

# Implementing value-based pricing for pharmaceuticals in the UK

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The views expressed in this document are those of the authors alone.

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## Abbreviations

AIFA	: Italian Medicines Agency
ASMR	: Amelioration du Service Medical Rendu (Improvement in therapeutic benefit rendered)
AWMSG	: All Wales Medicines Strategy Group
CaHTA	: Catalan Agency for Health Technology Assessment
CEPS	: Comité Economique des Produits de Santé
CT	: Commission de la Transparence
DACEHTA	: Danish Centre for Evaluation and Health Technology Assessment
DAHTA	: German Agency for Health Technology Assessment
DH	: Department of Health
ED	: Evidence Development
EU	: European Union
FinOHTA	: Finnish Office of Health technology Assessment
FJC	: Federal Joint Committee (Germany)
FPM	: Financial Push Mechanism
GDP	: Gross Domestic Product
GP	: General Practitioner
HAS	: Haute Autorité de Santé (France)
HLPF	: High Level Pharmaceutical Forum
HTA	: Health Technology Assessment
IAA	: Innovation Assessment Algorithm
ICD	: Implantable Cardioverter Defibrillator
ICER	: Incremental Cost Effectiveness Ratio
IQWiG	: Institute for Quality and Efficiency in Health Care (Germany)
MRC	: Medical Research Council
NAO	: National Audit Office
NCCHTA	: National Coordinating Centre for Health Technology Assessment (UK)
NHS	: National Health Service
NICE	: National Institute for Health and Clinical Excellence
NME	: New Molecular Entity
NPM	: Non-financial Push Mechanism
OECD	: Organisation for Economic Cooperation and Development
OFT	: Office of Fair Trading
OLS	: Office for Life Sciences
PAS	: Patient Access Scheme
PDP	: Product Development Partnership
PET	: Positron Emission Tomography
PM	: Pull Mechanism
PPB	: Pharmaceuticals Pricing Board (Finland)
PPRS	: Pharmaceutical Price Regulation Scheme
PROs	: Patient Reported Outcomes
RM	: Regulatory Mechanism
RS	: Risk Sharing
QALY	: Quality Adjusted Life Year
QoL	: Quality of Life
R&D	: Research and Development
ROCE	: Return on Capital Employed
SBU	: Swedish Council on Technology Assessment in Health Care
SMC	: Scottish Medicines Consortium
SPC	: Supplementary Protection Certificate
STA	: Single Technology Assessment (NICE)
TLV	: Dental and Pharmaceutical Benefits Board (Sweden)
UK	: United Kingdom
VBP	: Value Based Pricing
WT	: Wellcome Trust

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## About This Publication

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In September 2009 2020health.org published their interim report on 'value-based pricing' (VBP), the pricing mechanism described in the Office of Fair Trading report of 2007. The concept of 'value', what it actually means and how value-based pricing (VBP) is perceived and defined by those from the front-line of health to high level stakeholders were explored in this first publication.

This second report explores both the opportunities and limitations of VBP as applied to innovative medicines pricing, and seeks to identify the barriers to be overcome if it is to be introduced in ways which genuinely enhance the UK's overall approach to patented medicines pricing and spending. We worked closely with Panos Kanavos of the London School of Economics (and his team) and David Taylor of University of London on this report and are very grateful to them for their wisdom and insight.

We are also indebted to the team of six pharmaceutical companies who enabled these two reports to be undertaken, and to all our sponsors for their unrestricted funding on which we depend. As well as driving our on-going work of involving frontline professionals in policy ideas and development, sponsorship enables us communicate with and involve officials and policymakers in the work that we do. Involvement in the work of 2020health.org is never conditional on being a sponsor.

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March 2010

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## Executive Summary

In our interim report<sup>1</sup> we redefined value-based pricing (VBP) as *'the price that reflects the value to patients, carers, society and the economy which delivers health benefits that exceed the health predicted to be displaced both elsewhere in the NHS and in the welfare economy, due to their additional cost'*. We also demonstrated that the concept of what determines 'value' has different meanings depending on who you are asking, be it the public, managers, clinicians or patients.

The UK has a strong history of innovation in medicines and it is vital to the economy that this continues to be the case. During the lifetime of the NHS, the British research based pharmaceutical industry has enjoyed considerable success. NHS spending on medicines at manufacturers' prices has remained relatively modest as a proportion of both total health costs and the gross national product, at about 10 per cent and 1 per cent respectively. At the same time the UK has been a major pharmaceutical exporter, and domestic research spending has been about double that on promotional and allied activities. In much of the rest of the world more is spent on medicines promotion than research.

The NHS' Pharmaceutical Price Regulation Scheme (PPRS) has played a significant part in the achievement of this healthy record. However, critics of the PPRS argue that on occasions it has allowed companies to charge unduly high prices for some individual products, even though their overall profits have been kept within defined limits.

Other commentators argue that in today's globalised economy national level profit and cost controls are outmoded, and that a more objective way of setting fair price limits for patented medicines is required. VBP, based on setting a maximum affordable cost per Quality Adjusted Life Year (QALY) generated by the use of new medicines, seeks to provide the solution to this challenge.

Although in principle the prices of goods like patented medicines should reflect their overall value to individuals and communities, this cannot in practice simply be achieved. Despite the enthusiasm of some VBP advocates, the health economic techniques used by HTA agencies currently only cover a relatively narrow spectrum of factors relating to the overall value of health and allied technologies. For example, in the case of dementia treatments, the well-being of carers is not included in current NICE calculations relating to the benefits generated by medicines use. Nor, at a more general level, are the long term returns associated with investing in research programmes that – if sustained through less productive periods – will ultimately open the way to fundamental new ways of treating conditions like cancer and neurological diseases, and which will also contribute to building a stronger knowledge based UK economy capable of earning its future living in a changing world.

This new 2020health report is based on an acceptance of the fact that many stakeholders in health and pharmaceutical care believe that introducing VBP as a concept is a desirable way forward. It explores both the strengths and weakness of VBP as applied to innovative medicines pricing, and seeks to identify the barriers to be overcome if it is to be introduced in ways which genuinely enhance the UK's overall approach to patented medicines pricing and spending.

This report's key message is that – although there are important elements of the established PPRS that should be retained to protect public interests - within a reformed structure VBP techniques could and should play a useful part in determining the reasonableness of individual pharmaceutical product prices. It is apparent that the British economy will not be able to recover from its current crisis without fostering vigorous and financially viable science-based industry, and that monopsonist state purchasers should not be in a position to artificially depress the prices of valued innovations of any sort. But politicians and the public they serve must almost be confident that companies are not in a position to unfairly exploit the public purse. It is with respect to the latter that VBP could if intelligently utilised have an important strategic role to play.

1. Camps-Walsh G, Aivas I, Barratt H (2009) *How can Value-based Pricing improve access to and adoption of new treatments?* 2020health, September.

Against this background our detailed observations can be summarised as follows:

1. The current agreement (PPRS together with elements of VBP) balances UK health and industrial policy in the pharmaceutical sector; abandoning that agreement altogether could have an adverse impact on pharmaceutical and biomedical R&D investment and is in itself unlikely to have a sizable effect on the level of NHS spending on medicines. Building on it, by enhancing the VBP component while also developing and strengthening other strategic elements could have a welfare-enhancing effect.
2. Should the PPRS cease to exist in its current form, its replacement should be a constructive agreement between government and industry that builds positively on the spirit in UK pharmaceutical policy over the past half century. A pricing committee would need to be established in the Department of Health to negotiate prices and finalise pricing arrangements with manufacturers. If a manufacturer requests a premium over existing treatments then the product will undergo a 'health technology assessment' (HTA), though this process will have to be reviewed to ensure the different components of 'value' (economic plus patient, carer and society) are acknowledged and appropriately rewarded.
3. VBP, as it is currently applied, contains limitations that will need to be addressed such as a) the arbitrary basis for affordability b) relative lack of evaluation of other health benefits, e.g. to carers or/and to society c) how to consider long term benefits d) meeting humanely the needs of people who can reasonably be regarded as 'exceptional cases' and e) catering for treatment that has shown to benefit end stage disease but could also be used at an earlier stage.
4. NICE uses a fixed threshold with occasional deviations from it. Greater representation of factors such as unmet medical need, severity of disease, clinical judgement, prevalence of the condition, patient preference, public health impact and societal impact would imply that the QALY threshold of £20-30,000 may need to be raised for areas of high unmet clinical need (eg. cancer) and reduced for low areas of unmet clinical need (eg. treatment of Dislipidemia).
5. The 2007 OFT report proposed two pricing options. a) Free pricing at launch followed by reviews afterwards to assess the effectiveness of the treatment and an adjustment in pricing over time (known as ex-post assessment); and b) set pricing at launch with data that is already available (known as ex-ante assessment). Evidence prior to the launch of a new product is not always available and there may be significant data limitations. Ex-post assessments may prove instrumental in many cases in determining product value for the NHS, patients and society. But criteria, methods and processes need to be set up as to which products should undergo these, together with arrangements allowing access to patients in the meantime. An ex-ante price premium in the case of ex-post assessments would provide a signal to the innovator of the willingness by the payer to reward high risk-taking.
6. Varying medicine prices raises the issue of the resistance to raising the price paid by the NHS and other purchasers if a product is shown to be more effective than originally thought. So a high initial price needs to be considered to ensure a) the public interest is protected by ensuring that high-risk research is incentivised b) industry is reassured that it is worth taking risks with new research. A provision for reimbursement by industry to repay excess profit can be built in to ensure fairness once the full potential of the product is known.
7. If the PPRS in its current form is abandoned, then VBP should assume a key but not necessarily dominant role in informing pricing through HTAs. Final pricing decisions will rest with the DH; a Pricing Committee may be established within the DH to confirm prices with manufacturers on new products based on evidence submitted; the Committee will be responsible for pricing policy and pricing decisions at national (UK) level. In this new environment, thought will need to be given to how HTA activities will be coordinated across all UK-based HTA agencies.

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8. If the PPRS in its current form is abandoned all new patented or other single source products that enter the UK market place may need to undergo an HTA if they request a price premium over existing alternatives. If price parity is requested, then the inclination from the Pricing Committee should be to accept the proposed price. As the workload for appraisals is likely to increase, there may be a requirement for an increase in the available resources for HTA.
9. Currently, HTA assessments are undertaken at a country level (NICE in England, SMC in Scotland, AWMSG in Wales). In order for HTAs to inform pricing decisions at national (UK wide) level if the PPRS is abandoned, the three agencies (currently having different protocols) would have to share the burden due to the increased number of product appraisals and coordinate their activities.
10. Implementing VBP as defined in the report may require more joint work and greater coordination among HTA agencies; consideration should be given to a) the possibility that workloads and, as a result, funding may need to increase; b) the differences between the three agencies and the way they work; c) the timeliness of appraisals and the implications for access; d) the evaluation of benefit in conditions where insufficient study populations exist; and e) returning a verdict on insufficient data in an independent and transparent way.
11. A critical determinant of price is the duration of the intellectual property on the product. To further attract investment in areas of high unmet medical need, rare diseases, personalised medicines or other, we should consider re-defining market exclusivity periods and potentially revisiting the length of supplementary protection certificates. Both these may require international coordination.
12. Patient access schemes (PAS) or risk-sharing agreements mean that payers who are looking for increased certainty when funding new medicines are able to obtain new technologies at acceptable prices without de-incentivising innovators. Irrespective of the type of agreement in place (whether coverage with evidence development, conditional coverage, outcome guarantee scheme, or price-volume agreement), PAS arrangements need to ensure that risk-taking is fairly distributed among the stakeholders involved. The administrative burden associated with running such schemes should also be considered and evaluated.
13. Ex-post value assessment, combined with an ex-ante price premium provides an incentive to the innovator to continue investing in high risk projects, therefore contributing to long term investment in innovation activities and dynamic efficiency. This type of approach should become practice particularly in areas of high unmet medical need.
14. From a welfare perspective, separating production and pricing from innovation and removing the direct market incentives could have a stagnating rather than a welfare enhancing effect. Continuing to link pricing with investment in innovation through the provision of direct financial incentives imbedded in product prices, as is currently the case under the PPRS, should have a welfare-enhancing effect.
15. To ensure overall R&D incentives are provided to encourage innovation there may need to be: a) a multi-disciplinary, cross-departmental 'innovation commission' building along the lines of the OLS initiative, b) continuation of knowledge transfer and research commercialisation arrangements, including the provision of opportunities to extend market exclusivity periods where warranted and c) as required multi-agency initiatives aimed at setting research priorities and supporting relevant implementation strategies.
16. The Innovation Commission would develop and expand a package of actions to support UK pharmaceutical and biomedical R&D, create vertical links within the life sciences community, invest in disciplines to produce a critical mass of appropriately trained scientists. It would also assist in the diffusion of new treatments in the NHS and continue to form a bridge between research and commercialisation. If and when judged necessary it might also seek to provide new supra-market incentives to manufacturers to invest in targeted R&D programmes.

## 1. Background

This paper builds on a series of earlier reports reviewing the UK's current system of pharmaceutical regulation and incentives for innovation and exploring viable alternatives for implementation. In this context, the paper builds on previous work already undertaken by 2020Health (Camps-Walsh et al, 2009), the Kennedy report (Kennedy, 2009), the Cooksey Review (2007), the Office of Fair Trading report on the PPRS (OFT, 2007), the Life Sciences Blueprint from the Office for Life Sciences (OLS, 2009) and the latest PPRS Report to Parliament (DH, 2009).

There is a view amongst some commentators that the case for 'value-based' pharmaceutical pricing has been proven (Claxton, 2007), and that it will in future provide a means of calculating fair NHS prices for new medicines that in the UK will obviate the need for the current Pharmaceutical Price Regulation Scheme (PPRS). Some also argue that the latter has already become redundant because of the establishment of NICE, and the criticisms of it contained in the Office of Fair Trading's 2007 report on pharmaceutical pricing (OFT 2007).

