

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

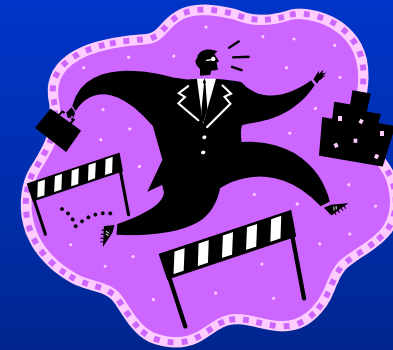


Clinical & Cost effectiveness



'4th Hurdle'

Affordability and impact on services



'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**

Rational

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

Rational

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”

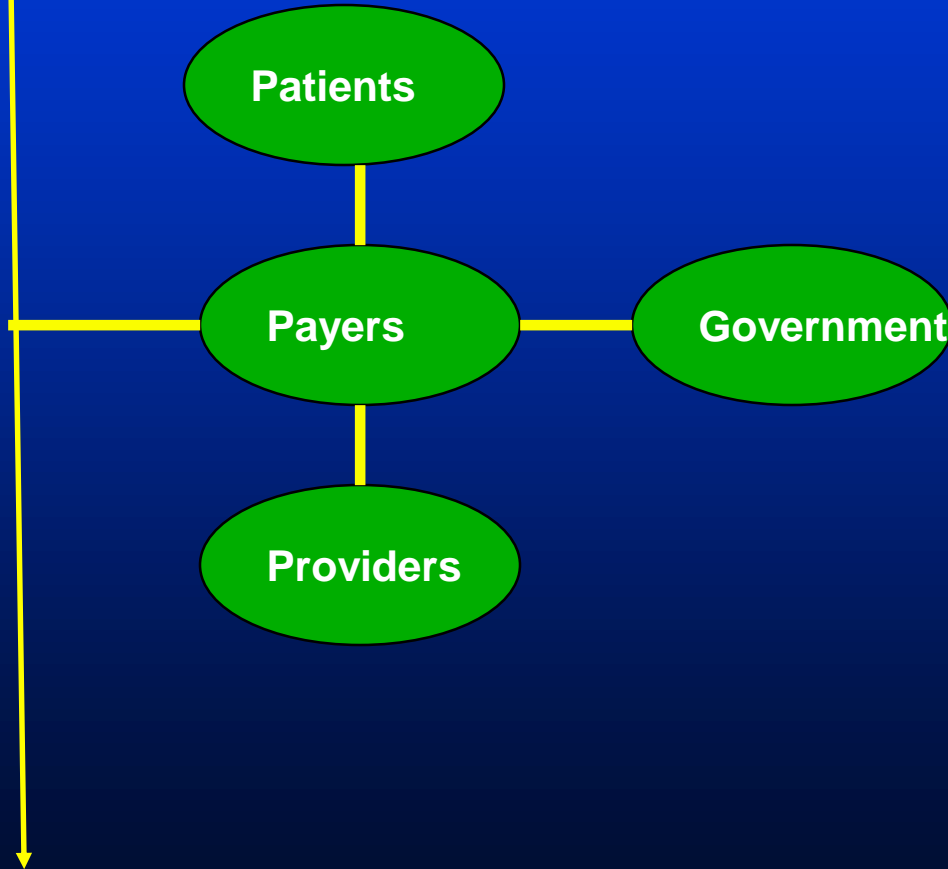
- More Keynes than Friedman
- Strong control by government
- No free market
- Perspective: payers, hospitals - national
but what about “investors” – international market?



