Access to high priced and orphan drugs: some thoughts

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Conflicts of interest:
LOTS

Orphan diseases

- Different regions have different standards/criteria (CORD, 2005)

Country/Region	Ratio	Total Number Affected
United States	7:10,000	~200,000
Europe	5:10,000	~185,000
Australia	1:10,000	~2000
Japan	5:10,000	~50,000

South Africa??

Ultra-Orphan Diseases

- Even more rare than orphan
- Varying definitions
- Increasing knowledge of genomics breaks down diseases into a larger number of Ultra-Orphan diseases

(Hughes et al, 2005)

Ultra-orphan diseases

Country	Prevalence
United States	0.18 case per 10,000 or less
United Kingdom	<1 case per 50,000, or <0.20 case per 10,000

(CORD, 2005)

Orphan drugs

- These are drugs that are unlikely to be manufactured by private industry unless special incentives are provided

(Gericke, 2004)

Why?

- Used to treat rare diseases
  - Manufacturer unlikely to make a profit due to the limited number of patients requiring the drug
- Used to treat diseases (often called “neglected” diseases) that are prominent in developing countries
  - Where countries cannot afford to pay for the drugs
  - Examples: malaria, TB

(Gericke, 2004)

Orphan Drug Development: Legislation to Improve Access

- 1983 – United States Orphan Drug Act
  - Key Components:
    - Research and Development tax incentives
    - 7 Year market exclusivity
    - Additional support in developing research protocols
    - Expedited reviews for market approval
  - Incentives for pharmaceutical companies to develop these drugs

(CORD, 2005)

Orphan Drug Development: Legislation to Improve Access

- 1993 – Japan
  - Amendment to taxation and drug regulatory laws to incentivize drug companies
- 1993 – Australia
  - Similar policy – focussed on facilitating market access to drugs that had received orphan status in the US
  - No specific incentives for R&D

(CORD, 2005)

Orphan Drug Development: Legislation to Improve Access

- 2000 – European Union
  - Lower application fees
  - 10 year market exclusivity
  - Country-specific research incentives

Main ethical issues

- How much value should be placed on health as opposed to other societal goods (e.g. education)?

- Is it morally legitimate to base health care allocation decisions on “cost-effectiveness”?

Main ethical issues

- Health care allocation
  - Who should receive treatment and why?
  - How should relative benefits be weighed?
  - How should decision-making work for individual patients and patient groups?

- Research funding dilemma
  - The 10/90 gap in global health research (WHO, 1996; London, 2011)

Why is this an important ethical discussion?

- Rationing and priority setting in health care contentious, often random.
- Ongoing debate regarding measures of cost-effectiveness (e.g. QALYs)
- Opportunity costs of provision of expensive treatments
- Public and media interest

A principlist approach

- Autonomy
- Beneficence
- Non-maleficence
- Justice

(Beauchamp and Childress, 2009)

- Conflict between beneficence and justice in resource allocation decisions for orphan diseases

A principlist approach FOR the provision of orphan drugs

- Justice
  - Human right to health
    - Constitution of the World Health Organisation (WHO):
      - "*The enjoyment of the highest attainable standard of health is one of without distinction of race, religion, political beliefs, economic or social condition*" (WHO, 1946/2006)

A principlist approach FOR the provision of orphan drugs

- Justice
  - Value of equality (Gericke et al, 2005)
    - Cost effectiveness arbitrary from a moral point of view
    - Avoid giving preference or denying treatment based on morally arbitrary reasons
  - Right to treatment as an equal (Dworkin, 1977)
    - "*Right to be treated with the same respect and concern as anyone else*"

A principlist approach FOR the provision of orphan drugs

- Justice
  - Priority to the worst off (Daniels, 2008)
    - How to determine "worst off"?
    - Might limit provision of expensive treatment for all orphan diseases
  - Priority to those who have suffered "*brute bad luck*" (Dworkin, 2000)
    - Difficult to delineate "*bad luck*"

A principlist approach FOR the provision of orphan drugs

- Beneficence
  - Non-abandonment (Landman & Henley, 1999)
    - Moral (and public policy) commitment not to abandon patients needing specialized and/or expensive treatment

A principlist approach FOR the provision of orphan drugs

- Beneficence
  - Rule of rescue (Jenni and Loewenstein, 1997)
    - Often more instinctive/emotional than rational
    - Might support expensive treatment only in certain cases
    - Does this rule facilitate fairness in resource allocation?

A principlist approach FOR the provision of orphan drugs

- Beneficence
  - Capacity to benefit from treatment
  - Withholding or removing treatment may cause harms
  - Public utility
    - Satisfaction of helping those in need

A principlist approach FOR the provision of orphan drugs

- Autonomy
  - Importance of maintaining good doctor-patient relationship to promote autonomy
    - Withholding treatment may adversely influence trust
    - *If doctor becomes involved in resource allocation decisions, this may undermine relationship and the provision of "best treatment"*

(Boy et al, 2011; Hunter et al, 2011)

A principlist approach AGAINST the provision of orphan drugs

- Justice
  - Utility
    - "The greatest good for the greatest number"
  - Right to equal treatment (Dworkin, 1977)
    - "*The right to an equal distribution of some opportunity or resource or burden*"

A principlist approach AGAINST the provision of orphan drugs

- Justice
  - Discrimination
    - Provision of expensive treatments may amount to unfair discrimination in favour of patients with orphan diseases

(Hunter et al, 2011)

A principlist approach AGAINST the provision of orphan drugs

- Beneficence
  - Prioritizing health (Daniels, 2008) vs. prioritizing health care (Segall, 2010; Wilson, 2009)
  - Low cost effectiveness of most orphan disease treatments
    - More benefits could be provided to a greater number at the same cost (Fijn et al, 2002; Hunter et al, 2011)

Does the principlist approach provide clear resolution?

- Unfortunately not!
- Helps to unpack complexities of resource allocation for orphan diseases
- Allows for assessment of individual cases BUT may not facilitate ethically consistent decision-making
- Need a transparent process for decision-making to achieve sustainable solutions

Accountability for reasonableness: the best response?

- May maximise justice in resource allocation decisions
- Allows for transparent decision-making based on best current evidence

(Daniel and Sabin, 2002; Gibson et al, 2004)

Accountability for reasonableness: the best response?

- Model consists of four main conditions (Daniel and Sabin, 2002; Gibson et al, 2004)

Condition	Description
Relevance	Decisions based on relevant reasons in specific circumstances that "*fair-minded*" people are able to agree to
Publicity	Decisions should be transparent and publically accessible
Revision	Opportunities to review decisions based on evidence, and mechanisms to challenge decisions
Enforcement	Public or voluntary regulation of the resource allocation or priority setting process

Summary and conclusions

- Resource allocation for orphan diseases contentious
- Principlist approach assists in identifying ethical issues
- Accountability for reasonableness model may assist in transparent and consistent decision-making
- South Africa requires policies for resource allocation for treatment of orphan/rare diseases, and orphan drug research

South Africa: An Approach

- Determine need – Stakeholder input
- Gap analysis of needs and current policies and systems
- Legislative requirements – fees, regulatory exclusivity
- Resources

There is no disease so rare that it does not deserve attention *Orphanet*

Thank you

QUESTIONS?