An innovative pricing model to assess the price of expensive drugs with an orphan indication

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RATIONAL
Rational
Rational

Reimbursement

- Registration: efficacy and safety
- Reimbursement
  - Efficacy, safety, but also effectiveness and QoL
  - Cost-effectiveness: cost per QALY
  - Budget impact:
    - Annual cost per patient
    - Annual cost on national budget
- Other criteria: equity and social values
Rational

Safety, Efficacy & Quality

Clinical & Cost effectiveness

Affordability and impact on services

‘4th Hurdle’

‘5th Hurdle’
Rational

Orphan drugs

- Efficacy and safety - clinical evidence may vary:
  - Low sample size
  - Heterogeneity
  - Relevance of clinical outcomes

- Cost-effectiveness: ICER>threshold €100,000/QALY

- Budget impact:
  - Annual cost per patient: high
  - Annual cost on national budget: low

- Equity and social values: low to medium weight
Price orphan drugs

- Small number: high drug price necessary due to spread same costs over small number of potential patients:
  - R&D costs
  - Operational costs

- Higher risk:
  - Clinical evidence
  - Reimbursement (BIA and ICER)
  - Small firm premium
Rare disease – equity issues:

- Low sample size – more uncertainty in clinical evidence at time of launch - variance in ICER
- High drug price necessary due to spread same costs over small number of potential patients – high ICER
- Cost-effectiveness: high ICER > threshold

Equity: is it fair to be punished for having a rare disease
Rational Economy

- Keynes - “socialistic”
  - Public perspective
  - Control government
  - Taxpayer

- Hayek and Friedman – “liberal”
  - Free market
  - Financial markets
Rational

Health Care “Market”

- More Keynes than Friedman
- Strong control by government
- No free market
- Perspective: payers, hospitals - national

but what about “investors” – international market?

Our approach: bridging concepts from health economics and business economic valuation
Rational

Free Market

- Governments leave innovation to business entrepreneurship
- Medical innovation relies on the market mechanisms in the finance market
- Investors, who demand a required return of investment – determines price
  - Cash flow
  - Cost of capital
Rational

High price of orphan drug

- Pharma versus the public community (“the others”)
  - Governments, payers and providers
  - Patients and medical community (KOLs)
  - Media

- Subjective – excessive high price
  - High profits
  - High marketing / R&D costs ratio

Lack of understanding: bookkeeping value ≠ value
Rational

Justification of high price of orphan drug

- Objective concept - Discounted Cash Flow method
- Validate the price of the new drug from investor’s perspective
- Lower limit: price does not include all other monetary and non-monetary values for the society (patients, physicians, payers, providers and employers
  - Reduction other medical costs
  - Reduction lost productivity
  - Gain in Quality of Life
Rational

Conclusion

- Innovation relies on business entrepreneurship
- Ophan drugs – ICER > threshold
- Health authorities
  - Not only consider a willingness to pay (ICER) from public perspective
  - Have to accept the market mechanisms in the finance market
- Discounted cash flow method – price justification
APPROACH
Rational

Discounted Cash Flow method

\[
DCF = \frac{CF_1}{(1+r)^1} + \frac{CF_2}{(1+r)^2} + \cdots + \frac{CF_n}{(1+r)^n}
\]

Where

DCF = discounted cash flow

CF = (free) cash flow

n = the time in years before the future cash flow occurs

r = cost of capital

- **Free cash flow**: the cash flow from operations flow (> corporate tax)
  - Sales from the pharmaceuticals
  - Costs for research & development (R&D) and marketing

- **The cost of capital**: the opportunity cost of making a specific investment - required return of investment
Approach

Cash Flows
Approach

Sales - forecast

- Population size – global market
- Incidence - prevalence
- Proportion eligible patients
- Annual growth
- Uptake
- Off-label
Approach

Expenditures

- **No actual accounting data:**
  - Confidential
  - Allocation
  - Value ≠ bookkeeping data
  - If company is managed efficiently, leading to lower costs, it should not be punished with lower drug price

- **Standard costs:**
  - Phase I, II and III and marketing
  - Finetuning for specific rare disease
Approach

Failures clinical program
- Phase 1 to 2
- Phase 2 to 3
- Phase 3 to registration

Failures market access
- Probability of reimbursement
- Business models:
  - Conditional reimbursement
  - Pay for performance
Application SPINRAZAZA (nusinersen)
Main issues

- SMA – spinal muscle atrophy: rare, progressive disease
- Prevalence: 1:6,000 to 1:10,000
- Spinraza: added to best supportive care (BSC)
- Zorginstituut (December 2018):
  - Approved clinical benefit
  - Annual cost per patient: €240,000
  - BIA: €23.2 million
  - ICER = €1,700,000 per QALY
Price negotiations

