**CLINICAL INNOVATION:** Fair & Effective Incentives for New Uses of Established Drugs

# The Payor's Perspective: Regulating to incentivise value creation and repair a failed market

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## The Payor's Perspective: regulating to incentivise value creation and repair a failed market

Numedicus provides expert advice in the area novel uses for existing drugs, and initiates drug repurposing programs

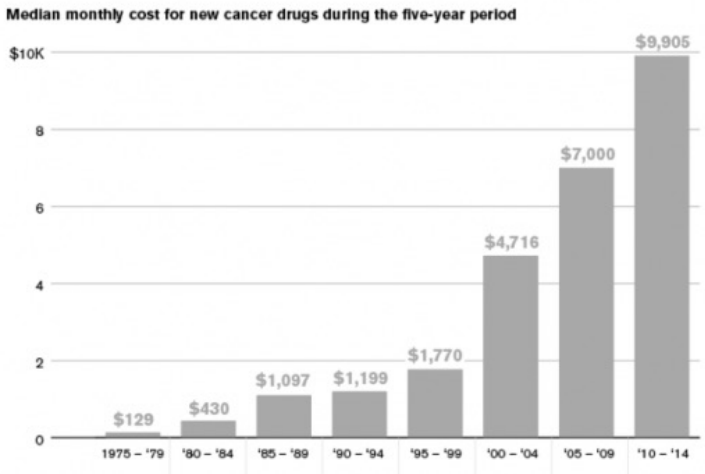
2

## Payor's objectives

- Improved health for patients
  - Outcomes
  - Quality of life
  - Pharmacoeconomic benefit
  - Prevention vs cure
- Value for money
  - Control of costs
  - Better alignment of cost and value
  - Obtain health value at underpriced costs
- US vs UK Perspective
  - Monopolistic NHS
  - Co-payments
  - Employer desire for access to latest medicines

3

## Problem #1: more expensive drugs…




4

## Problem #2: leads to more expensive premiums…

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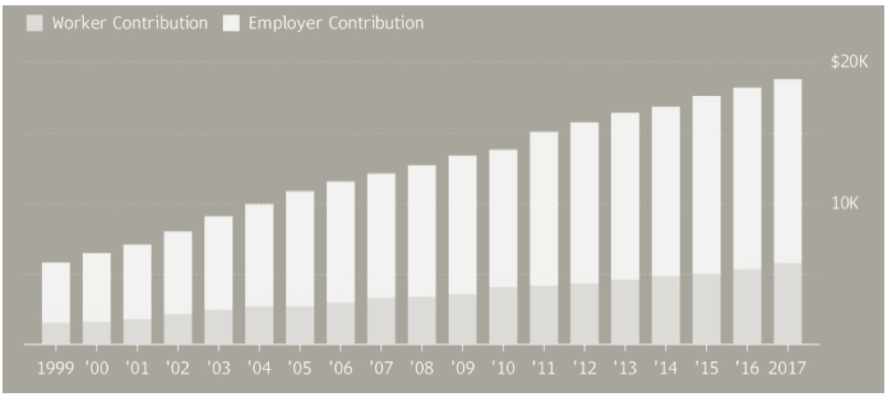


Source: Kaiser Family Foundation and Health Research and Education Trust

- Increased costs of drugs feeds through into increased annual insurance premiums.
- Increases faster than inflation; employers and employees burdened

5

## Problem #3: possible solutions don't work in a failed market

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- Drug repurposing reduces time, risk & cost of new products
- Protectable: Method of Use patents

…BUT

- Patent is usually necessary but insufficient requirement for R&D
- Generic off-label substitution (in >90% of cases) leads to
- NO commercial incentive to spend R&D dollars developing secondary uses outside a monopolistic position

…SO

- **Pharma invests in programmes that take longer, are more risky and cost more, because products can be sold expensively**

"You can have any car you want so long as it is a Rolls-Royce"

6

## Problem #4: commercial incentives ≠ value for money

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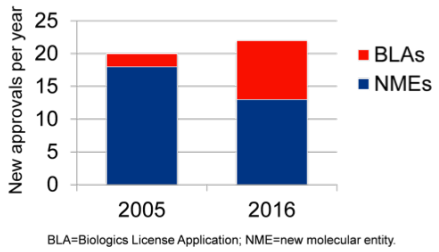


BLA=Biologics License Application; NME=new molecular entity.