It is certainly the case that the PPRS no longer covers off-patent pharmaceuticals, which in volume terms already represent more than 80 per cent of all the drugs prescribed by GPs. Further, in the context of products such as, for example, high cost new cancer medicines the de facto situation is that there is already a version of VBP in place, which defines their maximum acceptable NHS prices. Even if the PPRS would allow higher prices (or, where market conditions permit, earnings from other products' sales to carry a proportion of the costs attributed to such medicines) NICE interventions restrict or block the use of innovations that incremental cost effectiveness analysis indicates cost in excess of around £25-£30,000 per quality adjusted life year (QALY) yielded.

The situation relating to the appropriate pricing of new medicinal goods is more complex than is on occasions assumed. In commodity markets like those for generic medicines, prices act to balance supply and demand. Their role is to facilitate the efficient allocation of resources, which involves minimising good quality production costs and normalising the profitability associated with the supply of any given product or service. However, in more complex markets like those for health care innovations the role of price mechanisms is more plural. In addition to taking into account the immediate value attached to a good or service by consumers, they may also reflect factors such as the premiums needed to encourage highly risked investment that in the long term should either directly or indirectly contribute to very significant societal gains, yet in the short term (that is, within the likely effective patent life of an average medicine) may fail financially and/or produce only modest health benefits.

The pricing of new pharmaceuticals can be especially difficult for a variety of additional reasons. They range from the fact that in some instances drug costs are seen, rightly or wrongly, to be a key barrier to patient access to life saving treatment, through to the existence of the medical agency problem and that of moral hazard. These last can be said to centre on the fact that typically doctors prescribe medicines, patients consume them and the state (or the insurer) funds them. This means that normal market mechanisms for preventing over-payment may be impaired. In the UK debate about pharmaceutical outlays has also sometimes been an apparent proxy for questioning the affordability of the NHS as a whole, about 87 per cent of the costs of which remain non-pharmaceutical.

Given the above background, the paper takes further the earlier discussion on value and Value-Based Pricing (Camps-Walsh et al, 2009). Having provided a definition of value and VBP for innovative pharmaceutical products, it explores how the latter could be implemented in the UK setting, what the logistical implementation of such an initiative would entail and how it might be operationalised. In considering the policy options to meet the above objective, the paper has operated under two key and overlapping assumptions: first, the environment in which the pharmaceutical sector operates will continue to be characterised by stability, credibility, flexibility, predictability, whilst at the same time ensuring that the NHS continues to receive value for money from innovative prescription medicines; and second, pharmaceutical/biomedical innovation continues to be a priority so that the UK maintains and potentially enhances, its global leadership in the field.



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## 1. Background

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A viable VBP approach must deliver efficiency defined as value for money for the NHS, ensure that the system is stable and predictable over time and also provide appropriate incentives for pharmaceutical innovation to flourish and deliver increased results over the long term. To do so, a number of caveats must be addressed. First, a viable VBP approach must be practical and workable, including applicability given various levels of information constraints, uphold patient access to therapies by providing quick access to cost-effective therapies and maintain supply, as well as be legally defensible. Second, a fine balance of financial stability and flexibility must be struck both for companies and the government. Third, transparency of process is key as it upholds all other factors presented here. Fourth, incentives for innovation are also key, particularly in the UK context, as the country is one of the leading global hubs for pharmaceutical R&D, behind the USA and Japan (DH, 2009).

In this paper we first of all outline the methodology employed in collecting, analyzing and presenting the material (section 2). Section 3 discusses the concept of value and value-based pricing for innovative pharmaceutical products within the NHS (based on 2020health's interim report). Section 4 provides an international perspective into the way different countries and regulatory settings value (pharmaceutical) innovation. Section 5 discusses the key issues that are relevant in the implementation of VBP in the UK. Section 6 outlines an enhanced series of incentives, the aim of which will be to foster pharmaceutical and biomedical innovation in the UK and discuss how these can be operationalised. Finally, section 7 draws the main conclusions.

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## 2. Methods

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The material and reflections on the issues surrounding the implementation of VBP in this paper build on consultation from two broad sources: the first is the earlier primary research work conducted by 2020health (Camps-Walsh, 2009), which included interviews and meetings with stakeholders, conducted for this purpose. The second is additional consultation with a select group of stakeholders, including patients, policy experts and manufacturers in order to tease out some of the logistical arrangements for VBP implementation.

As discussed above, there are two working assumptions underpinning this paper: first, the parameters in which VBP is implemented guarantee a stable, flexible and credible environment for the assessment of value of new products in the UK; and second, that incentives for encouraging pharmaceutical and biomedical innovation will continue to be provided in order for the UK to maintain and potentially enhance its leading position globally. The paper was written between November 2009 and February 2010.

## 3. Valuing medical treatments: What benchmarks?

### 3.1. Value and medical ethics

In purely semantic terms, value can be thought of as the amount of money considered a fair equivalent for a 'product,' or simply a feature that renders an object desirable. In this sense, the absolute value of an object is independent of the user. But value is also a relative concept: how much a desired object is worth relative to other objects, or the property of an object which represents its importance or rarity. So it can be subjective, dependant on culture and personal view.

When we start to consider 'value' in terms of medical ethics, we encounter even more questions. Beauchamp and Childress (2001) outlined four principles that provide a framework for considering ethical issues. Each must be considered and weighed up against the others. Firstly, respect for autonomy, facilitating individuals to make informed choices. Secondly beneficence, or 'doing good' for the patient, which must be considered alongside non-maleficence, the principle that no harm should be done. The benefits and risks, as far as they are known, must be balanced with financial costs. Finally the principle of justice, brings in a social perspective in which patients in similar positions should be treated similarly.

These concepts are useful, but only to a point. What does value really mean in practice for the patient? The now familiar methodology of assessing value is the QALY. This uses a basic equation to consider quantity of life alongside quality of life. The scale of quality of life measurement ranges from negative values indicating worst health, to a maximum of 1 indicating the best possible health, and incorporates pain and side effects. There are limitations however as not only does the QALY attempt to attribute a financial value to life, it also uses a 'one size fits all' approach which fails to acknowledge that all patients are different. Additionally, it omits factors that may be significant to patients and their families such as the ability to return to work or live independently for longer.

This abstract concept becomes a poignant reality when one considers specific scenarios such as providing a 64 year old man with metastatic colon cancer the chance to live longer, or the 43 year old mother with advanced breast cancer and family responsibilities the opportunity to spend more time with her children and make arrangements for when she has gone. For the 75 year old man with wet age-related macular degeneration that could have been halted by appropriate treatment and who now can no longer care for his wife with dementia, the personal and societal costs are enormous. Yet again for the 38 year old woman with rheumatoid arthritis who commutes to work, treatment for her is just as much about enabling mobility and independence.

From the patient perspective, there are perhaps different spheres of value, which go beyond the health outcomes that dominate the QALY model, to include the true costs or value of a treatment. This might be portrayed in the following way:

There is no doubt that it would be a significant challenge to include more detailed personal costs in the process of valuing a product. At the moment a 'generic' patient is considered and the differing priorities and needs of individual patients are ignored. This however raises the issue of whether we should allow for differences in personal circumstances and then include these different considerations and importantly, how would we measure them?

At the same time, the potential benefits need to be balanced with fairness and justice - how do we ensure that costs and benefits are distributed fairly? And what are the most significant benefits? It is important that we do not lose sight of the need for equity in healthcare, ensuring that there is equal provision for equal need. This then raises the question of which needs are the most important, who should decide? And how does all this sit alongside patient autonomy and choice?

Evidence based medicine, through appraising the findings of research and applying them to clinical practice to ensure that patients receive the best care, must remain central. Additionally resources are limited and there will always be a need to think about demand management. Alongside this there needs to be public discourse about how priorities are set, and above all what really matters to the patient.

### 3.2. Value in the NHS

At the launch of the NHS in July 1948, the three core principles were outlined: first, that it meets the needs of everyone; second that it be free at the point of delivery and third, that it be based on clinical need, not ability to pay.

As noted on page 17 the NHS Constitution includes six 'NHS values' –

- respect and dignity
- commitment to quality of care
- compassion
- improving lives
- working together for patients
- everyone counts

However, these do not define how we value medical treatments. A stakeholder analysis by 2020health of the factors that are most important in valuing medical treatments revealed a series of interesting results.

The first two parameters receiving the highest ratings were effectiveness/efficacy (98% amongst all stakeholder representatives) and safety (94% amongst all stakeholder representatives). These were followed by health outcome/success of treatment (90%), loss of dignity and individualism (57%), complications and readmissions, side effects and cost to the patient.

Stakeholder analysis adopted in the definition of 'value' across medical treatments, suggests that different values are important to different stakeholder groups, including patients, health care professionals, NHS/health care managers and pharmaceutical manufacturers.

This previous work by 2020health showed that while the benefits most highly valued by all stakeholder groups are effectiveness/efficacy and safety, which NICE and the NHS evaluate at present, other highly rated costs and benefits were not widely considered (Camps-Walsh et al, 2009). For instance, whereas costs to the NHS are always considered, costs to patients, their families, their employers and society are not, although they fund the NHS. These costs can be significant and in a publicly funded, or indeed any healthcare system, must be taken into account and include, among others:

- patient time to feeling completely well/ returning to work
- loss of dignity and individualism
- costs to patient of side effects
- invasiveness of treatment
- care needed from friends and family
- where they are treated i.e. hospital, primary care, home
- convenience of treatment
- cost to the economy
- cost to employer

Different values were attributed to acute, chronic and end-of-life treatments and these should be viewed differently when assessing value, as side effects for chronic disease are more important than those for the other two categories.

### 3. Valuing medical treatments: What benchmarks?

To ensure that value is delivered both now and in the future most, but not all, thought that NICE should oversee this process, but that patients and doctors should be much more involved in the process.

Overall, when assessing the ‘value’ of new or even existing treatments the NHS, NICE, the Department of Health (DH) and the Government, ought to take a societal perspective which includes the costs to patients, their families, society, their employers and the economy.

### 4. Value of (pharmaceutical) innovation – The European perspective

#### 4.1. Valuing innovation in the context of drug reimbursement

Few would disagree that pharmaceutical innovation is worthwhile, although many would argue that there are significant differences in opinion across different settings, often dominated by individual value judgements about “what is innovation” and how value is defined. Indeed, the debate surrounding the value of innovation centres not only around clinical, but also socio-economic as well as budgetary criteria. This is done with a view to deciding on how new products should be reimbursed and whether the decision to reimburse them meet a number of criteria. The type of criteria applied in this context and across the study countries are shown on Table 4.1 and range from therapeutic improvement to assessment of cost effectiveness and budget impact, to cross-country price comparisons.

Countries typically apply a multiplicity of criteria to inform decisions about inclusion of new products in the reimbursement list and the rate at which a new product might be reimbursed. More often than not, valuing an innovative new medicine becomes a function of the price that the same medicine commands in neighbouring countries.

Despite the wide range of criteria that are explicitly or implicitly used to inform pricing and/or reimbursement decisions, the explicit strategies or modalities used in practice to value pharmaceutical innovation are limited in number. The evidence suggests that European countries apply three different approaches to valuing pharmaceutical innovation: the first is through rate of return regulation, which includes incentives to conduct R&D.

The second is the assessment of the clinical/therapeutic benefit of individual technologies, by means of ranking new treatments based on their therapeutic potential, as is currently undertaken in France and, to a certain extent, in Italy.

The third approach to valuing innovation relates to the use of Health Technology Assessment (HTA) in informing relative effectiveness of new treatments. Several countries apply HTA explicitly (UK, The Netherlands, Sweden, Switzerland, Finland, Poland), while in others HTA plays an increasing role but is not used explicitly in the decision making process.

All three approaches are pursued at national level as health and pharmaceutical care budgets are managed nationally. Supra-national bodies such as the European Commission have no competence in deciding on how health care budgets are allocated or spent and by default, have no competence in passing judgement on how new technologies or treatments should be valued and what approach or methodology should be used. They have, however, attempted on several occasions – the last time during the High Level Pharmaceutical Forum (HLPF) – to bring Member States together with a view to sharing common practices in pharmaceutical policy and creating consensus about the future.

The following sections outline each of the three approaches identified in this section and also discuss the role of European institutions in value assessment.

## 4. Value of (pharmaceutical) innovation – The European perspective

**Table 4.1 Criteria for assessing new technologies in 15 EU countries, 2008**

	UK	Germany	France	Italy	Spain	Netherlands	Sweden	Switzerland	Denmark	Finland	Czech Republic	Portugal	Greece	Poland	Slovakia
Therapeutic benefit	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Patient benefit	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Cost efficacy/ cost effectiveness	X				?	X	X	X	?	X	?	X?		X	?
Budget impact	X		X	X	X	X	X			X	X	X		X	X
Pharmaceutical/ Innovative characteristics			X			X			X						
Availability of therapeutic alternatives	X					X	X		X						
Equity considerations	X						X		X		X				
Public health impact	X		X				X								
R&D	X								X						
Unmet need	X	X						X			X				
Price in other countries			X				X		X		X	X	X	X	X
Price of similar/ comparable products												X	X		
Other	X														
Price freedom	X?	X	X??												

X?=applies in part in the case of the UK and Portugal; X??=applies in part in the case of France; ?= not a formal requirement to arrive at decisions, but local expertise exists, which may feed into the decision-making process.

Source: Kanavos et al, 2009.

### 4.2. Rate of return regulation

Rate of return regulation applies in the case of the UK, through the Pharmaceutical Price Regulation Scheme (PPRS), a scheme that regulates the profits of pharmaceutical companies and, through profits, the prices of medicines indirectly. The scheme has been in operation in the UK for over 50 years now and is administered by the UK Department of Health (DH).

The objectives of the scheme are firstly to deliver value for money for the UK NHS by securing the provision of safe and effective medicines at reasonable prices, and encouraging the efficient development and competitive supply of medicines. Secondly, to encourage innovation by promoting a strong and profitable pharmaceutical industry that is capable and willing to invest in sustained research and development to encourage the future availability of new and improved medicines for the benefit of patients and industry in this and other countries. Thirdly, to promote access and uptake for new medicines and fourthly, to provide stability, sustainability and predictability to help the NHS and industry develop sustainable financial and investment strategies.

