

Rewarding innovation; one step forward, two steps back?

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Topics

- Introduction
 - Current situation and scales
 - Contrasting perspectives
 - Historical decisions
- Rewarding innovation – problems and challenges
- Case studies (interactive)
- Rewarding innovation – possible solutions

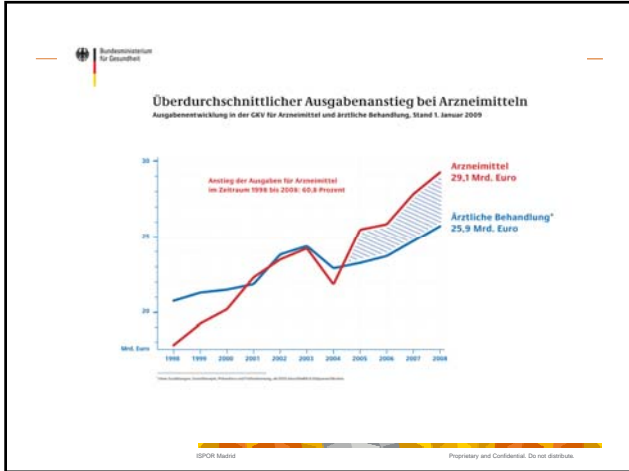
Introduction

Current situation – health care systems EU

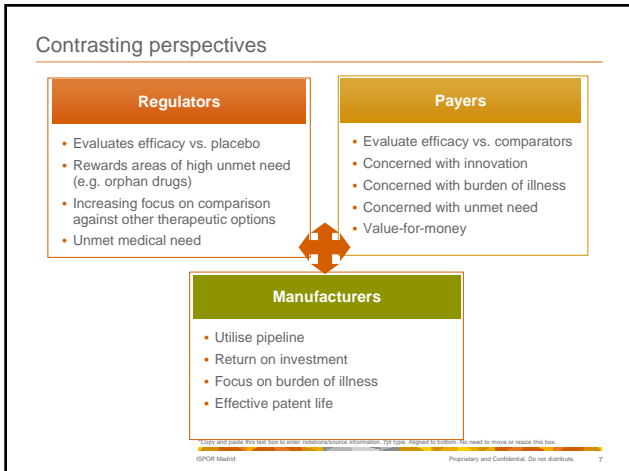
- Major increases in health care costs since 1970s
- Cost containment measures in place in most health care systems but have not been able to contain increase
- Ageing of population
- Health policy makers in the EU strive to:
 - Ensure access to new (affordable) technologies
 - Guarantee equity
 - Control costs
 - Monitor affordability
- Increase regulation / development of HTA

1. The European Medicines Agency Road Map to 2015: The Agency's Contribution to Science, Medicines, Health. Available from http://www.ema.europa.eu/docs/en_GB/document_library/Other/2011/06/WC507227251.pdf

2. A call to make innovative medicines accessible in the European Union. Available from <http://www.ispor.org/congresses/PragmaticApproachtoInnovativeMedicineAccessintheEU.pdf>



- ### Current situation manufacturers
- Decrease in discovery of new blockbuster
 - Reduced yield of pipelines
 - Few compounds reach market (1 in 10,000)
 - Increasing cost of development
 - Reduction in effective patent life
 - Increased demand for demonstration of value / regulations
 - Need to consider value during development process
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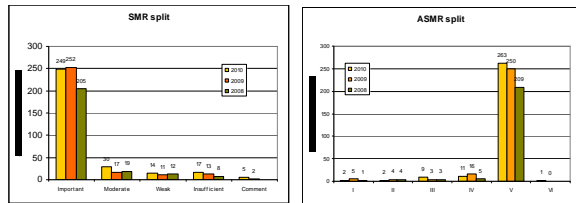


Comparison of scales

FR: ASMR	DE: AMNOG	UK: NICE
<ol style="list-style-type: none"> 1. Innovative product with significant therapeutic benefit 2. Therapeutic benefit, in terms of efficacy and/or reduction of side-effect profile 3. Therapeutic equivalent available, moderate improvement in efficacy and/or reduction of side-effect profile 4. Moderate improvement in terms of efficacy and/or utility 5. No improvement but listed 6. Not listed 	<ol style="list-style-type: none"> 1. Substantial additional benefit (survival; AEs) 2. Meaningful additional benefit (improvement in patient-relevant endpoints) 3. Small additional benefit (minor improvement) 4. No quantifiable additional benefit (insufficient evidence base) 5. No indication of additional benefit 6. Negative additional benefit 	<ol style="list-style-type: none"> 1. Unrestricted 2. Restricted indication to populations where product is most cost-effective 3. Not reimbursed <ul style="list-style-type: none"> • Budgetary impact considering only direct medical costs • Established cost per QALY threshold of £20,000- £30,000

