Use of Cost-effectiveness in Reimbursement Decisions – a Perspective on Rare Diseases

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Disclaimer

• These views are my own
• I am a member of the BC EDRD Advisory Committee
• PI – CIHR New Emerging Team for Rare Diseases
• I cannot disclose confidential information
Valuation of benefits

• Objective of health care and clinical “need”
  • Maximise health gain?
    • Capacity to benefit (individual/societal)

• Alternatives
  • Equality of health outcome
  • Equality of resource use/treatment access
  • Severity of ill health, potential health outcome

• Implications beyond orphan indications
• We may sacrifice health gain (or other investments)
HTA/Cost Effectiveness Analysis?

Drug Benefits Committee

Orphan Drug Benefits Committee
What is a rare disease?

- 6000 – 8000 rare diseases identified
- 80% genetic / 50% affect children
- No cure or treatment for vast majority
- Unmet need
- Many have high mortality without treatment
- Rare diseases are rare – having a rare disease is not rare
Innovation in the Biopharmaceutical Pipeline: A Multidimensional View

- 5,400 drugs / 8,000 projects
  - >50% potentially ‘first in class’
- 1,795 projects in orphan diseases
- 155 personalized medicine trials
The EDRD Advisory Committee has been established by the Assistant Deputy Minister, Pharmaceutical Services Division, Ministry of Health on an interim basis until such time as a Canadian Access Program for Rare Diseases is instituted through the National Pharmaceutical Strategy (NPS). The purpose of the Committee is:

- To develop a fair, transparent process to assist in pharmacological management of rare diseases in BC;
- To provide expert advice to the Division on rare diseases and the associated drug treatment
Mandate

- Create guidelines to determine appropriateness of treatment in the course of rare genetic diseases using an evidence-based approach that reflects medical and scientific knowledge and current clinical practice.
- Make recommendations for drug coverage in the initiation and ongoing treatment with expensive drugs for those individuals who are diagnosed with rare genetic diseases to the BC-EDRD Advisory Committee (identified as the “Committee) of the Ministry of Health (MoH) Pharmaceutical Services Division (PSD)
Scope

- Review of all patients in the province that fall within the scope of EDRD
- Drug coverage for individuals diagnosed with a genetic disease which are rare as determined by incidence/prevalence in the population
- Currently lysosomal storage disorders are the group of diseases for which new drugs/therapies have been developed
Factors in reimbursement / policy decisions!

- DTC advertising
- Safety
- Consumer expectations
- Efficacy
- Productivity, satisfaction and QOL
- Physician support
- Budget Impact
- PBM, physician and pharmacist contracts
- Societal values
- Regulatory Issues
- Disease management programs
- Cost-effectiveness
- Moral and Ethical
- Politics and public image
- Acquisition cost
- Effectiveness
- Decision
Current paradigm – common diseases

- DTC advertising
- Safety
- Consumer expectations
- Productivity, satisfaction and QOL
- Physician support
- Budget Impact
- PBM, physician and pharmacist contracts
- Societal values
- Effectiveness
- Acquisition cost
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DECISION

Effectiveness

$50K/QALY
New Paradigm?

- DTC advertising
- Safety
- Consumer expectations
- Budget Impact
- Physician support
- PBM, physician and pharmacist contracts
- Societal values
- $50K/QALY

Politics and public image

- Efficacy
- Productivity, satisfaction and QOL

Acquisition cost

- Effectiveness
- Moral and Ethical

Cost-effectiveness

- Regulatory Issues

Disease management programs

Effectiveness

Moral and Ethical

Societal values

Decision
Putting it into context

- **Aldurazyme** – MPS1 - $435,000/yr
- **Galsulfase** – MPS VI - $900,000/yr
- **Idursulfase** – MPS II - $500,000/yr
- **Miglustat** – NPC - $240,000/yr
- **Alglucosidase** – Pompe - $450,000/yr
- **Agalsidase** – Fabry - $250,000
- **Velaglucerase** – Gaucher’s - $350,000/yr
- **Ivacaftor** – CF - $321,000 / year
- **Sapropterin** – PKU - $ 10 - $150k / year
PNH

- $450k / yr / patient
- Prevalence 1/200,000
- Population 4.45M
- ~ 23 PNH patients in BC
- 15% - 30% eligible for tx
- Budget impact $0.67M - $2.93M
  - To treat 4 – 6 patients.
Eculizumab – CEA in PNH

