Developments in the appraisal and pricing of new drugs in England

John.Cairns@lshtm.ac.uk

London School of Hygiene & Tropical Medicine, og Universitetet i Bergen

Helseøkonomi-konferansen 2016

Sundvolden Hotel, 24th May
Themes

- Pharmaceutical Price Regulation Scheme (PPRS), Patient Access Schemes
- Cost-effectiveness threshold
- Value-based assessment
- Special position of cancer drugs
  - Life-extending end-of-life treatments
  - Cancer Drugs Fund
- Speeding up decision making processes
Pharmaceutical Price Regulation Scheme 2009

PPRS has regulated pharmaceutical prices since 1978

**Profit control**: sets a maximum level for the profits that a company may earn from the supply of branded drugs to the NHS. Excess profits repaid to the DH. Can increase prices if profits below a set minimum.

**Pricing**: companies set initial individual prices but over time may be required to cut overall prices in the future. However, companies can choose how to achieve the overall negotiated price cut.

PPRS2009 encouraged **Patient Access Schemes** [PAS]. Schemes proposed by a pharmaceutical company & agreed with the DH

- to improve the cost-effectiveness of a drug
- to enable patients to receive access to cost-effective innovative medicines
Patient Access Schemes [PAS]

Need to ensure that the cumulative burden on the NHS is manageable

Financially-based schemes:
Where the company does not alter the list price of the drug, but offers effective discounts or rebates that may be linked to (e.g. number of patients treated, response of patients treated, and numbers of doses required). Confidential simple price discounts have become common in England.

Outcome-based schemes: (not common in England)

1) Agree a later increase in price subject to additional evidence
2) Agree a price subject to collection of additional evidence (rebate if evidence is not forthcoming)
3) Risk sharing – adjustment of prices in light of outcomes different from those anticipated
### Patient Access Schemes 2007-2016

- About 4 per year 2007-2011 [42% discount on list price]
- Over 12 per year 2012-2016 [87% discount on list price]

<table>
<thead>
<tr>
<th>Outcome based</th>
<th>Patient level</th>
<th>#</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-outcome based</td>
<td>Patient level</td>
<td>7</td>
<td>Discounted treatment initiation</td>
</tr>
<tr>
<td></td>
<td>Population level</td>
<td>62</td>
<td>Discount on list price</td>
</tr>
<tr>
<td>Fixed cost per patient</td>
<td>Patient level</td>
<td>10</td>
<td>Utilisation cap</td>
</tr>
<tr>
<td>Fixed cost per patient</td>
<td>Patient level</td>
<td>1</td>
<td>Refund for patients who do not reach agreed target</td>
</tr>
</tbody>
</table>
“The selection of an appropriate scheme will be facilitated if schemes can be incorporated as part of the HTA performed by bodies such as NICE. This could allow for the HTA body to begin to suggest prices at which the products under review become cost-effective, giving innovators greater clarity around the value assessment and potentially reducing the length of time required for decisions to be made on products (e.g., rather than a product requiring the development of a patient access scheme).

Fundamental to these negotiations will be the need for confidentiality on net pricing, which innovators have expressed the need for in light of international reference pricing. The NHS and DH will need to confirm to what extent this is possible in the context of the EU Transparency Directive although we know that commercial confidential agreements are already in place in the UK and other EU countries.”
Secret Pricing

• Less information $\rightarrow$ less competition $\rightarrow$ greater profits for pharma & reduced social welfare

• Is it the secrecy or the price discrimination (possibly aided by secrecy) which causes the welfare loss?

• Is it the distribution of the surplus which is the major concern?

• Is facilitating pricing which just enables cost-effectiveness thresholds to be met an appropriate way in which to share the surplus?
Pharmaceutical Price Regulation Scheme 2014

The basic cost-effectiveness threshold used by NICE will be retained at a level consistent with the current range and not changed for the duration of the scheme [5 years]

Simple price discounts are to be preferred to complex PAS (such as, dose caps & outcome-based schemes)

Introduced a limit on growth in the overall cost of the branded medicines purchased by the NHS from members of the scheme. Allowed Growth Rate for 2014 is 0% & then for each subsequent year is 0%, 1.8%, 1.8%, 1.9%

Manufacturers must make payments to the DH if overall cost exceeds the prescribed limit

Pricing of new products at discretion of manufacturer “It is assumed that prices at launch will be set at a level that is close to their expected value as assessed by NICE”
Cost-Effectiveness Threshold

- Stated £20,000 - £30,000
- End-of-Life £50,000
- With £12,936 additional spending NHS can add a QALY (Claxton et al. HTA 2015)
- £61,346 WTP for a QALY based on value of statistical life
In Feb 2007 OFT published a report reviewing how drug prices are regulated in the UK.