The relatively free pricing in the UK – which is, nevertheless, subject to negotiation and moderate reduction in prices each time the scheme is re-negotiated – makes it an attractive market for the launch of new pharmaceutical products. It also provides clear incentives for innovation through the return on capital employed (ROCE) and R&D allowances. A thorough assessment of the true socio-economic value of innovative pharmaceutical products in the UK is particularly important as it is a price-leader with regards to international reference pricing. The countries which reference prices to the UK represent approximately 25% of global pharmaceutical markets, though not all products in each country are referenced to the UK [OFT, 2007].

The scheme has been criticised on several occasions for leading to capital over-investment and for being inefficient.<sup>2</sup> In addition, the divergence between price and value was the main focus of the Office of Fair Trading investigation report (OFT, 2007), calling for a radical overhaul of the scheme in favour of value-based pricing. The key argument in favour of a new approach from the OFT perspective was that “...neither the profit nor the price controls take account of the therapeutic value of drugs. This undermines the extent to which they can help secure value-reflective prices for the NHS. For a scheme that sets out to deliver value for money for the NHS and give companies the right incentives to invest, we consider this to be a significant flaw... the UK is almost unique in the world in not taking explicit account of the therapeutic benefits of drugs in its pricing system.”

The 2009 PPRS became effective on January 1st, 2009 (DH, 2008), following a re-negotiation, and will include several options for patient access schemes, whether financially or outcome-based, the latter implying flexible pricing based on the clinical evidence produced and risk sharing between the Department of Health and individual companies.

### 4.3. Assessment of clinical/therapeutic benefit

Surveys have shown that countries shown on Table 4.1 examine the available clinical evidence very closely (Table 4.1). However, in two of the study countries it appears that the strength of the clinical evidence forms the basis for a classification of drugs as highly innovative, innovative, or me-too.

In this context, France applies the principle of therapeutic benefit rendered (Amelioration du Service Medical Rendu, ASMR). In France, pricing and reimbursement of pharmaceuticals is decided by negotiations between the pharmaceutical industry and a variety of organisations. The Transparency Committee (Commission de la Transparence, CT) initially decides whether or not reimbursement is granted and the scope of indications for which the drug is to be prescribed, ultimately determining rate of reimbursement (ranging from 30% to 65%).

2. The criticism on non-transparency arises from the fact that discussions between industry representatives and the PPRS Branch on ROCE, target profits and price modulations are never made public; on the other hand, they could never be publicised given the confidential nature of such discussions. Capital over-investment (and the inefficiency that may arise as a result) is a corollary of the link between capital invested in the country and justifiable profit. Whereas there is a link from a conceptual perspective, it is not clear what the economically optimal rate of capital investment in the country is as a result of the PPRS.

## 4. Value of (pharmaceutical) innovation – The European perspective

However, prices are determined by the Comité Economique des Produits de Santé (CEPS) based on the ‘improvement in medical benefit rating’ (ASMR), or ‘incremental medical benefit’ as judged by the CT. The ratings are categorised as shown on Table 4.2.

**Table 4.2**  
**ASMR categories in France**

Amelioration du Service Medical Rendu (ASMR) Group	
<b>ASMR 1</b>	significantly innovative and of substantial clinical benefit
<b>ASMR 2</b>	significant improvement in efficacy, and/or amelioration of adverse reactions
<b>ASMR 3</b>	some improvement in efficacy, and/or reduction of adverse reactions, compared with existing medications
<b>ASMR 4</b>	little improvement of clinical benefit compared with existing products
<b>ASMR 5</b>	no improvement in clinical benefit, as compared with existing products

The ASMR rating is not the only factor taken into account when deciding the final price. Although ASMR 1 to 4 products will be priced higher than their existing alternatives, with ASMR 5 pharmaceuticals not given a price premium compared to existing products, expected sales levels and external reference pricing are also considered. If the new pharmaceutical is expected to increase the overall level of sales in that therapeutic group, a lower price than existing pharmaceuticals may be justified. In addition, the CEPS wants to keep prices at the EU average or below.

In Italy, a study illustrated the development of an algorithm to quantify the value of innovation, in the hope of capturing patients, policy-makers and pharmaceutical companies’ perspectives in the innovation process (Caprino and Russo, 2006). The Innovation Assessment Algorithm (IAA) had 3 key aims: first, to take into account and incorporate different properties of drug innovation; second, to provide a numeric weight as a measure of the innovative value of a drug; and third, to re-assess innovation over time, by incorporating clinical evidence that has emerged after marketing authorization.

The IAA differentiates between therapeutic innovation, common innovation and industrial innovation. A schematic version of the algorithm is shown on Table 4.3.

**Table 4.3**  
**The IAA algorithm**

The IAA algorithm			
Stage 1		Stage 2	Stage 3
<b>Therapeutic Innovation</b>	Subdivided to recognise medications for which there was no current satisfactory treatment, known molecular entities but used for novel indications and unclassified substances	patient-centred issues, such as compliance, tolerability and the societal consequences of the new drug	factors of importance to the pharmaceutical industry in the clinical trial phase, such as clinical outcome, number of indications, patient population tested and type of overall benefit
<b>Industrial Innovation</b>	Classified according to whether discovered through an advanced technology (e.g. biotechnology), whether a new preparation or administrative route, or whether of limited innovative value		
<b>Common Innovation</b>			
<b>Evaluation of Efficacy</b>		<b>Evaluation of Effectiveness</b>	

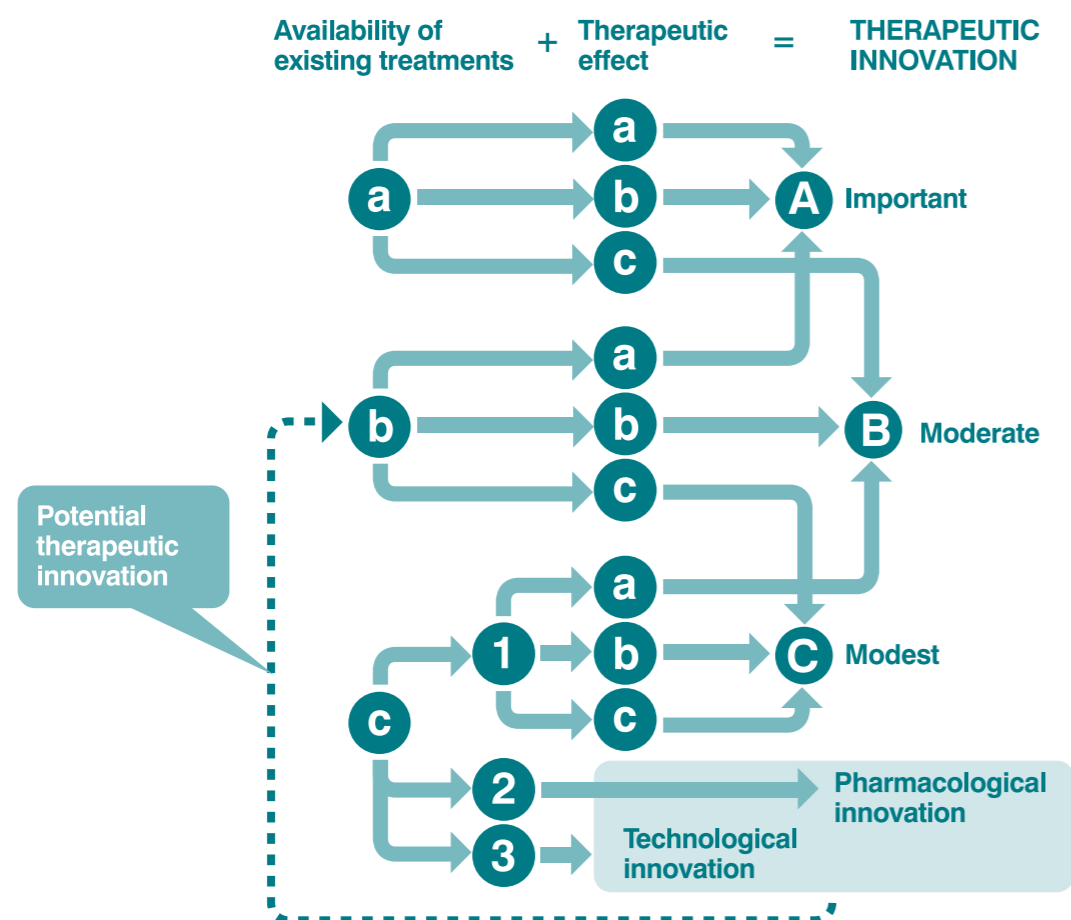
Source: Caprino and Russo, 2006

The final score produced by the algorithm gave greater weight to the earlier ‘efficacy’ branches than the effectiveness branches. Whilst several models have been suggested to explicitly quantify innovation in such a manner, this model is significant in that it identifies aspects of innovation in the early-intermediate R&D stage. Recent evidence suggests that this type of approach to analysing innovation per se is influencing policy directly in Italy. Indeed, a similar hierarchical scheme which has been devised by AIFA along very similar lines. Indeed, a similar hierarchical scheme which has been devised by AIFA along very similar lines. Pharmaceuticals are divided into three broad categories; those for fatal or serious conditions which result in permanent disability/hospitalisation, those that eliminate or reduce the risk of serious diseases (e.g. hypertensive treatments) and lastly those for ‘non-serious’ diseases such as hayfever. Interestingly, a clear distinction is made between pharmacological innovation (i.e. a new method of action, with necessarily increased efficacy) and technological innovation which may similarly not provide a therapeutic innovation. Other things being equal, the former would be rated higher than the latter under their new scheme. AIFA have also stressed the importance of incorporating post-marketing data into their algorithm. A schematic approach to this model is shown on Figure 4.1.

Although the IAA algorithm may appear to have high informational requirements, a similar framework might be useful in structuring the economic information required from pharmaceutical companies and enabling greater transparency of the priorities of the health system. Such scientific approaches provide a robust and reliable method of quantifying innovation and are also attractive as they pacify several stakeholders in the system simultaneously. The particular model also takes into account economic information that emerges after clinical authorisation (ex-post).

## 4. Value of (pharmaceutical) innovation – The European perspective

**Figure 4.1**  
Assessing therapeutic innovation in Italy



Source: Atella, 2008, personal communication.

### 4.4. Health Technology Assessment and value-based pricing

The varying nature and emerging complexity of health technologies, in combination with limited national budgets, has resulted in tensions between delivering cost-effective health care and improving or sustaining a country's manufacturing and research base. As a result, it has become increasingly important to achieve a balance between affordable healthcare and the use of innovative health technologies, including pharmaceuticals. To meet this end, it is necessary to not only consider the medical and economical value of a product, but also who benefits from innovations, the optimal usage<sup>3</sup> and the appropriate placement in the spectrum of care (Drummond, 2006).

HTA can assist in meeting these challenges by determining which technologies are ineffective versus those with value and by defining the most appropriate indications for use of the technology (Drummond, 2001). Moreover, HTA can serve to validate a new technology and define its role in healthcare system. HTA thus provides important benefits by enabling governments to make decisions driven by value, which concurrently supports innovation, and garners patients and physicians with the information needed to make the best treatment choices (Sorenson et al, 2008).

However, the effectiveness of HTA in achieving the above benefits, particularly in terms of encouraging innovation, hinges on properly performed assessments and the appropriate implementation and use of subsequent recommendations. HTA can encourage innovation if the assessments are properly done and consider a wide range of costs and benefits associated with a new technology, rather than focus solely on acquisition costs. In particular, the costs of adoption need to be viewed in terms of the broader benefits that would ensue if a technology were integrated into the health system, as budget driven constraints on the general diffusion of technologies do not necessarily result in the selection of the most effective or cost-effective products. This may require governments to allow additional funding and flexibility between budgets, so that expenditure levels are driven by value, as opposed to arbitrary spending caps (Drummond, 2001).

The utility of HTA in encouraging innovation and value-added health care also depends on the assessment process, including when and how the review was performed, and resulting decision-making procedures. In particular, the following issues can potentially affect the effective use of HTA in meeting these objectives (Drummond, 2006; Zentner et al., 2005; Anell, 2004; Busse et al., 2002):

- delays in the HTA process can result in deferred reimbursement decisions, restricting patient access to needed treatments;
- evidence requirements can pose a significant hurdle for manufacturers, particularly small, innovative companies, which may serve to discourage sponsors from pursuing breakthrough technologies;
- as HTA becomes increasingly widespread, assessments are occurring earlier in the technology diffusion process, which may introduce greater uncertainty in the process and the potential for innovations to appear more or less beneficial when assessed at an early stage;
- current assessment methodologies may limit the comparability and transferability across countries and studies;
- lack of transparency, accountability, and stakeholder involvement in the HTA process can decrease the acceptance and implementation of assessment results;
- limited skilled HTA personnel and international collaboration between review agencies can stymie the efficiency and effectiveness of assessments;
- separate processes for and organizations dedicated to economic assessments, reimbursement/pricing decisions, and practice guideline development may hinder the effectiveness and efficacy of the overall decision-making process, and lead to unnecessary duplication of efforts and resource use.

In addition, HTAs are more likely to be utilised by decision makers if policy instruments (e.g. reports, practice guidelines) are available to act on the assessment and if prior commitments to effectively use the assessments are established. Moreover, as the cost-effectiveness of a technology can change over time, in addition to patient demand, it is important to review the recommendations of HTA agencies on a consistent basis. To achieve these objectives, greater participation and collaboration among stakeholders, particularly HTA personnel, government officials, industry, health providers and patients, is required. Without adequate input and understanding of the HTA process, stakeholders may mistrust the evidence and subsequent recommendations of the assessment.