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

Rational

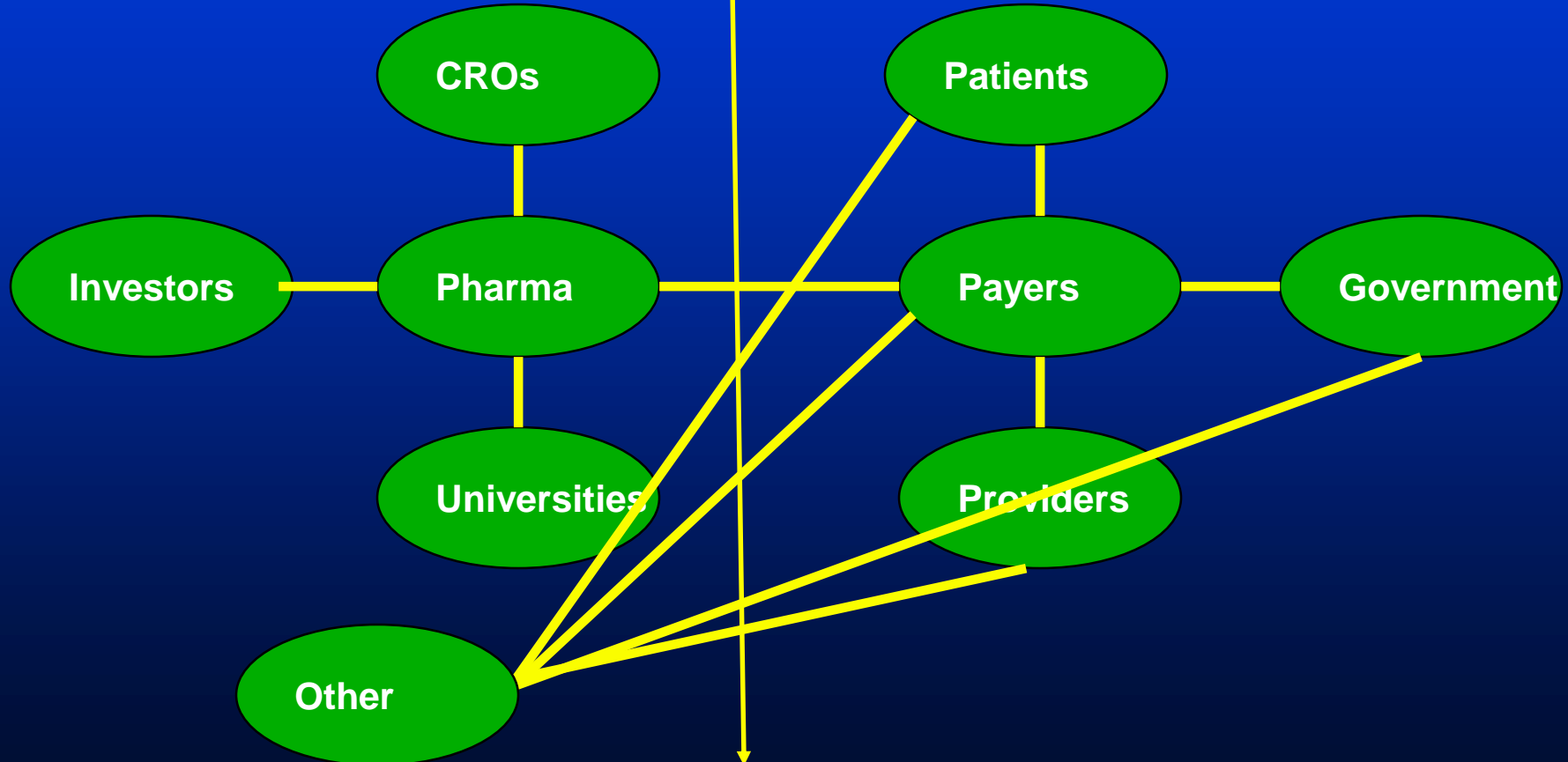
Regulated market



Rational

Free market

Regulated market



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 \neq 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