Source: AMWA Engage

| Drug | Launch date | 2015 Global Sales ($bn) |
|---|---|---|
| Humira (adalimumab) | 2002 | 14 |
| Enbrel (etanercept) | 1997 | 8.7 |
| Remicade (inflixamab) | 1998 | 8.7 |
| Rituxan (rituximab) | 1997 | 8.3 |
| Avastin (bevacizumab) | 2004 | 7.0 |
| Lantus (insulin) | 2000 | 7.0 |
| Herceptin (trastuzumab) | 1998 | 6.6 |
| Neulasta (pegfilgrastim) | 2002 | 4.6 |
| Lucentis (ranibizumab) | 2006 | 4.2 |

Source: GEN

- Increased
  - numbers of BLAs
  - costing more
  - much slower to genericise
- Problem with drugs approved narrowly and used widely (e.g. EPO)
- CNS less attractive as an area

7

## Payor's perspective: off-label uses

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- Evidence
- Consent
- Indication
- Jurisdiction

Physician

Regulator

Payor

- US – FDA
- UK – MHRA ≅ payor

- US – compendia
- US – oncology
- UK – NICE

Increasing acceptance of indication-based pricing?

9

## Payor's perspective: second medical uses

- Off-label → on-label
  - Better understanding of risks and benefits (e.g. trials of Avastin in AMD)
  - Reduction in higher SAEs associated with off-label drugs
  - Greater patient acceptance
- Extend discovery and development of other SMUs
  - Most existing drugs have unexploited SMUs
  - New uses still being discovered for very old drugs
  - Greater R&D efficiency
  - Better allocation of resources for healthcare benefit
- Concerned about gaming the system
  - Pfizer pregabalin epilepsy/pain
  - Shkreli-type schemes (Turing Pharmaceuticals)

10

## Pricing by value

- Compare same drug in different situations:
  - Aspirin for headache or cancer
  - Thalidomide for insomnia or leprosy
- Pricing by outcome models exist: Velcade (JnJ)
- Tension between what the customer needs, what the payor will pay and what the provider can get away with?
- Monopoly provides commercial framework for R&D but at risk of predatory pricing

11

## Value in data: retrospective evidence in cancer

| Cancer type | Drug type |
|---|---|
| Breast | Beta-blockers |
| Colorectal | Calcium-channel blockers |
| Liver | HMG CoA inhibitor |
| Lung | $Na^+/K^+$ ATPase inhibitor |
| Melanoma | Metformin |
| Oesophageal | NSAIDs |
| Ovarian | PPAR agonists |
| Pancreatic | Quinolone antibiotic |
| Prostate | TNF antagonists |
| Stomach | |

…but sometimes not repeated prospectively (metformin in pancreatic cancer)

## Other indications…

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| | | |
|---|---|---|
| Age related macular degeneration | Depression | Pneumonia |
| Alzheimer disease | Diabetes (type II) | Psoriasis |
| Asthma | Epilepsy | Rheumatoid arthritis |
| Autism | Glaucoma | Sepsis |
| Burn injury | Influenza | Stroke |
| Cachexia | Myocardial infarction | Systemic vasculitis |
| Cataracts | Osteoporosis | Transplant rejection |
| Chronic renal failure | Parkinson disease | |
| COPD | Periodontitis | |

13

## Regulatory incentives

- **Data exclusivity**
- EMA: additional *1 year exclusivity* for repurposed drugs
  - Only applies to drugs still within 8 years of original MAA
- FDA: 3 years data excl for SMUs

- **Marketing exclusivity**
- US Orphan Drug Act (1983), replicated in EU, JP, AU, Singapore and Taiwan
- Marketing exclusivities, 7yr in US; 10yr in EU
- Plus other R&D tax breaks, reduced regulatory payments
- Designation given for two possible reasons:
  - Prevalence (or incidence) below 200,000 in US or 5 per 10,000 in EU
  - *Development of drug otherwise likely not to return R&D investment*

14

## Regulatory incentives for SMUs

- Most current versions work poorly outside monopolistic position
- Differential pricing?
  - What price, and for how long?
  - Enforcement
  - Questionable public acceptability
- Tax credits
  - Work on a country-by-country basis.
- Priority review *vouchers*
  - Can be sold (up to $350m)
  - Value to healthcare ≠ price when sold

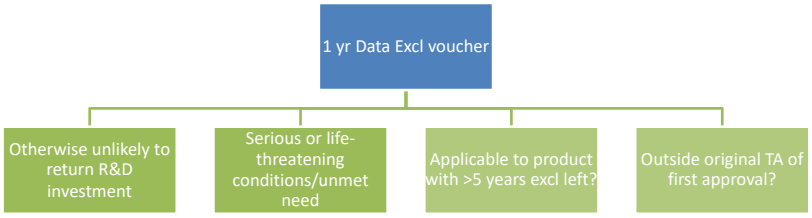

*If you develop a new drug for malaria, your profitable cholesterol-lowering drug could go on the market a year earlier.*

*Bill Gates, Davos, 2008*

- Stretch FDA resources, additional payment req
- Only 12 so far issued

15

# Regulatory incentives




- Very little additional work required
- Can be sold
- Value to healthcare ≠ price when sold
- Balanced effects on generic producers
- Can be refined by adding or subtracting conditions for grant

16