3. Variation in uptake and diffusion can signify the sub-optimal use of technology. Excess use is signified when the costs outweigh the benefits for any additional level of technology diffusion or use. Under-use can occur when the foregone benefits outweigh the costs of additional diffusion or use. Both scenarios are sub-optimal, potentially resulting in economic costs and/or reduced health outcomes.

## 4. Value of (pharmaceutical) innovation – The European perspective

Overall, in order for HTA to be of optimal benefit, the assessment process needs to be linked with innovation and other aspects of policy-making. To the latter, it is important that HTA recognise the complexities of decision-making, whereby subjective and normative concerns are duly considered. Otherwise, HTA may be limited in its powers to impact upon the policy process and subsequent access to new and effective products. The role of HTA in encouraging innovation and value in health care could be improved by better understanding and addressing the inherent challenges in the HTA process, as outlined below.

The introduction and growth in HTA in Europe parallels an era in health policy that places greater emphases on measurement, accountability, value for money and evidence-based policies and practices. Moreover, the advent of randomised control trials and subsequent availability of data, growth in medical research and information technology, and increased decentralisation of health system decision-making, all contributed to an increased need for HTA activities (OECD, 2008).

In Europe, the first institutions or organisational bodies dedicated to the evaluation of health care technologies were established in the 1980s, initially at the regional and local level in France and Spain and, later, on the regional level in Sweden in 1987 (Velasco-Garrido & Busse, 2005; Garcia-Altes et al., 2004). Over the following decade, in almost all countries, HTA programmes have been established either through the provision of new agencies or institutes, or in established academic units or governmental and non-governmental entities (Table 4.4). Broadly speaking, such bodies fall into two general strands: 1) independent (“arms-length”) review bodies that produce and disseminate assessment reports on a breadth of topics, including health technologies and interventions, and 2) entities under governmental mandate (e.g., from health ministries) with responsibilities for decision-making and priority-setting, typically pertaining to the reimbursement and pricing of health technologies. The latter type of HTA body serves either an advisory or regulatory function.

In parallel with establishing HTA entities, many EU countries are investing resources in HTA and associated evaluation activities. For example, Sweden dedicates €5 million per year on the Swedish Council on Technology Assessment in Health Care (SBU) and the Dutch Fund for Investigative Medicine spends €8.6 million per year on health evaluations (Sorenson et al, 2008).

**Table 4.4**  
**Institutions and advisory bodies responsible for HTA activities in selected EU countries, 2008**

<b>1. Denmark</b>	Reimbursement Committee/Danish Centre for Evaluation and Health Technology Assessment/ Center for Evaluering og Medicinsk Teknologivurdering (DACEHTA/CEMTV)
<b>2. Finland</b>	<ul style="list-style-type: none"> <li>• Pharmaceuticals Pricing Board – PPB (Laakkeiden hintalautakunta)</li> <li>• Finnish Office of Health technology Assessment (FinOHTA)</li> </ul>
<b>3. France</b>	<ul style="list-style-type: none"> <li>• Economic Committee for the Health Products (CEPS)</li> <li>• Transparency Commission (CT)</li> <li>• Haute Autorité de Santé (HAS)</li> </ul>
<b>4. Germany</b>	<ul style="list-style-type: none"> <li>• Federal Joint Committee (FJC)</li> <li>• Institute for Quality and Efficiency in Health Care (IQWiG)</li> <li>• German Agency for Health Technology Assessment (DAHTA)</li> </ul>
<b>5. Italy</b>	<ul style="list-style-type: none"> <li>• Committee on Pharmaceuticals (CIP Farmaci)</li> <li>• Italian Medicines Agency (AIFA)</li> </ul>
<b>6. Netherlands</b>	National Health Insurance Board/Committee for Pharmaceutical Aid
<b>7. Spain<sup>1</sup></b>	<ul style="list-style-type: none"> <li>• Spanish Agency for Health Technology Assessment</li> <li>• Catalan Agency for Health Technology Assessment (CaHTA)</li> </ul>
<b>8. Sweden</b>	<ul style="list-style-type: none"> <li>• Dental &amp; Pharmaceutical Benefits Board (TLV)</li> <li>• Swedish Council on Technology Assessment in Health Care (SBU)</li> </ul>
<b>9. UK</b>	<ul style="list-style-type: none"> <li>• National Institute of Health and Clinical Excellence (NICE)</li> <li>• National Coordinating Centre for Health Technology Assessment (NCCHTA)</li> <li>• Scottish Medicines Consortium (SMC)</li> <li>• All Wales Medicines Strategy Group (AWMSG)</li> </ul>

*Note: 1. These are not an exhaustive list of the agencies available in the country.*

*Source: The authors from various sources; adapted and enhanced from Velasco-Garrido & Busse, 2005; Zetner et al., 2005.*

## 4. Value of (pharmaceutical) innovation – The European perspective

### 4.5. Reflections on value from a European dimension

Over the past five years, the High Level Pharmaceutical Forum (HLPF) has provided some impetus for debate and potential coordination among national policy makers in the field of pharmaceuticals. As part of this process, a questionnaire was submitted to all Member States, with the aim of identifying the demand-side benefits which are seen as important when assessing the value of an innovative medicine (European Commission, 2007). The benefits identified by the Member States themselves, fell into three broad categories; (a) therapeutic/clinical benefits, (b) quality of life improvements and (c) socio-economic benefits. A list of these benefits and the way in which they were categorised is shown in Table 4.5.

Despite the fact that EU institutions have no competence in health care and pharmaceutical policy harmonisation, it has been an important achievement to gather the Member States and other stakeholders around the table. This was with a view to understanding some of the levers driving “value of pharmaceutical treatments” at Member State level, as well as to “work out a set of guiding principles which demonstrate that dialogue between Commission, Member States and multiple stakeholders is possible in an attempt to meet the needs of patients, payers and industry alike” (Cueni, 2008).

**Table 4.5**  
**Valuing pharmaceutical innovation<sup>1</sup>**

Benefits of innovative drugs	
<b>Clinical/ Therapeutic benefits</b>	Higher probability of recovery
	Faster partial/total recovery
	Slower disease progression
	Increased ability to cope with disease symptoms
	Higher probability of preventing re-emergence of a disease
	Survival rate, life expectancy
	Reduced side effects
	Reduced interactions with other medicines
	Higher tolerability
	Broader/easier dosing/administration - improved compliance
<b>Quality of Life benefits</b>	Higher physical self-sustainability/self-management
	Higher psychological self-sustainability
	Higher social self-sustainability
	Higher convenience/comfort for the patient
<b>Socio-economic benefits</b>	Avoiding Pandemics
	Addressing Resistance
	Reduced total cost of medication/treatment
	Reduced cost of sick-leave
	Higher productivity

*Note: 1. Adapted from EC Progress Report.*



## 4. Value of (pharmaceutical) innovation – The European perspective

Contextually, the output of the HLPF in terms of defining pharmaceutical innovation and therefore, ‘value’, presents striking similarities with the value benchmarks discussed in section 3 and the earlier work by 2020health among UK stakeholders.

Two critical aspects are immediately compelling across the two: first, that strict cost-effectiveness criteria do not dominate the discussion or, indeed, the decision making process on what determines “value”; and second, a societal perspective occupies the high ground in the assessment of value of pharmaceutical innovations. As a result, VBP encompasses all aspects of value and in which an assessment of costs and benefits, as exemplified by a narrowly defined cost/QALY ratio, is neither a necessary nor a sufficient condition for assessing value and revealing affordability.

Whereas it may be socially desirable to adopt a societal perspective in the assessment of value, rather than only therapeutic or health system value, the practical limitations of the former over the latter options are twofold. Firstly, the complexity and breadth of data required to demonstrate value mean that it is normally impossible to assess the full clinical value of any medicine at the time of its initial launch. The types of difficulty this leads to with regard to implementing value-based pricing are discussed in the next section. The second limitation is the frequent silo mentality in budget setting. Whereas the former can be addressed with improvements in methodology and data reporting, the latter requires a mentality shift across the payer community.

## 5. Implementing VBP in the UK

### 5.1. Current practice

The previous section highlighted the complexities in value determination and the fact that a cost - benefit (or cost - effectiveness) assessment is one of the criteria used rather than the leading criterion.

For VBP to be a viable option in the UK it must deliver efficiency defined as value for money for the NHS but also provide correct incentives for the pharmaceutical industry to invest in innovation. To do so, a number of caveats must be addressed. First, the new VBP system must be practical, including applicability given various levels of information constraints, uphold patient access to therapies by providing quick access to effective therapies and maintaining supply, as well as be legally defensible. Second, a fine balance of financial stability and flexibility must be found for manufacturers and government. Third, transparency of process is key as it upholds all other factors presented here.

The options for in-patent therapies are complex, as the reflection of value and incentive for innovation must be more explicit.

Current practice, as well as recent suggestions (e.g. through the OFT recommendations), maintain that there are two possibilities, ex-post and ex-ante scenarios (see Table 5.1). The method of valuation of the therapy follows the Incremental Cost Effectiveness Ratio (ICER) principle:

$$\text{ICER} = \frac{\text{Cost NEW DRUG} - \text{Cost COMPARATOR DRUG}}{\text{Benefit NEW DRUG} - \text{Benefit COMPARATOR DRUG}}$$

Using this cost effective method, a maximum ICER would be set and currently NICE sets an ICER threshold of £20,000-30,000/QALY. A decision needs to be made about whether a fixed or a flexible threshold is desirable, but, in the authors’ view, consideration should also be given to criteria other than economic/QALY, such as severity of disease, which may imply a flexible threshold. Once price agreement is reached based on assessment of product value, it cannot be changed by the manufacturer, unless further evidence emerges in the medium term on the value of the product. This is in order to ensure budget stability for the NHS. The definition of a comparator therapy is paramount. NICE defines this as the current best available treatment which may be branded or generic, the most popular clinically-effective or cost-effective treatment.

The most controversial portion of determining ICER is measurement of benefit. NICE uses the QALY, where survival outcomes are modulated by a quality of life factor. The major criticism is in diseases where new therapies may not lengthen survival, however, do make a significant impact in quality of life. This problem is further compounded in situations where the study population is scarce, such as in paediatric diseases, orphan diseases and cancer. Mental illnesses, certain chronic illnesses and geriatric diseases may also suffer under the QALY as outcomes may again be related more to quality of life rather than length of life, in addition to impact of quality of life for the carer (which is currently unmeasured in the QALY).

The use of generic comparators is also controversial, however, the views that have already been expressed are that the NHS does not have enough flexibility to be generous in this point (OFT, 2007). Nevertheless, one possible downside of the VBP model as employed by the OFT is that it is in effect designed to curtail patent holders’ rights to charge a premium for their products during the full life of their patent. While there is a temptation for the NHS to consider generic comparators where possible, one needs to reflect on the further disincentive it provides to the innovator, if the payoff is driven by a generic low cost alternative. This provides neither short nor long term

4. Relating to the arguments about static and dynamic efficiency.

## 5. Implementing VBP in the UK

incentives to innovate<sup>4</sup>, whilst at the same time it provides a strong incentive to the innovator to select less risky investment options, which potentially, can lead to less innovation and lower welfare in the future.

Thus, design and implementation of VBP is paramount to its success and continued underpinning of NHS goals and values. Ideally, reform gradually, perhaps even with pilots in certain classes of medicines, in order to either phase in ex-post reviews of all drugs currently reimbursed to bring their pricing in line with their clinical value, or ex-ante analysis of all New Molecular Entities (NMEs) entering the market (or a combination thereof).

**Table 5.1**  
**Methodological options of value based pricing reforms for on-patent therapies**

Value Based Pricing Scenario	Description	Advantage	Disdvantage
Ex post VBP <sup>5</sup>	<p>a) Keep initial pricing freedom for pharma for new active substances</p> <p>b) Replace current PPRS profit controls and price cuts with ex post reviews on cost-effectiveness of individual drugs or drug classes</p> <p>c) The ex post review would set maximum price depending on clinical benefit compared to an appropriate clinical comparator</p> <p>d) The timing of ex post reviews should coincide with major events, ie new drug entry, comparator post-patent, Phase IV trial results</p> <p>e) Regular pricing reviews, every 5 years</p>	<p>Continues rapid access to new medicines, beneficial to manufacturers and patients</p> <p>Preferred option by industry by continuing free pricing it currently enjoys along with its international ramifications, while potential for future cuts are offset</p>	<p>Weaker bargaining position of the NHS, as withdrawal of product from the market is a less viable threat (versus ex ante method)</p>

**Table 5.1 (continued)**

Value Based Pricing Scenario	Description	Advantage	Disdvantage
Ex ante VBP <sup>6,7</sup>	<p>a) Delete current PPRS profit controls and price cuts, and limit current pricing freedom of new active substances at launch</p> <p>b) Develop ex post reviews for existing drugs as described above</p> <p>c) Initiate fast track ex ante reviews for new drugs cost effectiveness begun during the licensing process</p> <p>d) Concurrent reimbursement and pricing decisions when sufficient cost-effectiveness data is available. If insufficient data is available, a risk sharing mechanism would be agreed upon until further data is collected</p> <p>e) Regular ex post reviews, particularly when new information emerges or when comparator product goes off-patent</p>	<p>Refuses reimbursement for new substances not cost effective</p> <p>Better bargaining power of the NHS</p> <p>Early stage cost effectiveness assessment may encourage uptake of new medicines (reflecting increased uptake after positive NICE recommendations), benefiting both patients and companies</p> <p>Ideal for medicines applied in acute conditions where data is easy to collect</p> <p>Unlikely to require new legislation as current pricing is not devolved</p> <p>Removes current timely referral process for new medicines passed to NICE</p>	<p>Potential for lengthy negotiations between company and reimbursement agency when insufficient data available and risk sharing is produced as an option. This approach is likely most applicable in chronic conditions, paediatric applications, cancer and orphan diseases where the population base for trial is minimal and observed outcomes longitudinal</p> <p>How to address initial non-profitable new molecular entities or pharmacological mechanisms, but may have an application in the future</p> <p>The reformed system would allocate this risk to the manufacturer, as there is currently no room for ineffective therapies to be reimbursed by the NHS</p>

5. Examples of other ex ante pricing and reimbursement schemes are free pricing with immediate reimbursement (Germany, UK), pricing relative to a substitute (Australia, Canada – non-innovative drugs, Finland, France, Netherlands, Spain, Sweden, Switzerland, US), international reference pricing (Canada – innovative drugs, Finland, France – innovative drugs, Netherlands, Spain, Switzerland) and price volume agreements with rebates (Australia, France, Germany, Spain, US)

6. Examples of other ex post pricing and reimbursement schemes are price cuts (Finland, France, Spain, UK), profit controls (UK), pricing relative to substitute ((Australia, Finland, France, Germany, Netherlands, Spain, Sweden, Switzerland, US), and international reference pricing (Canada, Finland, Netherlands, Switzerland)

7. Deemed by the OFT to be the most viable option for reform in the UK

## 5. Implementing VBP in the UK

### 5.2. Reflections on VBP implementation and key issues arising

If VBP is the preferred option for valuing pharmaceuticals in the UK, then the implementation of a VBP system, where prices reflect their true value, would require discussion around and clarification of a number of issues, as follows:

- the current regulatory system surrounding the PPRS;
- the actual limitations of VBP in its current form;
- what are the implications for pricing decisions in the context of VBP?
- for which products would VBP be applied?
- what would be the role of the current HTA agencies operating in a devolved health care system?
- who would be responsible for pricing?
- would there continue to be a fixed/revealed threshold?
- would preference be given to ex-ante or ex-post evaluations? or is there scope for a combination of the two?
- who would be responsible for industrial policy, particularly fostering innovation?