$$DCF = CF_1 / ((1+r)^1) + CF_2 / ((1+r)^2) + \dots + CF_n / ((1+r)^n)$$

Where

DCF = discounted cash flow

CF = (free) cash flow

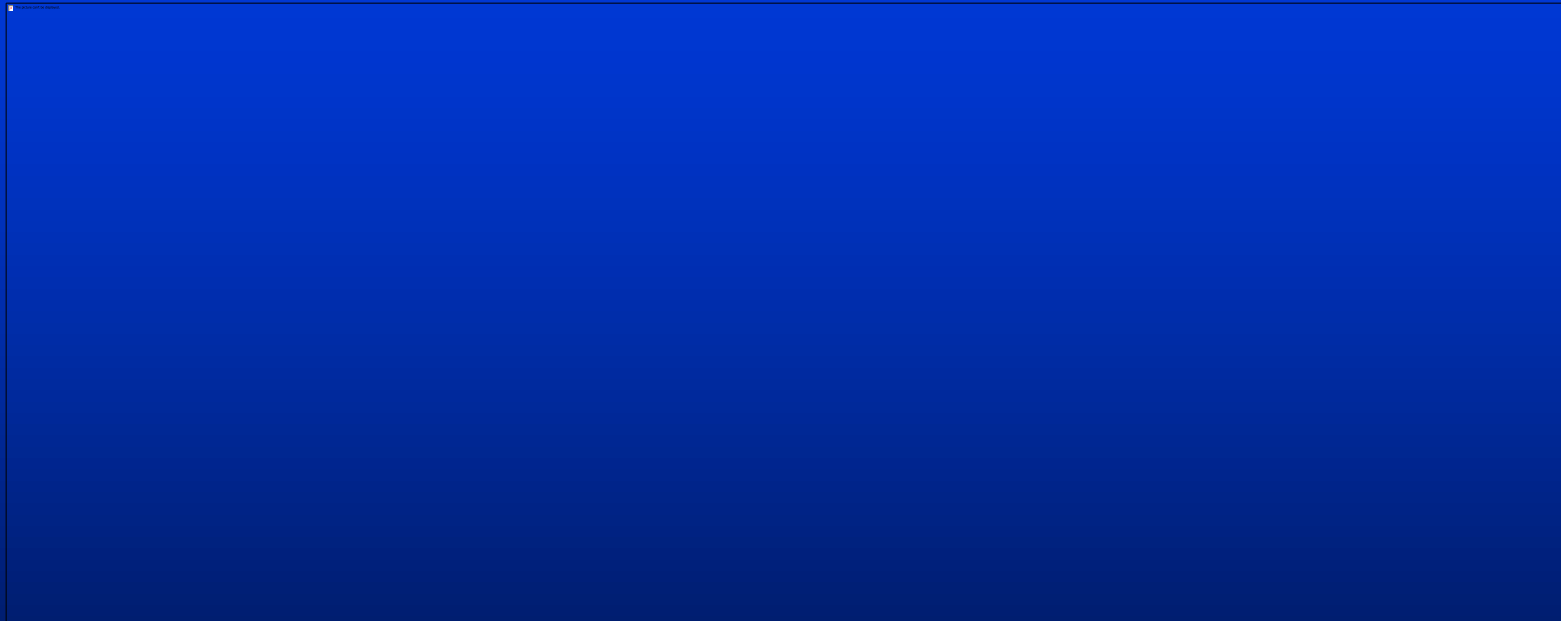
n = the time in years before the future cash flow occurs

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 \neq 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
SPINRAZA
(nusinersen)**

Application

Main issues

- **SMA – spinal muscle atrophy: rare, progressive disease**
- **Prevalence: 1:6,000 tot 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**

Application

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

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

Application

Break-even price based on DCF

Actual price		€240,000
BE price	investor	€114,837
ICER	payer	€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

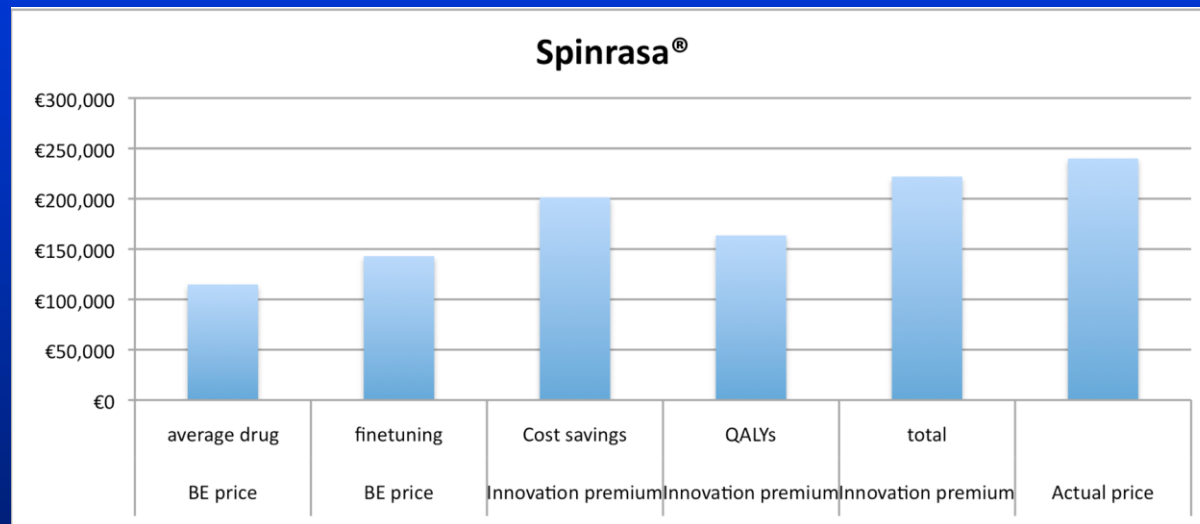
Application

Results for Spinraza®

Drug price		Spinraza®				
Discounting	costs		4.0%		4.0%	
	QALYs		1.5%		4.0%	
			savings	price	savings	price
Actual price				€ 240,000		€ 240,000
BE price	average drug			€ 114,837		€ 114,837
	fine-tuning			€ 143,052		€ 143,052
Innovation premium	cost savings	total costs	€ 58,402	€201,454	€ 58,402	€201,454
	gain QALYs		€ 20,554	€163,606	€ 14,494	€157,546
	total		€ 78,966	€222,018	€ 72,896	€215,948

Application

Results for Spinrasa®



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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