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French decisions



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German decisions

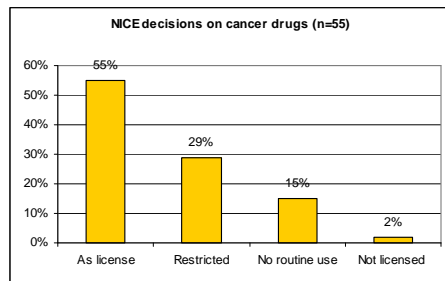
- Limited number of decisions available; 7 awaiting decisions
- Reasonable level of transparency

Active ingredient	Trademark	Indication	Decision
Dexmedetomidin	Dexdor	Hypnotics/sedatives	Exempt as minimal effect on GKV
Pivastatin	Livazo	Hypercholesterolemia	No dossier – Reference priced
Ticagrelor	Brilique	ACS	Level 2: + ASA vs clopidogrel + ASA for IAINSTEMI; benefits in STEMI not shown
Prasugrel	Effient	ACS	No add benefits compared to clopidogrel
Ezetimib	Zetia/Ezetrol	Hypercholesterolemia	No additional benefits vs existing treatments

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NICE decisions



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Overview of historical decisions

Drug / Active Ingredient	Indication	HAS	GBA	SMC
MabThera / rituximab	Severe, active RA + methotrexate. Adults with inadequate response / intolerance to other DMARDs including one or more TNF inhibitor	II	Premium price	Restricted - Specialists
Lucentis / ranibizumab	Age-related macular degeneration (AMD)	II	Premium price	Listed
Herceptin / trastuzumab	In addition to adjuvant therapy in early breast cancer	I	Premium price	Restricted - Specialists
Tysabri / natalizumab	MS	III Restricted Population	Premium price	Restricted - Population

Tysabri: Restricted to patients with rapidly evolving severe RRMS defined by two or more disabling relapses in one year and with one or more gadolinium-enhancing lesions on brain magnetic resonance imaging (MRI) or a significant increase in T2 lesion load compared with a previous MRI.
Safety concerns

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Conclusions

- Decisions are not consistent across countries
- Different systems lead to different decisions
- Lack of clarity around definitions
- Is innovation synonymous with clinical benefit?
- To what extent do the available scales adequately value a new technology?
 - Definition of the levels of the scales
 - Sensitivity of the scales
 - Definition / inclusion of unmet need and burden of illness
- Is innovation really measured in these scales?



Rewarding innovation – Problems and challenges

Problems and Challenges

- Some benefits of innovation are not captured in current measures of health gain
- Some benefits of innovation take a long time to become apparent
- Much innovation is incremental
- Incentives to innovate should be given at the time R&D investments are being made

Inadequacy of Current Measures of Health Gain

- Measures such as the QALY focus on health gain
- Many of the benefits of innovation may relate to increased convenience of use, or greater adherence
- Policy makers in many jurisdictions are resistant to considering estimates of benefit from stated preference studies (eg contingent valuation or discrete choice experiments)

Time Lag in the Benefits from Innovation

- The full benefits from major innovations may take time to become apparent
- May be the case for a new mechanism of action that delays progression of disease
- 'Risk-sharing arrangements may be difficult to devise, or maintain, over a period beyond (say) 5 years
- Product may be out of patent before some long-term benefits are apparent

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Incremental Nature of Innovation

- Much pharmacologic innovation is incremental in nature - first product in a new class, or its use in the first indication, may deliver only modest benefits
- The main gains may be from follow-on products, which may be from a different manufacturer

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Giving the Incentives at the Time of R&D Decisions

- Pharmaceutical R&D decisions are long term and subject to considerable risk and uncertainty
- These decisions are made on an international level – risks the 'free-rider' problem
- The main current policy instrument, patent protection, may not deliver the 'appropriate level of R&D

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Potential Agenda for Research and Policy

- Expanded use of stated preference studies, going beyond the QALY
- New designs for risk-sharing schemes
- Develop ways of 'internalising' the benefit to the original developer of innovations that turn out to be incremental
- Consider alternatives to the current patent system
- Develop VBP on an international level and minimise the free-rider problem

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Case study

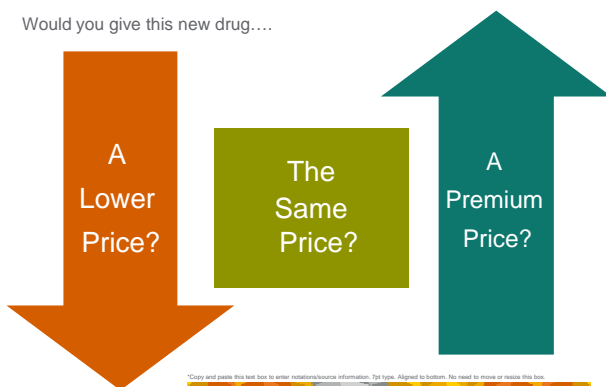
Drug 1: NOTSOLO

Innovation claim: **UNMET NEED**

- Indication: Adjunctive therapy for myoclonic epilepsy adolescents/ adults 12+
- Details: Twice-daily oral tablet
- Efficacy data:
 - More effective than placebo when used as combination therapy
 - Improved drop-out profile for efficacy versus placebo
 - Similar safety profile
- Burden of illness:
 - Limited cost of illness as few patients have juvenile myoclonic epilepsy
 - **Juvenile myoclonic epilepsy is still a cause of major disability for which no other combination treatment is available**

Show of hands

Would you give this new drug...