These questions are examined in the following paragraphs and highlight the issues that arise for decision-makers.

#### 5.2.1. Considering the PPRS in the context of UK pharmaceutical policy

Critics argue that the PPRS has in the past encouraged excessive capital investment in this country, and led to the UK paying unduly high prices for individual products. But against this, aggregate NHS spending on medicines has been and remains relatively low, as compared to the figures recorded elsewhere in the OECD (OECD, 2008). The same holds for UK pharmaceutical prices (DH, 2008).

This country has in addition had an unusually robust record of pharmaceutical research and export from the 1950s through to the early twentieth century, coupled with what is, in international terms, low spending on advertising and other forms of promotion. PPRS advocates point out that it does not guarantee 'as of right' target returns, because of price competition between alternative medicines. The validity of this view depends in part on the extent of the medicines' price sensitivity that can be found in the GP and, today more importantly, the hospital pharmaceutical markets. The proportion of NHS resources spent on drugs has fallen since the end of the 1990s, although within the total 'drugs bill' the proportion due to hospital costs is rising. (The current figure is in the order of 25 per cent, or less than 5 per cent of gross hospital costs).

It is of additional note that low drug prices are not synonymous with low drug spending. Many countries with limited unit prices for medicines have relatively high total pharmaceutical costs, because of factors such as high volume prescribing (as in the case of France) and/or rapid take up of new medicines (as in Spain). Furthermore, the OFT's 2007 analysis indicated that while the UK remains a successful pharmaceutical research and exporting nation relatively high domestic prices should, at least in instances where other countries use the NHS price as a reference, advantage the country. It may also be suggested that the free new product pricing environment in the UK permitted by the PPRS has fostered early medicine launches, so potentially enhancing public access to therapies.

However, against this suggestion there is substantive evidence that the NHS is typically slow to adopt innovative products and practices of any sort (Richards 2009), presumably because of the extent of institutional level financial and other bureaucratic controls on professional freedom of action. NHS pharmaceutical purchasers drive down the actual prices paid for medicines to below 'list' levels. But even so, this does not appear to have been effective in encouraging rapid innovation uptake rates. In the case of oncology, for instance, gross UK per capita spending on cancer medicines appears to be only about two thirds of the western European average. This contrasts with the fact that total per capita cancer research spending (public plus private plus charitable) in the

UK is when expressed as a proportion of Gross Domestic Product (GDP) probably the highest in the world (Kanavos et al 2009).

What is the economic case for abandoning the PPRS and relying on a product by product VBP regulatory approach?

From an academic/OFT standpoint the case against the PPRS is in essence that it, like profit control systems in other similar sectors, may allow companies with new products that are only of marginal extra value to price them up in order to reach target returns. A product by product pricing approach should prevent this. From an industry viewpoint, the removal of national and/or regional controls other than those based on VBP principles should allow companies more freedom to concentrate production and other activities in the most cost effective settings. That is, they could cut investment and activity in higher cost areas such as the UK/EU whenever spending elsewhere would enhance profitability.

The scrapping of the old PPRS and the introduction of VBP may therefore be expected to promote increased global economic efficiency. However, factors such as the movement of pharmaceutical goods within Europe, the high level of generic prescribing in Britain, the work and impact of NICE and the pressures on, for example, NHS hospital pharmacies to buy as cost effectively as possible, complicate the actual picture. Given the real-world situation of the UK market today, removing the remaining elements of the PPRS, as they emerged in January 2009, would almost certainly have little effect on the level of NHS pharmaceutical outlays. But it could reduce overall UK pharmaceutical sector activity, income and expenditure and might have an impact on the UK's advantage as a global pharmaceutical/biomedical R&D hub.

#### Box 5.1

##### Key Observation 1: Considering the PPRS in the context of UK pharmaceutical policy

The current agreement (PPRS together with elements of VBP) balances UK health and industrial policy in the pharmaceutical sector; abandoning that agreement could have an adverse impact on pharmaceutical and biomedical R&D investment and is in itself unlikely to have a sizable effect on the level of NHS spending on medicines. Building on it, by enhancing the VBP component while also developing and strengthening other strategic elements could have a welfare-enhancing effect.

#### 5.2.2. Pricing options for medicines

The previous section has highlighted the value added of the PPRS. Should for some reason the current PPRS cease to exist, serious consideration should be given to the scheme that replaces it. It will be essential to frame this as a collaborative process for instance, a voluntary agreement between government and industry. If it is essential to move away from the PPRS terminology, it should be emphasised that the complexity of the vision around VBP requires genuine and ongoing collaboration with stakeholders to enable implementation.

If this scenario materialises, it may be the case that a Pricing Committee be established within the DH to negotiate and finalise pricing arrangements with manufacturers. Prices for newly introduced medicines will need to be confirmed, whether they undergo an HTA appraisal or not. Prices will be applicable across the UK. Products requesting a price premium over existing therapies may need to be subjected to an HTA, whereas for all other products an HTA is unlikely to be required and submitted prices will be confirmed. Pricing criteria and formal procedures (e.g. evidence submitted) will need to be established for this purpose.

Whereas for products not in need of an HTA the process may be straightforward, this is not the case for products requesting a price premium. An appraisal of the innovative potential will need to take place for this purpose. In order to do so, manufacturers will submit a proposed price plus cost effectiveness evidence to the designated institution (either NICE, SMC or AWMSG), ideally at early stages as recommended by the Cooksey review.

## 5. Implementing VBP in the UK

Although HTA as it is currently performed by NICE and SMC, may need to change significantly to comply with the definition of VBP, typically, HTAs would make one of three recommendations:

- if the treatment is below an acceptable cost effectiveness threshold, whether this is going to be a fixed or a flexible threshold, also taking into account other criteria beyond the cost/QALY; in that case, the treatment is to be recommended to the NHS;
- if the treatment is above an acceptable cost effectiveness threshold (whether fixed or flexible): HTA institution assesses maximum acceptable price for each indication to aid DH in subsequent price negotiations;
- if there is insufficient data for analysis: potential for risk sharing or ‘only in research’ designation. The HTA institution would give DH estimated volumes per indication and clinical data needed to help future decision making.

The Secretary of State for Health, with the Pricing Committee, will negotiate prices with manufacturers based on the analyses performed by NICE, SMC and AWMSG. These negotiations would be compliant with any EC legislation (e.g. Transparency Directive). The Pricing Committee would consider pricing of new products whether they have been subjected to an HTA appraisal or not (at parity, below parity, at premium, with evidence development and ex-post assessment, etc). Pricing procedures could consider:

- price levels, including fixed price (most common) or fixed budget;
- price structure, including price-volume agreements and rebate agreements and brand premiums;
- Patient Access Schemes (PAS) or/and Risk-Sharing (RS) agreements if and when the circumstances (e.g. quality of the available data) require.

Finally, in this environment, consideration ought to be given to the question of what happens to products that are currently in the PPRS, as VBP is assumed to apply only to new products. Arrangements will need to be in place for this group of medicines as well.

### Box 5.2

#### Key Observation 2: Pricing options for medicines

Should the PPRS cease to exist in its current form, its replacement should be a constructive agreement between government and industry that builds positively on the spirit in UK pharmaceutical policy over the past half century. A pricing committee would need to be established in the Department of Health to negotiate and finalise pricing arrangements with manufacturers. If a manufacturer requests a premium over existing treatments then the product will undergo a ‘health technology assessment’ (HTA), though this process will have to be reviewed to ensure the different components of ‘value’ (economic plus patient, carer and society) are acknowledged and appropriately rewarded. While these arrangements will apply to new products, arrangements will also need to be made for products that are already in the system and have undergone HTA reviews or other negotiation(s).

### 5.2.3. The limitations of the current VBP for medicines

Value-based pricing, as was defined in the previous sections, clearly has a potential to help inform the fairness or otherwise of the amounts NHS bodies pay for patented medicines. Its introduction could at a political level, not unlike that of the original VPRS in the 1950s, for a time at least allay concerns about whether or not the use of tax payers’ money to pay for NHS supplied ‘free’ medicines is legitimate.

Yet at a fundamental level the techniques embodied in VBP, as it is currently applied in the HTAs in the UK and elsewhere, do not address the issue of how much money it is right for the health service to channel into the private (or public) sectors for pharmaceutical research aimed at generating inherently uncertain future welfare or other benefits.

Even ignoring such concerns, there also remain a range of lower level methodological and allied limitations relating to the practical application of VBP for medicines. They include:

1. The essentially arbitrary nature of the incremental gain affordability thresholds set. Associated with this there is the fact that in other areas (like maintaining public order and providing care for people considered a danger to the public) such thresholds may be very higher or lower than those used by NICE in relation to the QALY, or not be taken into account of at all in public policy making and service and product purchasing processes.
2. As recently highlighted by Professor Sir Ian Kennedy in a report commissioned by NICE (Kennedy, 2009), there may be a lack of evaluation of the additional health related benefits of items such as new medicines for conditions like, say, dementia. In this last instance, for example, the model employed by the National Institute for Health and Clinical Excellence appears not to take into account the gains that may be enjoyed by informal carers and family members as a result of better symptom or disease management.
3. Beyond this, NICE is also not presently charged with evaluating the long term external benefits that will in time be generating as a result of, for instance, an improved understanding of cancer genomics and/or the provision of high quality employment in the pharmaceutical sector. Although it may in this context be argued that other agencies, such as the newly established Office for Life Sciences (OLS), may be better placed to take on an industry ‘sponsorship’ role, the arguable reality is that if the NHS is as the single purchaser (monopsony) of prescription medicines only willing to pay medicine prices based on immediate individual patient level gains, that will be the de facto driver of the overall national system.
4. Problems associated with the use of aggregated data in circumstances where there is substantial variance within populations, and a lack of appropriate provision for identifying and meeting humanely the needs of people who can reasonably be regarded as ‘exceptional cases’. The potentially severe harm to public confidence associated with NHS patients having to, or seeming to have to, ‘plead for their lives’ with the support of doctors who wish them to have access to non-approved treatments is one cost linked to this area;
5. Lags between best practice developments and the publication of supportive evidence. In the oncology context such problems may become apparent because although the effectiveness of anti-cancer drugs is normally first demonstrable in late stage disease treatment, their optimally effective use may be at an earlier stage. If because of an unduly crude application of VBP principles clinically informed logical extrapolations cannot be used in a timely manner to justify new treatment applications, health outcomes will on occasions be impaired.
6. The inherent challenges of measuring and comparing utilities of different types, both within the health sphere and between that and other areas, including industrial development. The possibly special nature of end of life care illustrates this area of concern.

## 5. Implementing VBP in the UK

### Box 5.3

#### Key Observation 3: The limitations of the current VBP

UK policy makers should be aware that in its current form, VBP, as it is currently applied, contains limitations that will need to be addressed, such as a) the arbitrary basis for affordability b) relative lack of evaluation of other health benefits, e.g. to carers or/and to society c) how to consider long term benefits d) meeting humanely the needs of people who can reasonably be regarded as 'exceptional cases' and e) catering for treatment that has shown to benefit end stage disease but could also be used at an earlier stage. Introducing VBP for medicines as defined earlier in this paper, will also require addressing the limitations of VBP as it is applied today.

#### 5.2.4. Variable affordability thresholds (fixed v flexible threshold)

It may be that some areas of health related innovation are likely to be more valuable in the long term than others because, for instance, of their potential for application outside the health sphere. Alternatively, as suggested above, achieving some health related social goals may be widely regarded as inherently more desirable than attaining others, contrary to the assumptions currently underpinning incremental cost effectiveness analysis. Thus being able to cure life threatening or disabling diseases in young people may be regarded fundamentally more important than reducing mortality and morbidity amongst those who have enjoyed a 'fair innings'. Similarly, democracies may wish to pay special attention to the needs of people affected by rare disease on social inclusion grounds.

Were this so, it means there is a case for applying in a transparent manner varying affordability thresholds in differing health care fields, albeit that a more viable way forward in practice might simply be to raise the average incremental affordability threshold used. If as can reasonably be expected the genericisation of the high volume medicine market continues, one check to be employed in this context is whether or not overall medicines spending is remaining constant as a proportion of all health spending.