Introduced the idea of Value-Based Pricing (VBP).

Prices of individual pharmaceutical products reflect their ‘clinical and therapeutic value to patients and the broader NHS’.
DH Value-based pricing consultation

VBP: Prices of individual pharmaceutical products to reflect their 'clinical and therapeutic value to patients and the broader NHS’

“Proposal” went out for consultation in 2011. No material change introduced by DH following consultation

Negotiations subsequently started autumn 2012 between government & industry

July 2013 NICE received terms of reference from ministers for value assessment of new medicines
NICE remit for developing methods of assessment from DH June 2013

- Adopt the same benefit perspective for all technologies falling within the scope of VBP, and for displaced treatments
- Include a simple system of weighting for burden of illness that appropriately reflects the differential value of treatments for the most serious conditions
- Encompass the differential valuation of ‘End of Life’ treatments in the current approach within the system of Burden of Illness weights
- Include a proportionate system for taking account of Wider Societal Benefits
- No additional weighting for Therapeutic Innovation and Improvement
DH proposal for Wider Societal Benefits

- Concerned with the effect of treatment on others
- The DH defines WSB as the difference between the amount of resources a patient contributes to society (production) and the amount they utilise (consumption)
- The adoption of any proposed treatment will lead to a change in WSBs (e.g. as one treatment is replaced by another)
- Also if an intervention has a positive incremental cost other NHS activities will be displaced & these activities will also have associated WSBs
Net Resource Impact

\[ WSB = \text{Production} - \text{Consumption} \]

Production:
- Unpaid labour AGIQ
- Paid labour AGQ

Consumption:
- Formal care AQ
- Personal paid consumption AQ
- Informal care AGIQ
- Informal child care AG
- Personal unpaid consumption A
- Government services A

A = age
G = gender
I = disease
Q = quality of life
Held several meetings over the summer of 2013. Commissioned the NICE Decision Support Unit to produce two briefing papers:

[1] Department of Health proposals for including Burden of Illness into Value Based Pricing: A description and critique


Public consultation on the subsequent proposal March-June 2014
The **burden of illness** is measured from the point at which the new treatment is to be used. The shortfall in QALYs will be considered *relative to what people could expect without the condition at the time of treatment and is therefore called the ‘proportional QALY shortfall’.*

We propose calculating **wider societal impact** by ... subtracting the total QALYs expected as a consequence of having the condition from the total QALYs expected for people with the same age & gender distribution without the condition.

The **end of life** treatments protocol ... will be replaced by the new burden of illness modifier... we propose setting a maximum cumulative weight of 2.5 in circumstances where all modifiers apply.
No changes to the technology appraisal methodology should be made in the short term. This will mean that the current End of Life treatments protocol will be retained in its current form.

Using the response to consultation, further consideration should be given to the use of QALY shortfall as a means of quantifying burden of illness.

Taking into account the response to consultation, the desirability and practicality of incorporating wider societal benefits into the appraisal methodology should be reviewed, in conjunction with the DH.
Special place of cancer drugs

- Sustained increase in the cost of new drugs
- Perception of NICE recommendations being restrictive relative to other European countries
- Life-extending end-of-life treatment
- Cancer Drugs Fund 2011-2016
- New Cancer Drugs Fund
## Twenty Oncologic Drugs Approved 2009-2013

<table>
<thead>
<tr>
<th>Drug</th>
<th>Cost per year of treatment (USD)</th>
<th>Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>sorafenib</td>
<td>140,984</td>
<td>radium-223</td>
</tr>
<tr>
<td>crizotinib</td>
<td>156,544</td>
<td>erlotinib</td>
</tr>
<tr>
<td>ibrutinib</td>
<td>157,440</td>
<td>trastuzumab emtansine</td>
</tr>
<tr>
<td>obinutuzumab</td>
<td>74,304</td>
<td>pomalidomide</td>
</tr>
<tr>
<td>pertuzumab</td>
<td>78,252</td>
<td>bevacizumab</td>
</tr>
<tr>
<td>nab-paclitaxel</td>
<td>82,233</td>
<td>ponatinib</td>
</tr>
<tr>
<td>afatinib</td>
<td>79,920</td>
<td>abiraterone</td>
</tr>
<tr>
<td>lenalidomide</td>
<td>124,870</td>
<td>cabozantanib</td>
</tr>
<tr>
<td>trametinib</td>
<td>125,280</td>
<td>omacetaxine</td>
</tr>
<tr>
<td>dabrafenib</td>
<td>109,440</td>
<td>regorafenib</td>
</tr>
</tbody>
</table>