• 3 UK CEA done (Cost ~£252,000)
• ~£257,100 (~C$447,300) per patient achieving a stabilised haemoglobin
• ~£340,500 (~C$592,500) per patient achieving normalised LDH.
• £1.2M (C$2.1M) to £1.4M (C$ 2.4M) per LYG for patients like those in clinical trials
• £2.8M (C$ 4.8M) LYG to £3.2M (C$ 5.5M) LYG for all diagnosed PNH patients
CEDAC FINAL RECOMMENDATION and REASONS for RECOMMENDATION

LARONIDASE
(Aldurazyme® - Genzyme Canada Inc.)

Reasons for the recommendation:

1. One six-month, double-blind, placebo controlled randomized controlled trial (RCT) in

3. The medication costs between $100,000 and 900,000 per year, depending on patient weight. Given the average weight of patients enrolled in the clinical trial (40kg), the average annual cost for laronidase would be $434,720 per patient.

quality of life, as measured by the Childhood Health Assessment Questionnaire (in children) or the Health Assessment Questionnaire (in adults).

2. The majority of patients develop antibodies against laronidase. Their significance for benefit, harm, and dose requirements are unknown. In the above noted RCT, mild infusion reactions were common in patients treated with either active medication or placebo. Of the 45 patients from the RCT who enrolled in the open label observational study and received laronidase, one developed a life-threatening infusion reaction requiring emergency tracheotomy.
CEDAC FINAL RECOMMENDATION and REASONS for RECOMMENDATION

ALGLUCOSIDASE ALFA (Myozyme® – Genzyme Canada Inc.)

Recommendation:
The Canadian Expert Drug Advisory Committee (CEDAC) recommends that alglucosidase alfa be listed in patients with infantile-onset Pompe disease, as demonstrated by onset of symptoms and confirmed cardiomyopathy within the first 12 months of life. The Committee further recommends that drug plans develop specific criteria for monitoring and stopping alglucosidase, in consultation with experts in the management of lysosomal storage diseases.

Reasons for the Recommendation:
1. Information from uncontrolled trials in patients with infantile-onset Pompe disease indicate that alglucosidase alfa significantly improves survival in comparison to historical controls who did not receive enzyme replacement therapy.

2. There is insufficient evidence to evaluate the effectiveness and safety of alglucosidase alfa in other forms of Pompe disease.

Alglucosidase alfa costs $847 per 50 mg vial and the annual cost for patients between 5 – 10 kg ranges from $44,000 to $88,000.
Myozyme – Pompe - CEA

• Scottish Medicines Consortium
  – Infantile pompe - £244k and £318k / QALY
  – Late onset - £819k / QALY

• Australia
  – A$15,000 to A$45,000 per additional metre walked at 52 weeks (late onset Pompe)
The Evidence

- Small sample, heterogeneity
- Lack of natural history disease models
- Inability to recruit patients into RCTs
- Lack of validated treatment response and no standard of care
- Rarely alternative therapy
- No effectiveness data/ limited CE analysis
- High Cost
- ? Re: societal willingness to pay
Implications

- Existing methods and processes:
  - Can estimate costs and effects using available evidence
  - Lower standards of evidence (more decision uncertainty)
- What is our threshold WTP?
  - Revealed preferences would say it is significantly higher than $50k/QALY
  - Opportunity cost
Making the Recommendation

- Clinical evidence
  - Given patient heterogeneity
- Current guidelines (if they exist) / Other Jurisdictions
- Patient specific considerations
  - Clinical picture/alternative treatments
- Clinical monitoring/stopping criteria
- Price / Budget impact / Cost (offsets)
- Societal willingness to pay??
The Issues

• Finite budget / Sustainability
  – Front edge of drug development curve
• Long term treatment
• Ethical/Moral/Equity considerations
• Opportunity cost
• Price
• Willingness to Pay
Are we willing to pay a premium for a QALY (health benefit) in this population?

If so, how much?
Is there a maximum?
Summary

• ‘Economics’ are certainly considered, but ‘cost effectiveness’ is rarely discussed
• Decisions are more about values (clinical evidence) than efficiency/cost effectiveness
• Question: How much should we (society) be paying for expensive therapies in very small populations?
  – Is there different value-based CE threshold