Currently, the UK operates in a more or less fixed threshold ranging between £20,000 and £30,000 per QALY. Aside from the economic/QALY – type judgments (or whatever unit of effectiveness individual countries are using other than the QALY), other parameters that should be considered are:

- a. unmet medical need
- b. clinical judgment
- c. prevalence of the condition
- d. patient preferences
- e. public health impact
- f. societal impact

Aspects that should be included in HTA analysis comprise:

- a. clinical
- b. economic
- c. budgetary
- d. ethical
- e. Patient-Reported Outcomes (PROs)
- f. public health impact (does the technology address a public health priority)

Explicit thresholds are often desirable but it should be borne in mind that such thresholds can be limiting, particularly in cases where patient needs are weighed against market size, for instance in oncology targeted treatments or in orphan drugs; these may require different treatment and most certainly higher threshold levels. It should be borne in mind, however, that it is very difficult to determine explicit thresholds (on a cost/QALY, or other, basis) under a flexible threshold perspective and a methodology would need to be established for that purpose.

### Box 5.4

#### Key Observation 4: Variable affordability thresholds

NICE uses a fixed threshold with occasional deviations from it. Greater representation of factors such as unmet medical need, severity of disease, clinical judgement, prevalence of the condition, patient preference, public health impact and societal impact would imply that the QALY threshold of £20-30,000 may need to be raised for areas of high unmet clinical need (eg. Cancer) and reduced for low areas of unmet clinical need (eg. treatment of dislipidemia).

#### 5.2.5. Ex-ante versus ex-post assessment

Ex-ante evaluation provides manufacturers with the incentive to invest in gathering the evidence that the health service requires to approve and encourage innovation in areas/therapies where a substantial clinical benefit can be demonstrated. One drawback, however, of the use of ex-ante as opposed to ex-post evidence is that there will be uncertainty surrounding the cost-effectiveness of the drug outside the RCT setting at the time of launch. Although further ex-post reviews can also be suggested, these may be difficult to ensure as once a pharmaceutical product is approved, the incentive to carry out further trials is diminished and may even be deemed unethical. There is also concern that if ex-post evaluation slips, the evidence-based approach to NHS care could be compromised (Claxton, 2007). Nonetheless, a balance between the value of the economic information surrounding the drug and the value of availability of the drug to patients needs to be achieved (as is often emphasised in HTA).

On the other hand, it should be made clear to manufacturers that ex-post evidence is as crucial as ex-ante evidence in proving the value of new treatments. In order to do this, there needs to be acceptance of data obtained in naturalistic settings and methodologies on how best to extract value from such data need to be strengthened. Ownership of such data is also important, as the cost associated with gathering such evidence is substantial and creating this evidence should provide the scope for collaboration between the payer community and manufacturers. Indeed, it can be the case that new products enter the UK market place via an expedited/rapid HTA review and for those that further evidence needs to be developed, to be re-assessed when that evidence has been gathered. In the meantime, the pricing option for a product that undergoes rapid review can be to award the price the manufacturer applies for, or to arrive at a (risk-sharing) type of deal between the Pricing Committee at DH and the manufacturer.

While ex-post appraisals are a key component to VBP, further reflection and consultation will be required to determine criteria and processes for ex-post appraisals to take place. There may be no sense in requiring ex-post HTA for all products (even if only applied after a specified starting date). It is likely to be most beneficial where there is either a complex value proposition for a chronic condition (e.g. disease modifying medications for Alzheimer's disease) or a level of uncertainty related to the evidence available at time of Market Authorisation. Consideration should be given to how best to deal with products that might never be able to demonstrate cost-effectiveness e.g. orphan medicines, and to whether products with a very small budget impact should be excluded from ex-post HTA. As discussed in the next section, rewarding risk-taking behaviour by the innovator is critical and could take place by allowing a price premium at launch, rather than ex-post.

## 5. Implementing VBP in the UK

### Box 5.5

#### Key Observation 5: Ex-ante vs. ex-post assessment

The 2007 OFT report proposed two pricing options. (a) Free pricing at launch followed by reviews afterwards to assess the effectiveness of the treatment and an adjustment in pricing over time (known as ex-post assessment); and (b) set pricing at launch with data that is already available (known as ex-ante assessment). Evidence prior to the launch of a new product is not always available and there may be significant data limitations. Ex-post assessments may prove instrumental in many cases in determining product value for the NHS, patients and society, but criteria, methods and processes need to be set up as to which products should undergo these, together with arrangements allowing access to patients in the meantime. An ex-ante price premium in the case of ex post assessments would provide a signal to the innovator of the willingness by the payer to reward high risk-taking.

### 5.2.6. Varying medicine prices – should they be increased post-launch, as and when a medicine’s efficacy becomes better demonstrated?

In response to the delayed evidence problem identified in the previous sub-section, some authorities have suggested that low initial reimbursable medicine prices could be raised if and when new evidence of treatment effectiveness comes available during the patent life. This is arguably especially relevant to areas like cancer care and/or long term neurological disease treatment. From a VBP perspective such a strategy would be entirely justified, and is theoretically attractive.

But in practice raising significantly the price of an established product is much more difficult than lowering it, especially in today’s pan-European and wider global markets. The danger for innovators is that if they were to introduce an expensive to develop new medicine at a relatively low initial price, this would become its international reference cost. From the perspective of assuring public interests in the ongoing financing of high risk research a more attractive option might be to permit a relatively high ‘free market’ reimbursable launch price, and to have a PPRS-like provision for repaying excess profitability as and when the full potential of the product is revealed.

### Box 5.6

#### Key Observation 6: Varying medicine prices – post-launch or ex-post price?

Varying medicines prices raises the issue of the resistance to raising the price paid by the NHS and other purchasers if a product is shown to be more effective than originally thought. So a high initial price needs to be considered to ensure (a) the public interest is protected by ensuring that high-risk research is incentivised (b) industry is reassured that it is worth taking risks with new research. A provision for reimbursement by industry to repay excess profit can be built in to ensure fairness once the full potential of the product is known.

### 5.2.7. VBP should PPRS cease to exist

The PPRS is currently responsible for health and industrial policy in the pharmaceutical sector in the UK. It monitors prices and profits/rate of return of pharmaceutical manufacturers, whilst at the same time it administers the incentives for innovation in the pharmaceutical sector that are part of the PPRS agreement.

If the PPRS ceases to exist and is replaced by a form of voluntary agreement, as discussed in section 5.2.2., VBP will need to inform pricing decisions, whilst the incentives for innovation under the PPRS may need to be transferred elsewhere<sup>8</sup>. Pricing decisions will be taken at national level. Assuming this is the case, a uniform price will apply in the UK and the responsibility for this will be with the DH and the scheme that will succeed the PPRS. For instance, arrangements might include the establishment of a Pricing Committee. It is in the national interest to avoid price disparities at national level, which will fuel intense debate about value and ‘willingness to pay’ in the constituent parts of the UK. For a uniform price to apply in the UK, there must be an acceptance of the fundamentals of VBP appraisals/evaluations, performed across institutions such as NICE, SMC and AWMSG, as well as a coordination of their activities.

### Box 5.7

#### Key Observation 7: VBP should PPRS cease to exist

If the PPRS in its current form is abandoned, then VBP should assume a key but not necessarily dominant role in informing pricing through HTAs. Final pricing decisions will rest with the DH; a Pricing Committee may be established within the DH to confirm prices with manufacturers on new products based on evidence submitted; the Committee will be responsible for pricing policy and pricing decisions at national (UK) level. In this new environment, thought will need to be given to how HTA activities will be coordinated across all UK-based HTA agencies.

### 5.2.8. Application of VBP across a range of products

VBP would in principle apply to all new products entering the UK marketplace but not generics. For the latter, different arrangements already exist in the context of the current pharmaceutical policy, resulting in low prices over time for the NHS.<sup>9</sup>

With regards to new, branded products entering the UK market, different arrangements may apply depending on their nature and the price proposed. Typically, manufacturers – upon entering the market - will propose a price. The following possibilities then exist:

- if the requested price of the newly introduced product is below that of an existing therapeutic alternative, then that price may be adopted as is;
- if the requested price is at the level of existing therapeutic alternatives, the tendency would be to accept as is, based on the clinical evidence submitted; and
- if the requested price is above those of all other therapeutic alternatives, or if the product belongs to a new therapeutic class or is a new and improved form, the case will automatically be referred to an HTA appraisal.

<sup>8</sup>. See discussion in section 6.

<sup>9</sup>. Generics are outside the scope of this paper.

## 5. Implementing VBP in the UK

As a result, in an environment where the PPRS ceases to exist, VBP will need to conduct value assessments on all new products entering the UK market that request a price premium over existing alternatives. This will automatically increase the workload of the UK-based HTA agencies quite significantly, in which case, there will need to be some prioritisation as well as cooperation among HTA agencies in order to ensure timely appraisals.

### Box 5.8

#### Key Observation 8: Who will be subjected to VBP assessments?

If the PPRS in its current form is abandoned all new patented or other single source products that enter the UK market place may need to undergo an HTA if they request a price premium over existing alternatives. If price parity is requested, then the inclination from the Pricing Committee should be to accept the proposed price. As the workload for appraisals is likely to increase, there may be a requirement for an increase in the available resources for HTA.

### 5.3. The UK HTA agencies

#### 5.3.1. NICE, SMC and AWMSG in a devolved healthcare setting

As the scope for VBP increases for all new branded products requesting a price premium, the implications for the total volume of appraisals are, in principle, quite significant. All UK-based HTA agencies (NICE, SMC, AWMSG) will have an increased workload. In order to avoid significant delays in the production of appraisals to feed pricing decisions, it is likely that the three agencies may need to work closer than they do now.

Current practice suggests that two different models exist as far as UK appraisals are concerned. The NICE model relies on a comprehensive review of the evidence, which also includes the production of independent evidence to inform the appraisal, and the SMC model, which conducts the appraisal in-house based on evidence submitted by the manufacturer. Both approaches clearly have merits and it is beyond the scope of this report to judge either of them and it may be the case that both models will continue to co-exist in some form. Based on the above, two scenarios are envisaged:

- The first scenario suggests that the three bodies carry on their “business model as usual”, but in a collaborative way. In this case and in order to meet the additional requirements for appraisals, they will need to be allocated more resources. This may be unacceptable on the grounds of scarcity of resources and likely duplication. The timeliness of producing appraisals is also going to be an issue.
- The second scenario suggests that they all share the burden of appraisals, which further implies that some of the activities currently pursued in great detail may need to be toned down significantly; this may be quite unpopular with NICE, which has already established an international reputation for the way it conducts appraisals. A potential solution might be to reserve NICE’s appraisal process to a limited number of cases. The budget impact in this case will be less dramatic than in the previous scenario and there is the additional benefit of faster appraisals.

Finally, there is need for greater clarity in an environment where decisions are often devolved. For instance, if prices are to be applicable across the UK, there needs to be a clearer role for the SMC after a medicine has been considered by the DH Pricing Committee, given that UK Government and Scottish Government health drivers and priorities are not entirely the same. The “value” of a medicine to the Scottish Government may be different to that accepted by the DH. The question arises as to whether SMC has any continuing ability to act as a separate gatekeeper for NHS Scotland. The potential exists for the NHS in Scotland to consider ways of getting

around a value-based price for a product which is regarded as having a higher value in the Scottish context than that ascribed to it by the UK wide HTA/pricing process. While differential pricing is highly unlikely, national Patient Access Scheme arrangements might then be encouraged.

### Box 5.9

#### Key Observation 9: Role of NICE, SMC and AWMSG in a devolved setting

Currently, HTA assessments are undertaken at a country level (NICE in England, SMC in Scotland, AWMSG in Wales) as health is a devolved power, rather than national level. In order for HTAs to inform pricing decisions at national (UK wide) level if the PPRS is abandoned, the three agencies (currently having different protocols) would have to share the burden due to the increased number of product appraisals and coordinate their activities.

#### 5.3.2. The UK HTA agencies and their role in value-based pricing

As NICE is considered a global leader in HTA, giving it, SMC and AWMSG responsibility for producing cost effectiveness analyses appears ideal. However, there still remain a few issues to consider with regards to feasibility. First, if ex-post reviews are also to be included, the initial increase of all currently available branded medicines would have short-term impact on their workload, regardless of gradual implementation. This would obviously impact their employment budget, albeit only acutely and perhaps filled with contractual versus permanent staff. Considering that over their first decade only 165 appraisals were produced, evaluation of workload appears significant.

Second, continued ex-ante reviews of all NME would also require additional staffing and quarters, again impacting the institutions’ respective budgets. These ex-post and ex-ante budgetary requirements, along with all other aspects of VBP implementation including developing of a new Pricing Commission in the DH and increasing bureaucratic complexity of NICE, SMC, AWMSG, the NHS and DH, must be considered and weighed against potential cost saving of implementing VBP.

Third, there is a more global issue with regards to evaluating benefit in conditions where insufficient study populations exist (i.e. paediatric diseases, cancer, orphan diseases), where quality of life is the goal over quantity of life or where medicinal impact may have greater measurable power to carers than to patients (i.e. mental illnesses and certain geriatric diseases where patients may be unable to give objective directions of benefit). Where insufficient data exists, insufficient statistical power or quality versus quantity of life, HTA agencies may be unable to give guidance with confidence, however, lack of confidence does not necessarily mean lack of clinical or cost effectiveness (Kennedy 2009).

Fourth, where risk sharing is likely to be considered when insufficient data exists to adequately perform HTA, is the definition of the role of NICE, SMC and AWMSG. The three agencies must be able to act independently and transparently in order to return a verdict of insufficient data. Further, the institution responsible for determining whether a medicine is eligible for risk sharing must be defined – will this be the HTA agency performing the appraisal, the DH, or a combination of these?

Fifth, if the workload between NICE, SMC and AWMSG is to be divided, however, methodological differences between these organisations, some theoretical and some practical, need to be taken into account. These variations would need to be resolved in order for the process to be as fair and as continuous as possible to patients and to manufacturers. In addition, the method for allocating medicines to each institution must be defined, either as a random process or based on each institution’s current methodological strengths.