What really happened

In France, NOTSOLO...

'...has a moderate (ASMR III) improvement in actual benefit in the treatment of adults and children over 12 with juvenile myoclonic epilepsy.'

In Scotland, NOTSOLO...

*'...is **not recommended** for use within NHS Scotland as adjunctive therapy in the treatment of myoclonic seizures in adults and adolescents from 12 years of age with Juvenile Myoclonic Epilepsy.'*

Drug 2: BLURBIGOHN

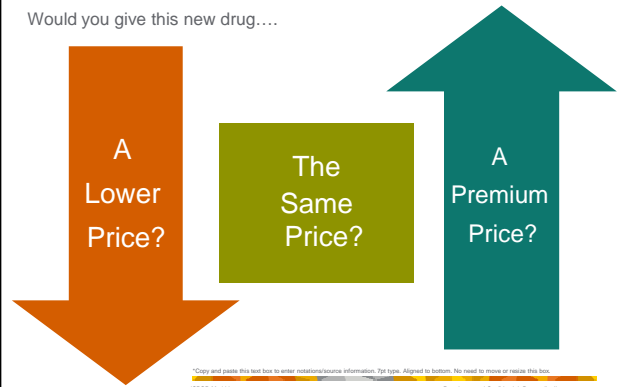
Innovation claim: **SUPERIOR EFFICACY**

- Indication: Neovascular age-related macular degeneration (AMD)
- Details: Intravitreal injection
- Efficacy data:
 - Statistically significant advantage for both primary and secondary end points against comparators
 - Clinical benefit of reduced rate of visual acuity loss and increases in visual acuity
- Burden of illness:
 - AMD is one of the leading causes of blindness worldwide and the primary cause of blindness in patients aged 50+ in many developed countries
 - Among severe forms of AMD, the exudative or neovascular forms are responsible for the greatest number of cases of severe visual acuity loss.

*Copy and paste this text box to enter relationship/source information. Tpl type: Aligned to bottom. No need to move or resize this box.
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Show of hands

Would you give this new drug...



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What really happened

In France, BLURBIGOHN...

- *'...provides a significant improvement in actual benefit (ASMR II) in the management of patients with AMD and subfoveal CNV.'*

In Scotland, BLURBIGOHN...

- *'...is accepted for use within NHS Scotland for the treatment of neovascular (wet) age-related macular degeneration (AMD) .'*

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DRUG 3: BETTERTHANSTATIN

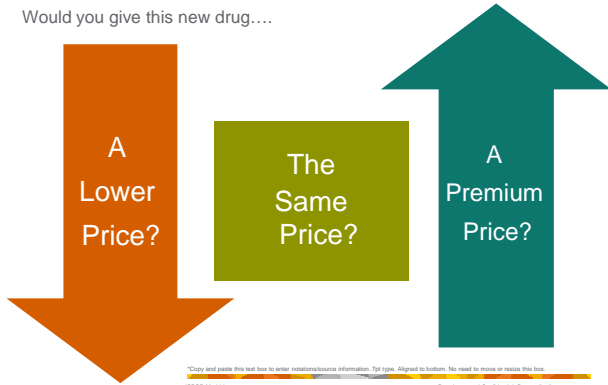
Innovation claim: **NEW MECHANISM OF ACTION**

- Indication: Primary hypercholesterolaemia
- Details: Once daily oral tablet
- Efficacy information:
 - Effective in combination with statins versus a statin alone in reducing LDL-c
 - Efficacy demonstration used intermediate outcome; not demonstrated for morbidity and mortality
 - Similar safety profile to statins
- Burden of illness:
 - Significant burden of cardiovascular disease due to hypercholesterolaemia
 - Most patients can be treated effectively with statins
- Other:
 - New mechanism for action (reduced absorption of cholesterol from the intestine; rather than preventing the production of cholesterol by the liver)
 - Crowded marketplace: many statins available
 - Suitable for patients intolerant to statins or in combination with statins for increased cholesterol reduction

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Show of hands

Would you give this new drug....



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What really happened

In France, BETTERTHANSTATIN ...