Mailankody & Prasad *JAMA Oncology* 2015;1:539-540
Trends in Launch Prices of Anticancer Drugs

- Howard et al. modelled launch prices for the 58 anticancer drugs launched in the US between 1995 and 2013
- In 1995 patients & insurers asked to pay USD 54,100 for an additional year of life, in 2005 this had risen to USD 139,100 and USD 207,000 in 2013.
- Argue there are incentives to set high prices in price insensitive market segments to offset discounts in price sensitive segments
- Suggest high US prices may result from pressure of low European prices

Howard et al. *Journal of Economic Perspectives* 2015;29:139-62
Criteria in order to qualify as a life-extending, end-of-life (EoL) treatment:

1) The treatment is indicated for patients with a short life expectancy, normally < 24 months

2) There is sufficient evidence to indicate that the treatment offers an extension to life, normally of at least an additional 3 months, compared to current NHS treatment

3) The treatment is licensed or otherwise indicated for small patient populations (≤ 7,000)

To date these criteria have been met on thirty-six occasions and the committee recommendations have been consistent with using a £50,000 per QALY threshold for these EoL treatments.
Criteria in order to qualify as a life-extending, end-of-life (EoL) treatment:

1) The treatment is indicated for patients with a short life expectancy, normally < 24 months

2) There is sufficient evidence to indicate that the treatment offers an extension to life, normally of at least an additional 3 months, compared to current NHS treatment
In April 2010 David Cameron pledged that any cancer patient should be allowed any drug licensed in the last five years, if their doctor seeks it, even if NICE had determined that it did not represent good value for money for the NHS.

Subsequently the Cancer Drugs Fund (CDF) was established by the new coalition government (interim funding of £60 million, & from 1 April 2011 £200 million per annum) as an additional funding source for cancer drugs not routinely available through routine commissioning.

NHS England took on its operational management on April 1 2013 & will continue to manage the CDF until 2016. NHS England recently pledged an additional £160 million over 2014-2016.
## Figure 1
Cost of the Cancer Drugs Fund

<table>
<thead>
<tr>
<th>Year</th>
<th>Cost (£m)</th>
<th>Budget (£m)</th>
<th>Cost as a percentage of allocated budget (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2010-11</td>
<td>38</td>
<td>50</td>
<td>77</td>
</tr>
<tr>
<td>2011-12</td>
<td>108</td>
<td>200</td>
<td>54</td>
</tr>
<tr>
<td>2012-13</td>
<td>175</td>
<td>200</td>
<td>88</td>
</tr>
<tr>
<td>2013-14</td>
<td>231</td>
<td>200</td>
<td>115</td>
</tr>
<tr>
<td>2014-15</td>
<td>416</td>
<td>280</td>
<td>148</td>
</tr>
<tr>
<td>Total</td>
<td>968</td>
<td>930</td>
<td>104</td>
</tr>
</tbody>
</table>

**Notes**
1. Costs are rounded to the nearest £ million.
2. Data for 2010-11 represent in-year funding provided by the Department of Health in October 2010.

Source: National Audit Office analysis of Department of Health data and NHS England data
CDF prioritisation consultation

Increasing concern over the sustainability of the CDF led to NHS England having to find additional resources during 2014.

A four week public consultation was held in October 2014 over plans to introduce a prioritisation process to assess the clinical benefit delivered in treating a patient with a drug, in relation to the cost of that drug.

NHS England issued a report on the consultation one week after it finished & new Standard Operating Procedures to guide the operation of the CDF four days later.
CDF prioritisation

- Focussed on clinical benefit score (points for improved overall & progression-free survival, changes in toxicity & quality of life, and for unmet clinical need)
- Overall score considers the clinical benefit score relative to the cost band in which the median drug cost falls
- This overall score is then subject to interpretation & modification by the CDF panel
- Reviewed 56 decisions to determine whether clinical benefit “insufficient to merit retention within current CDF funding” or “sufficient for a decision by the CDF panel to retain”. 26 drugs de-listed in March 2015.
- Some delistings have led to negotiations resulting in some being reinstated e.g. trastuzumab emtansine and ibrutinib
New Cancer Drugs Fund