## 5. Implementing VBP in the UK

Sixth, there remains a concern with timeliness of analysis and publication. Although the publication of guidance has become speedier over time, a concern remains with increased workload and the ability to remain independent. Furthermore, issuing clinical guidelines remains slow and intermittent, often inhibiting optimal new medicines uptake. A move to an online guideline database, including sections for patients, would aid in new medicine uptake, in ease of implementation and in reduction of practice variations.

Lastly, a concern remains with data provided for evaluation. Scientific literature is currently under scrutiny due to its abnormal over-representation of positive results, along with decreased likelihood of publication when negative or no difference is found. This represents a publication bias in data presentation with significant consequences. Criticisms continue on NICE and HTA existence, with average cost per appraisal reaching £325,000, while additional costs allocated to the manufacturer in data collection estimated at £4.5 million. Although NICE is now a decade old and manufacturers are aware of additional data required for analysis, particularly for innovative medicines, and have already made adjustments, this criticism continues. If ex-post analysis becomes a gold standard for real-life data collection, manufacturers and the state can co-finance these initiatives, thus providing global leadership in post-marketing data generation and use.

### Box 5.10

#### Key Observation 10: UK HTA agencies and their role in VBP

Implementing VBP as defined in the report may require more joint work and greater coordination among HTA agencies; consideration should be given to (a) the possibility that workloads –and, as a result, funding– may need to increase; (b) the differences between the three agencies and the way they work; (c) the timeliness of appraisals and the implications for access; (d) the evaluation of benefit in conditions where insufficient study populations exist; and (e) returning a verdict on insufficient data in an independent and transparent way.

### 5.4. Useful interventions within the context of VBP

#### 5.4.1. Implement comprehensive criteria and metrics

These should be considered when assessing drug value and setting pricing/reimbursement levels should include all elements of value. When they do assess value though, pricing/reimbursement systems have frequently chosen to focus on value almost exclusively from the healthcare system (payer) point of view rather than the broader societal or patient/physician (e.g., consider cost offsets to the healthcare system such as hospital stays and/or other drug costs avoided, but not from increased worker productivity or provider efficiency). Another problem is that most evaluations of drug costs are based on list prices, rather than actual observed net costs in a treatment setting.

It is imperative that standard guidelines for assessing benefits of drugs based on a broader range of applicable metrics are established. These should include:

- humanistic, patient focused benefits such as QoL;
- longer-term direct cost offsets;
- indirect system costs that might or might not be covered by payers such as worker productivity;
- benefits to caregivers as well as patients (e.g., enhanced patient and physician convenience that translates into improved compliance and better outcomes).

Finally, new standards and tools for more accurately and consistently assessing the more challenging metrics must be developed (e.g., patient reported outcomes such as QoL).

#### 5.4.2. Champion flexibility in decision-making

Total drug benefits and costs to the health system must be assessed over time, by segment/population and in a real-life context, with prices/reimbursement levels adjusted as new data on relative value becomes available. In many countries though, value assessments are conducted at drug launch, using only data collected during pre-approval studies. As new data becomes available, prices are only allowed to fluctuate downwards, rather than allowing them to increase as more value is demonstrated. Further, the value of a drug and its price is typically set based on the initial indication, with no flexibility to evolve it or change it for different indications in which the dosing and/or value over existing therapies could be significantly different. Optimal mechanisms must be determined, in order to allow for drug price/reimbursement variations across different indications/sub-populations based on value.

Pragmatic and viable processes must be created, so that pricing levels are allowed to fluctuate both up and down over time as meaningful new data becomes available, including potential for ‘temporary’ pricing for novel drugs with limited evidence at launch. Finally, it is important to establish appropriate requirements for ongoing data collection on the part of drug manufacturers to provide support for ongoing price adjustments.

#### 5.4.3. Foster collaboration between stakeholders

The NHS, providers and manufacturers must work together, not antagonistically, to establish pilots to investigate new pragmatic ways of managing drug spend, avoiding wholesale ‘top down’ change.

Unfortunately, most pricing systems are not always collaborative in their design and operation, with payers often issuing top down directives and little sharing of data. In addition, drug regulators give little or inconsistent guidance on trial design. Finally, reform often includes multiple changes to the current system wholesale, without a clear and open debate of the alternatives and/or productive piloting before roll-out.

In order to face these challenges, an inclusive process for defining pragmatic, effective changes to drug approval and pricing approaches must be developed, ensuring these are transparent to all (e.g., manufacturers understand what data will be required and pricing decisions well in advance). Pilots to test new approaches to drug pricing must also be established before large-scale implementation. Finally, effectively sequencing and staging the roll-out of any changes (e.g., begin with a few newly launched drugs and expand as required) rather than attempting to enact wholesale change could be an important part of the process.

#### 5.4.4. Explicitly recognising value

Some argue that any benefit ‘over and above a clinically beneficial outcome’ should not be rewarded. Although few would agree with accepting a price premium for a drug simply because it is innovative, innovation (both breakthrough and incremental) can lead to greater subsequent understanding of the aetiology of a disease (i.e. there could be said to be a positive externality from discovery and use of a new drug), recognition of which is achieved to a certain extent in the French ASMR system. This may have important dynamic implications for future R&D. In addition, the broader socioeconomic picture has to be considered if there is to be accurate recognition of the benefits that a drug brings.

It would be difficult to devise a ‘meaningful’ pricing system that would be able to deal with this problem. Whilst it is difficult to anticipate the future gains from innovation and directly incorporate these into a pricing system, governments must encourage such developments to take place. Stratified pricing arrangements such as these seen in systems where the (clinical) benefit is explicitly defined and recognised (e.g. ASMR approach) would send a clear message to the pharmaceutical industry that innovative products have recognisable value within the pricing system, although, clearly, the starting point vis-à-vis which ASMR a new medicine represents may be different for different stakeholders.



## 5. Implementing VBP in the UK

### 5.4.5. Demand-side policies rather than a budget

The notion of a fixed drugs budget should be rejected, as implementation of a budget restraint whilst avoiding the pitfalls of a ring-fenced budget would be too great a burden for any system if it were to also to undergo further substantial reform (e.g. by accepting and implementing VBP). However, greater work needs to be carried out into making GPs more price-conscious. A recent study by the National Audit Office found that GPs performed no better than chance at ranking drugs in 6 therapeutic groups in order of list price (NAO, 2007).

#### Box 5.11

##### Incremental changes to the context of VBP

Improving the environment for innovation within the context of VBP implies interventions at different levels, which could foster pharmaceutical/biomedical innovation in the UK. In particular, attention could be placed on:

- (a) implementing comprehensive criteria and metrics when assessing value, including a broader societal perspective;
- (b) enabling flexibility in decision-making to take into account new evidence on value propositions as and when it becomes available;
- (c) fostering further collaboration among stakeholders, particularly in what concerns the management of drug policy and achieving value for money and/or savings to the NHS;
- (d) explicitly recognizing the fact that in many cases innovation occurs incrementally; and
- (e) continuing to give emphasis on the demand-side and educating through an enhanced incentive structure.

### 5.4.6. Vary patent terms in relation to VB prices and returns on permitted investments?

The duration of a product's exclusivity of supply period is a critical determinant of the price needed to allow financial viability in relation to the marketing of any particular pharmaceutical innovation. In his recent evaluation of the work of NICE and its implications for the future, Professor Sir Ian Kennedy excluded from his analysis a consideration of issues like patent terms relative to changing research costs and productivity on the grounds that any change in current IPP provision would require pan-national agreement. However, although this is understandable, it is unhelpful regarding the wider policy debate on pharmaceutical pricing.

If the time taken to develop new medicines is increasing and the number of successful new medicines produced per quantum of resource invested is for whatever reason falling, then one potentially sustainable way of keeping product prices down to VBP defined levels would be to allow variable patent life extensions, in part determined (regionally or, ultimately, globally) via principles like those embodied in the PPRS. Such an approach might also provide a way of addressing 'evidence lag' related concerns to be resolved more elegantly than may be possible via post marketing price increases.

The viability of such a proposal is greater at regional level, through the patent extension term (USA) or the SPC (EU), rather than re-negotiating the patent protection term through the WTO. Similarly, an extension of the patent exclusivity period at regional level could also be considered.

#### Box 5.12

##### Key Observation 11: Varying patent terms in relation to VB prices

A critical determinant of price is the duration of the intellectual property on the product. To further attract investment in areas of high unmet medical need, rare diseases, personalised medicines or other, we should consider re-defining market exclusivity periods and potentially revisiting the length of supplementary protection certificates.

### 5.5. Caveats of value-based pricing and ways of addressing them

There are some caveats to overcome prior to implementation in order for VBP to be deemed a success both on behalf of the DH and on behalf of the pharmaceutical industry. The situation of insufficient data and risk sharing for instance needs to be outlined up front, so that manufacturers invested in diseases partial to this process are aware of the process and potential outcomes. Also, NICE, along with SMC and AWMSG, need to address major criticisms with potential modifications. Pricing under VBP should be closely examined in conjunction with industry to give realistic forecasting. Likewise patient access to innovative medicines must be maintained or improved under VBP in order for the scheme to be success. A balance between static and dynamic efficiency is needed in order to continue. Lastly, methodological issues in defining value, incorporating a societal perspective and the insufficiencies of the QALY concept need to be addressed in parallel with the implementation of VBP.

#### 5.5.1. Insufficient data and risk sharing

A main criticism of VBP is the situation where insufficient data is available to perform cost effectiveness analyses and potentially enters the medicine into a risk sharing agreement. Although the OFT believes this situation is limited, we believe this situation is not uncommon, particularly in the following conditions: paediatric diseases, cancer, certain chronic diseases and orphan diseases (Box 5.13).

Therapies for these diseases often have lengthy timelines before change in outcomes can be observed. Paediatric diseases and orphan diseases often do not have a sufficient population base in order to achieve statistical power for observation of clinical differences. Cancer is an increasingly complex disease, namely due to recent developments finding grouping of tumours based on genotype rather than location resulting in small populations and lengthy study timelines. As these situations are also the precise applications for innovation, this criticism is not trivial.

The situation for risk sharing will likely increase in those areas encouraged in new molecular entity (NME) development, either due to gaps in the market, new scientific evidence applicable translational research or overt encouragement via research grants, funding or taxation policies. In order for VBP to be viable, risk sharing should be defined, with its application and degree of cost sharing outlined, and perhaps broken down into various scenarios in order for the DH and industry to understand the playing field, encourage transparency and be able to forecast its frequency in application.

## 5. Implementing VBP in the UK

### Box 5.13

#### Value-based pricing in oncology: A case study

Cancer has recently become for many European countries the primary cause of death, replacing cardiovascular disease. Concurrently, cancer incidence is increasingly reflecting an aging population and the introduction of screening for specific cancers in some countries. The forecast for cancer is increasing disease burden and the transition into a chronic disease requiring lengthier treatment periods. As a result, innovation is welcomed and encouraged in oncology by the pharmaceutical market, funding agencies and government.

New evidence on cancer genotyping has found cancer to be increasingly complex, resulting in treatments that have also increased in complexity. Conventional cytotoxic chemotherapies are only partially effective and usually poorly tolerated, thus current interest lies in targeted treatments selecting only cancerous cells. However, due to the complexity of cancer cells and individual genotypes, development and application of new treatments requires combinatorial chemistry, structural biology, molecular biology and diagnostics, while attack targets include growth factor receptors, immune system modulation, cellular matrix, and cell proliferation, migration and survival.

In oncology R&D, due to the increasingly complexity of cancer itself, the cost of failure is high, with only 5% of NMEs actually entering the market (Clinton, 2007), and the cost of each NME estimated at €964 million, 20% higher than non-oncology entities. Thus innovation in oncology is paired with the highest costs and the highest failure rates, not a desirable situation for innovation.

Further issues unique to oncology R&D potentially impair innovation. First, oncology trials require ill versus healthy trial participants, making assessment of safety and efficacy more difficult due to many confounding factors. Drugs often fail in Phase III trials as patients are usually treated with multiple compounds, with the new compound requiring adapting new care standards.

Second, the transition of cancer treatment by tumour location to tumour genotype requires identification of tumour genotypes, leading to additional steps of identification of patients with specific tumour genotypes, further leading to difficulties in sufficient patients for statistical power and management of patients and data from multiple centres. Despite this, there are a number of oncology NMEs in development (Figure 5.1).

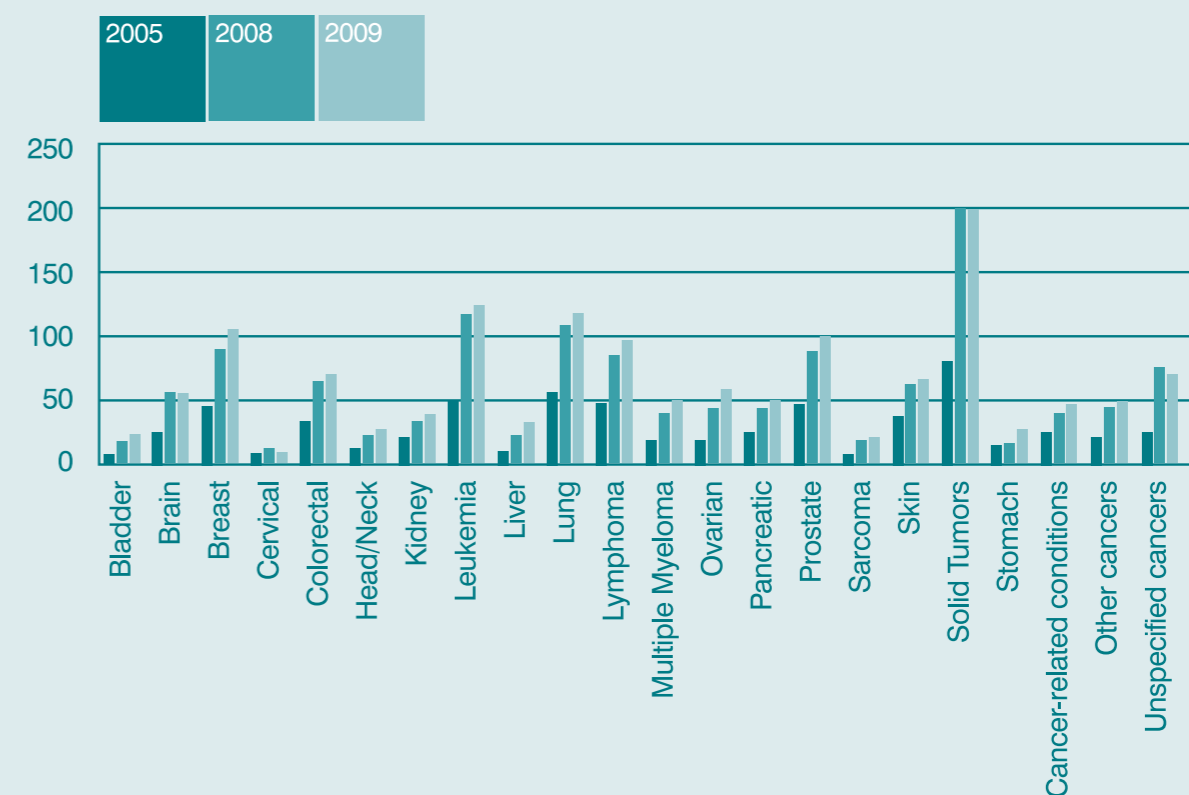
Third, the increasing complexity of cancer itself requires a number of players working together in order to find solutions. Various types of expertise are required to solve the significant and evolving puzzle, in addition to requiring multiple funding sources for R&D, including academia, industry, non-profit agencies and public-private partnerships. This requires a platform for cooperation unlike ever previously needed for other diseases.