- *'...in patients with primary hypercholesterolaemia who are not controlled by a statin alone, BETTERTHANSTATIN in combination with statins, provides better service minor medical benefit (ASMR IV) in the therapeutic strategy.'*
- *'...in patients with primary hypercholesterolemia for which treatment statin is against or poorly tolerated in the absence of morbidity and mortality, BETTERTHANSTATIN an improvement in actual benefit minor (ASMR IV) in the therapeutic strategy.'*

In Scotland, BETTERTHANSTATIN ...

- *'...recommended for restricted use within NHS Scotland...for patients who have failed to reach target cholesterol levels despite treatment with titrated/optimised statins alone. It may also be considered as monotherapy where statins are inappropriate or poorly tolerated.'*

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Rewarding innovation –
Possible solutions

Rewarding Innovation - Problem?

- 2 many targets too few instruments
- Targets
 - Incentivize R&D
 - Pay for product
- Policy instrument
 - Price
 - Patent (protects price)



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Rewarding Innovation – more of the same but different....

- Play around with price
 - VbP maybe the future
 - Let's say based on CEA
 - Maybe play with price established by CEA
 - More negotiation
 - Health outcome not the only benefit
 - Add to price if incremental benefit established
 - As based on patient preferences?
 - » Discrete choice experiments?

Still one instrument price Based on existing product not future R&D

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Rewarding Innovation – more of the same, but different

- Risk sharing agreements
 - Finance based schemes
 - » Price-volume agreements
 - » Patient access schemes
 - » Free or discounted access
 - » Price capping
 - Outcome/performance outcomes
 - » Refund of freely available
- Still one instrument
 - price

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Rewarding Innovation – extending the patent system

- But this is also based on existing product
 - Also uses NCEs rather than product
 - In any case protects price not product
 - Still 1 instrument (?)
- Not to say that price and patent do not interact
- Not to demean value of patent protection generally

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Rewarding Innovation

- 2 targets requires 2 instruments
- De-link reward for innovation from product price...
 - Separate product reward from R&D reward
 - » Patent tends to protect price
- Currently attempted with orphan drugs, vaccines, developing country interventions
- Problem is capital market failure in risk



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Rewarding Innovation – change nature of patent protection

- Patent on NCE not product
- But patents currently basically protect price
- Use patent to risk-share
 - Patent protection (guarantee purchase) if X% improvement in treatment benefit is seen
 - Tie to QALY gains

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Rewarding Innovation – Public-Private Partnerships (PPPs)

- Lots of examples
 - GAVI
 - Global Alliance for TB Development
 - Medicines for Malaria
- Not necessarily NGO and company limited
- UK had proposed matching public R&D levels to UK pharma R&D levels
 - A further step would bring these funds together

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Rewarding Innovation – International Finance Initiatives

- Structure international capital for ease of access for R&D monies
- UK proposed for some orphan drugs targeted at developing countries
- Not working for the Euro, can't see it working here

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Rewarding Innovation – Advanced Purchase Agreements

- Advanced Purchase Agreements
 - Legally binding commitments to purchase product
 - Medicines for a given disease with a given effect?
- May work best for products in late development
- Difficult to specify

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Rewarding Innovation – Tournaments and Prizes

- Tournaments and prizes
 - Reward outcome
 - Does not rely on product price reimbursement or the patent process
- Payers (governments and insurers) fund the prize
 - HIV in US proposed prize of 0.55% US GDP (\$8billion)
 - Open source dividend of 5% of prize to enhance public information
- Difficulties in specifying winning prize
 - Give if x% of health benefit gained
 - Tie to QALYs gained

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Breakdown reimbursement/reward for different parts of the R&D programme

- | | |
|---|--|
| • Basic research <ul style="list-style-type: none">– Public/private sponsorship– Matched grant funding (possibly prizes)<ul style="list-style-type: none">» To show mechanisms of action | Manufacturing <ul style="list-style-type: none">VbPCEA |
| • Early phase drug discovery <ul style="list-style-type: none">– Prizes | Problems <ul style="list-style-type: none">Difficult to manageEconomies of scale/scopeAlthough becoming much more industrialised |
| • Pre-clinical <ul style="list-style-type: none">– Competitive bidding for RCTs | |

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Rewarding Innovation - R&D tax credits

- Financial offsets for establishing R&D in a given area
- Not linked to outcome
 - But could be
 - Amassed over time, paid once the product leaves the gate

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Rewarding Innovation – Movement of R&D?

- Is R&D moving to the USA?
– If so, so what?
- Once product price is formally regulated in the USA attention will turn to the R&D process
 - De-linking of R&D from product pricing will follow

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Two steps forward, one step back

Progress has been made in that scales have been implemented that reward new technologies offering superior benefits to patients

Scales capture mainly clinical benefits

Other aspects of innovation are not being captured

Further progress is needed

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Thank you for your attention

Are there any questions?