- From 1 July 2016 the CDF is to become a managed access fund for new cancer drugs with clear entry and exit criteria.
  - NICE to issue draft guidance before marketing authorisation & final guidance within 90 days of marketing authorisation
  - Not recommended, recommended for routine use, recommended for CDF funding
  - After about 2 years NICE re-appraise and recommend or not for routine funding and the drug stops being provided by the CDF
- Cost control through explicit spending cap & delayed payment
- NICE to conduct rapid review of all drugs currently listed by CDF
1: All new cancer drugs expecting to be licensed are referred to NICE for appraisal prior to marketing authorisation

2: NICE makes an initial recommendation based on clinical and cost effectiveness

3: Interim funding is provided by the CDF whilst NICE undertake their full appraisal

4: NICE makes a final recommendation. Drugs recommended to enter the CDF must meet NHS England commercial requirements

5: CDF drugs are evaluated against specific criteria for a set period. After the evaluation period they are given a ‘yes’ or ‘no’ recommendation by NICE

6: Light blue shading denotes where CDF funding applies (subject to financial controls & £340m budget)
Challenges

- Observational data vs. RCT
- Can possibly make manufacturer responsible for collecting additional data on own product but what about the comparators
- Rapid assessment of cost-effectiveness at earlier stage even more reliant on manufacturer’s submission
- Saying no [a] at time of marketing authorisation, [b] after two years of routine (albeit CDF-funded) use
- Suggested that manufacturer has an incentive to price as high as possible in order to get the greatest share of capped expenditure
Speeding up decision processes

- NICE Single Technology Assessment 2006
- A number of earlier appraisal initiatives
- Accelerated Access Review
- New Cancer Drugs Fund
Earlier Appraisal Initiatives

- NHS England Commissioning through Evaluation (started 2013)
  - e.g. stereotactic ablative radiotherapy (SABR)
- MHRA Early Access to Medicines Scheme (started Dec 2014)
  - Access to medicines that do not yet have a marketing authorisation where there is clear unmet need
- Adaptive/Conditional Licensing
  - Enables new drugs where there is no current treatment to reach patients & to allow real-world data to inform regulators about future licensing of the drug
  - e.g. EMA Adaptive Pathways Pilot started Mar 2014 has 11 products under examination
Early Access to Medicines Scheme

Promising Innovative Medicine

The EAMS in facts and figures:
April 2014 - November 2015

Applications cover 7 therapeutic categories
- Oncology
- Central nervous system
- Cardiovascular
- Dermatology
- Blood disorder
- Ophthalmology
- Anti-infective

11 PIM designations awarded
7 Scientific Opinion applications
4 Positive Scientific Opinions

500+ Patients have received early access to innovative treatments through the EAMS

Overview of drugs granted early patient access via the EAMS

<table>
<thead>
<tr>
<th>Indication</th>
<th>Company</th>
<th>EAMS patient access period</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pembrolizumab</td>
<td>MSD</td>
<td>131 days 08 March – 17 July 2015</td>
</tr>
<tr>
<td>Nivolumab</td>
<td>Bristol-Myers Squibb</td>
<td>22 days 29 May – 19 June 2015</td>
</tr>
<tr>
<td>Nivolumab</td>
<td>Bristol-Myers Squibb</td>
<td>32 days 19 June – 20 July 2015</td>
</tr>
<tr>
<td>Sacubitril valsartan</td>
<td>Novartis</td>
<td>80 days 01 September – 19 November 2015</td>
</tr>
</tbody>
</table>

Early Access to Medicines Scheme: an independent review p.7

Innovative Medicines and MedTech Review

- Involving DH, Department of Business, Innovation & Skills, & Office for Life Sciences, Terms of Reference Mar 2015.
- Faster assessment of the safety & efficacy of innovations by adapting systems & better exploiting advantages as an integrated healthcare system.

- Adapt health economic assessment to:
  - reflect technological advances in genomics, precision medicine & informatics
  - take time & risk out of the traditional R&D model
  - better exploit the potential of our integrated healthcare system to pioneer new models of reimbursement for innovative products.

- How can the NHS can better support & drive medical innovation (including through specialist commissioning).
Accelerated Access Review

- Interim Report 27 October 2015, final report originally anticipated April 2016, now summer 2016
- Emphasis on “managing the entry of a product to the system as early as possible in the product cycle, when the evidence to determine its longer-term value has not been fully established”
- UK Early Access to Medicines Scheme “EAMS provides an opportunity for important drugs to be used in UK clinical practice in parallel with the later stages of the regulatory process”
- Documentation suggests that flexibility with respect to pricing will be a feature of the final report
Questions

- Has this short history suggested greater coherence than is warranted?
- Who are the likely gainers and losers from these developments?
- What are the implications for health economic evaluation?
- What is the relevance of all of this to Norwegian health policy?