beyond orphan indications
  - Sacrifice health gain
Valuation of benefits

• Inadequate measures of health gain
  – No alternative intervention
  – Poor prognosis/medical rescue
  – Irreversibility and regret
  – Statistical vs known lives (Heredity)

  – Not specific to orphan status
  – Empirical questions apply to all indications – not just rare ones
Valuation of benefits

• Equity issues?
  – Veil of ignorance
    • Value health gain equally

• Equity and rarity?
  – Patients p,q (prevalence of 1 per 20,000 and 1 per 4,000 respectively)
  – Same characteristics, prognosis without intervention and capacity to benefit
  – Acceptable that p does not get treatment?
  – Costs of treating p=10, costs of treating q=1, budget = 10
  – Choose to treat 1p rather than 10q?
  – if yes then outcome for p is valued at least 10x higher than q
  – Premium for rarity is \( \frac{q}{p} \) where indifferent
Conclusions

• Existing evaluation and appraisal methods
  – Can estimate cost-effectiveness
  – Can assess whether evidence is sufficient
  – Without arbitrary definitions of orphan/ultra orphan

• Cost of production are not sufficient justification

• Valuation of benefits
  – Different concepts of clinical need are not specific to orphan status
  – Inadequacy of measures of health gain are not specific to orphan status

• Equity issue – is there a premium for rarity alone?
  – Empirical question (if so what is the premium?)
  – Adjust the value of health outcome rather than changing the cost-effectiveness threshold
Dangers of orphan status

- **Incentives**
  - Reclassify drug indications
  - Reclassify diseases (phamacogenomics)
  - Multiple indications?
  - Skew future R&D towards ‘orphan’ indications

- **Lower requirements for effectiveness and cost**
  - Retirement home/fall back for failed therapies

- **Open ended commitment**
  - “Entitlement to the same quality of treatment”
  - What will be displaced in the longer run
Some suggestions

• Reiterate that evaluation and appraisal should only support provision of therapy which produces health gains valued at least as highly as those they displace

• Acknowledge that the ‘instinct’ to say yes is real but identify the underlying values and apply them consistently

• Where claims are made for a higher valuation of benefits (orphan indication or other issues) the existence and magnitude of any additional weight must be demonstrated empirically

• Research, development and appraisal placed within an explicit and transparent decision framework

• Acknowledge that explicitness, transparency and consistency are prerequisites for legitimate social decision making