85% reduction in price: ICER = €80,000/QALY

Price Spinraza: from €240,000 to €36,000

DCF Model: NPV = - €241 million

Conclusion: 85% reduction in price: NOT justified for investor
## Application

**Break-even price based on DCF**

<table>
<thead>
<tr>
<th>Model parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost of development (US$ million)</td>
<td>US$704.56 million</td>
</tr>
<tr>
<td>Phase I</td>
<td>US$84.07 million</td>
</tr>
<tr>
<td>Phase II</td>
<td>US$142.65 million</td>
</tr>
<tr>
<td>Phase III</td>
<td>US$189.73 million</td>
</tr>
<tr>
<td>Phase IV</td>
<td>US$68.33 million</td>
</tr>
<tr>
<td>Years of development &amp; approval</td>
<td>8 year</td>
</tr>
<tr>
<td>Population</td>
<td>Western markets: 872.5 million</td>
</tr>
<tr>
<td></td>
<td>Global markets: 1,670 million</td>
</tr>
<tr>
<td>Period reimbursement</td>
<td>1 year</td>
</tr>
<tr>
<td>Net patent life (years)</td>
<td>12</td>
</tr>
<tr>
<td>Uptake</td>
<td>80% from year 1</td>
</tr>
<tr>
<td>Cost of revenue (%)</td>
<td>40</td>
</tr>
<tr>
<td>Cost of capital</td>
<td>12%</td>
</tr>
<tr>
<td>Probability</td>
<td></td>
</tr>
<tr>
<td>- Phase I to II</td>
<td>0.70 (failure – 0.30)</td>
</tr>
<tr>
<td>- Phase II to III</td>
<td>0.39 (failure – 0.61)</td>
</tr>
<tr>
<td>- Phase III to EMEA/FDA approval</td>
<td>0.69 (failure – 0.31)</td>
</tr>
</tbody>
</table>
Application

Break-even price based on DCF

| Actual price | €240,000 |
| BE price     | €114,837 |
| ICER         | €36,000  |

**BE price:**

- **Lower limit:** price does not include all other monetary and non-monetary values for the society (patients, physicians, payers, providers and employers).
- **No specific data for orphan disease:** costs, failures, and risk.
Application

Finetuning of costs and probabilities failure

- Orphan disease and Spinraza is “first in class”:
  - Increase of hurdle rate from 12% to 18%
  - R&D costs: 10% increase
  - Failure: 10% increase of failure of clinical trials

Innovation premium:

- Substitution effects:
  - Reduction other medical costs
  - Reduction lost productivity

- Gain in QALY’s:
  - Threshold is €80,000/QALY
  - Gain in 2 QALYs = €160,000
## Results for Spinraza®

<table>
<thead>
<tr>
<th>Drug price</th>
<th>Spinraza®</th>
</tr>
</thead>
<tbody>
<tr>
<td>Discounting cost</td>
<td>4.0%</td>
</tr>
<tr>
<td>Discounting QALYs</td>
<td>1.5%</td>
</tr>
<tr>
<td>Actual price</td>
<td>€ 240,000</td>
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<tr>
<td>Average drug fine-tuning</td>
<td>€ 114,837</td>
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<tr>
<td>BE price</td>
<td>€ 143,052</td>
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<tr>
<td>Innovation premium cost</td>
<td>€ 58,402</td>
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<tr>
<td>Innovation premium QALYs</td>
<td>€ 20,554</td>
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<tr>
<td>Innovation premium total</td>
<td>€ 78,966</td>
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<tr>
<td>Total price</td>
<td>€ 222,018</td>
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<tr>
<td>Savings</td>
<td>€ 14,494</td>
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<tr>
<td>Savings</td>
<td>€ 72,896</td>
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<tr>
<td>Price</td>
<td>€ 201,454</td>
</tr>
<tr>
<td>Price</td>
<td>€ 157,546</td>
</tr>
</tbody>
</table>
Application

Results for Spinraza®

![Spinraza® Chart]

- average drug BE price
- finetuning BE price
- Cost savings Innovation premium
- QALYs Innovation premium
- total Innovation premium
- Actual price
OPPORTUNITY
Opportunity

Price negotiations

- ICER > €80,000 per QALY
  - Useful in informal price negotiations with health authorities e.g. NICE
  - Dutch Minister of Health proposes joint price negotiations with Netherlands, Belgium and Austria

- Budget impact: This approach may also be relevant for price negotiations in countries (e.g. Germany), when budget impact is the issue.
Opportunity

Perception of other stakeholders

- Stakeholders - misconception “excessive” price
  - Patients, patient associations,
  - Physicians, medical associations
  - Payers, hospitals
  - Other relevant organisations – politicians, press

- Convince stakeholders with objective scientific model that price is reasonable
CONCLUSION
Conclusion

- An alternative policy approach for the evaluation of ultra-innovative drugs from a broader perspective by bridging concepts from health economics and business economic valuation.
- This approach may justify a drug price, especially when ICER exceeds the threshold.
- For health care systems that do not use the ICER, our proposed alternative policy approach may put the usually high budget impact.
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