Fourth, pricing and reimbursement of these NMEs are far more uncertain than other NMEs. Due to the innovative nature of targeted treatments, increased R&D costs and high failure rates, industry would like to command higher prices. Many of the treatments are for Stage III and IV cancers, many with few options and poor survival (often less than 30% 1-year survival with current best treatment). However, this places treatments at times above the acceptable cost-effective threshold set out by NICE. Further confounding the issue is minimal or insufficient data due to the small numbers of patients available to enter trials.

This is where the situation of risk sharing and rebates (e.g. cetuximab for metastatic colorectal cancer), or under the current PPRS scheme, patient access schemes or refusal of reimbursement occurs. For example in metastatic colorectal cancer, cetuximab is reimbursed now, after initial reimbursement refusal, only when the manufacturer rebates 16% per patient, while bevacizumab, despite longer progression-free survival and reimbursement elsewhere in Europe, is refused reimbursement in the UK.

Figure 5.1

Number of oncology NME currently in development



Reportedly, the NHS has been said to be struggling with current implementation of Patient Access Schemes (PAS). Yet, the infrastructure, including the relevant information systems, is available to monitor these effectively. The implementation of VBP may improve access to new medicines, as explicit NICE guidance would reflect positively upon it. It would further encourage more cost conscious prescribing behaviours by clinicians, particularly for off-patent medicines. When guidance is further bolstered by timely clinical guidelines, the situation of access to patients may be ideal.

On the other hand, the process of VBP may be a barrier to patient access. As discussed previously, if analysis and guidance is not produced in a timely fashion, access to new medicines may be slower than in other leading countries. Considering the leading position of the UK in research, production and introduction of new medicines, such a development can prove detrimental to this leading position. Currently, medicines with insufficient data are often marked 'for research purposes only', which limits medicines only to those clinicians with an interest in research and expertise to apply it. This situation is more likely in academic teaching hospitals, usually located in urban centres and creates regional disparities. If the process for medicines with insufficient data for analysis are not transparent and considered fair by industry, some medicines may not even enter the UK market.

## 5. Implementing VBP in the UK

### Box 5.14

#### Key Observation 12: Risk sharing and improving access to patients

Patient access schemes (PAS) or risk-sharing agreements mean that payers who are looking for increased certainty when funding new medicines are able to obtain new technologies at acceptable prices without de-incentivising innovators. Irrespective of the type of agreement in place (whether coverage with evidence development, conditional coverage, outcome guarantee scheme, or price-volume agreement – see Table 5.2 and Appendix), PAS arrangements need to ensure that risk-taking is fairly distributed among the stakeholders involved. The administrative burden associated with running such schemes should also be considered and evaluated.

Table 5.2

Risk sharing mechanisms and “risks” addressed

	Right patients	Uncertain clinical value	Low cost effectiveness	Budget overspend
Coverage with ED	YES	YES	YES	NO
Conditional coverage	YES	YES	YES	YES
Outcome guarantee	YES	YES	YES	NO
Price-volume deal	NO	NO	NO	YES

Source: Kanavos and Checchi, 2010.

### 5.5.2. Prices of medicines under value-based pricing

There are a number of relevant variables in estimating potential prices with VBP. First, are the prices of currently reimbursed on-patent medicines evaluated via ex-post analysis? The OFT estimated transition to VBP on branded statins alone could save £500 million based on 2005 prescribing volumes. This estimation is based on the difference between the current list price and the 18-month average of generic price plus 50%. Although this simple analysis appears easy for ex-post analysis, a thorough analysis of more classes of high volume drugs should be examined to determine savings or additional costs. In addition, affects on more recent innovative medicines, such as oncology treatments, should also be evaluated. It is unsafe to assume that ex-post analysis of all current on-patent medicines would result in cost savings due to reduced pricing. The definitions under ex post analysis, and criteria for price increases or decreases need to be put forth explicitly.

Second, still regarding ex-post analysis for currently reimbursed on-patent medicines, is the method of determining prices. If many on-patent medicines, particularly those beyond the mid-point of their reimbursable patent period, are deemed less cost effective than previous with the DH pushing for price reductions, the issue of how are incentives for innovation to be maintained remains. And, if a medicine under the same conditions is still deemed more cost effective than any new entrants, does this warrant a higher price? These situations need to be set out explicitly in order to gain confidence from manufacturers in the revised system, and in order to

reasonably consider any savings.

Third, the method of negotiation (or ‘formula for innovation’) in ex-ante analysis is more complex to develop price and cost forecasting. Any examples may be drawn from current medicines entering NICE evaluations. However, this may not be realistically applicable to non-NICE evaluated medicines as they are related to a different segment of the pharmaceuticals market.

Fourth, the frequency and degree of risk sharing are also difficult to estimate in ex-ante price and cost forecasting. Definitions of risk sharing need to developed in order to give an idea of division of costs, and forecasting of potential classes of medicines more likely to experience this type of pricing. In certain diseases this situation may be more frequent than others, it is important that from a price perspective they are not penalised and thus creating a barrier to innovation.

### 5.5.3. Static vs. dynamic efficiency

The continuing debate over the pricing of pharmaceuticals has emphasised the relationship of pricing to value. In moving towards VBP, two aspects of efficiency must be considered; static efficiency, which relates to the pricing of a product about to enter or already on the market and dynamic efficiency which relates to product innovation as applied to future market conditions. Given the tensions in securing static and dynamic efficiency simultaneously there may be an optimal trade-off between the pursuit of both goals.

The proposed system would retain patent protection and combine this with a widened role for cost-effectiveness in pricing to pursue VBP. Emphasis therefore moves towards static efficiency with the emphasis on value for money at launch and potentially away from dynamic efficiency.

A number of problems exist in using cost-effectiveness which are pertinent to both existing use and the proposed use to establish VBP. A major issue relates to the use of clinical trial results to establish effectiveness. The objectives of such trials are normally to establish safety, tolerability and efficacy within a tightly controlled population. Such trials are normally short-term and therefore do not establish the long-term health effects required for a comprehensive cost-effectiveness analysis. The results from such trials are currently aimed at a different set of regulatory bodies than those concerned with pricing and reimbursement. Modelling, based on increasingly accepted methods, must therefore be undertaken not only for this reason but also as health economic data on endpoints and resource use are not routinely incorporated within clinical trial studies. For example, if QALYs are to reflect the outcome over which surplus is to be evaluated, as currently is the preferred norm, then note that most products will have to transform clinical trial outcome measures into QALYs. Given that pricing and reimbursement is required on launch an ex-ante fast track appraisal method<sup>10</sup> will place heavy demands on the evaluation data. This is not impossible to achieve, but it open to uncertainty; hence the combination of ex-ante and ex-post evaluations.

Currently NICE uses Single Technology Assessments (STAs) as a means of assessing comparator products within a limited time period. If used as the basis for VBP as envisaged by the OFT the data would have to be available quickly. This would, in principle, require head-to-head studies or indirect comparisons through some form of meta-analysis of new product with existing comparator therapy. It is unlikely that this information would be readily available across the board or that clinical trials, which are increasingly designed with a global perspective, would be tapered to fulfill regulatory criteria in one market for pricing purposes. There may in any case be different standard comparator therapies in different geographical markets. Data limitations will therefore be inevitable, as within the current STA assessments, with even greater pressure given the objective of realising a market price to ensure access to the product under evaluation. NICE currently lives within these data constraints so it may not be impossible that VBP cannot tolerate such constraints.

<sup>10</sup> Also as envisaged by the OFT, 2007.

## 5. Implementing VBP in the UK

NICE allows a considerable threshold of between £20,000 and £30,000 per QALY for acceptable treatment up-take, with QALY being the preferred measure of health benefit. If this form of analysis is to be used for VBP a stricter threshold value, is likely to become necessary as based on the changing opportunity cost of new treatments (Claxton, 2007). This would not only be the case if sub-group analysis and non-linear pricing were permissible. While this could lead to a more flexible regulatory pricing mechanism, in the extreme giving perfect pricing discrimination with all surplus being acquired by the manufacturer, this is extremely unlikely given the data required to substantiate such claims under the proposed VBP system. Even substantiating claim across a small number of sub-groups would be highly data intensive. Moreover if VBP is attached to a risk-sharing analysis in given circumstances where there is a lack of data available to perform an ex-ante analysis (e.g. with chronic disease treatments), sub-group analysis will be even more unlikely as the risk transfer to manufacturers increases with an increasing number of sub-groups. Note also that such risk sharing schemes erode patent protection in any case as the length of time required to establish regulatory worth is increased.

Therefore, data availability is a major constraint. Ex-post risk-sharing is only envisaged as a means of supporting situations where there is not enough available data for an ex-ante consideration. The lag time for the implementation of ex-post risk-sharing is of obvious interest. Too short a lag will not overcome data constraints and will not provide much incentive to participate; too long could lead to distortion of the perceived gains in static efficiency with firms gaining undue producers' surplus. Non-linear pricing within a VBP environment relies on greater availability of data and a greater willingness of companies to accept risky pricing strategies. Long lead times mitigate against a firm ex-ante consideration of non-linear pricing as a strategy unless pursuing from the beginning of their investment a very sophisticated data collection and pricing strategy. As investment progresses the firm would have to pursue evidence on sub-groups and a range of indications assuming it had the foresight to see the aggregate rewards early in the investment cycle. Alternatively if a firm became aware of potential benefits of market segmentation it would have to start collecting data at a late stage of development. While such data constraints are not insurmountable they are substantial and have to be faced as an additional investment to secure value for money pricing. It would seem of doubtful regulatory efficiency to allow firms to pursue extensive ex-post evaluations or risk-sharing agreements on the basis of non-linear pricing proposals. Most of the discussion above relates to issues of static efficiency. The impact of VBP has been less discussed with respect to dynamic efficiency. The envisaged regulatory environment is one where companies would pursue investment over a long time frame given that there is a chance of reward based on a product price set in accordance with achieved health benefit. The envisaged incentive being that firms will invest in areas where the achievable health benefit is greatest. Areas of high disease prevalence combined with unmet need are the obvious highest returns. But if these are also areas characterised by a long lag between research and product development as well as high risks for individual firms and either reason may mitigate against R&D; firms may place smaller value on R&D projects than society in certain areas leading to general underinvestment.

Even if VBP leads to a firm adopting concentration of investment in those areas where there is perceived to be greatest health gain, this may result over time in a narrowing of the general R&D base with subsequent loss in the external economies which tend to characterise larger R&D establishments. A narrow-based focus may tend to cause risk-avoidance within firms, without the broad base to spread risk, and to their valuation of research project less, in the absence of external economies, than society. Large R&D programmes in the pharmaceutical sector may have inherent advantages through economies of scale and scope that are difficult to identify but are nonetheless present (Sutton, 1998). The size of a firm may itself encourage innovation and wide range of potential products. In this sense VBP seems consistent with a narrowing of firms' technological capacity as they become more specialised in those areas with the greatest potential health gain for their investment portfolio. This seems to undermine one aspect of a productive R&D capability; the ability to maintain a broad technological base as this allows a form of insurance against inevitable research dead-ends. Within the context of VBP this occurs not only within companies but may occur across companies as they will have an incentive to compete for areas of highest health gain.

### Box 5.15

#### Key Observation 13: Dynamic efficiency

Ex post value assessment, combined with an ex ante price premium provides an incentive to the innovator to continue investing in high risk projects, therefore contributing to long-term investment in innovation activities and dynamic efficiency. This type of approach should become practice particularly in areas of high medical need.

Overall, it could be argued that the VBP approach is limited in its ability to deliver on dynamic efficiency and that this is one of its fundamental flaws. Therefore, compensating measures to incentivise R&D will need to be identified and robustly implemented. Further reflection on this particular aspect is offered in the next section.

#### 5.5.4. Prices of patented pharmaceuticals and the link with R&D

In conditions of market failure, such as those that arguably exist in poorer parts of Africa, Asia and Latin America, there is (despite widespread disease) little direct incentive for the private sector research industry to invest in the development of new medicines designed only for those markets. This is mainly because the intended consumers will not, without the intervention of third party payers, be able to afford such products at prices sufficient to provide a viable return. Indeed, they may not even be able to purchase (or, given the labour costs of medical and pharmaceutical care, to make appropriate use of such medicines) at the marginal production and supply cost.

In circumstances like these it is reasonable to argue that research funding should be separated from that of production and supply. Third party payers, governments, global NGOs, such as the Gates Foundation, and international agencies such as WHO and UNICEF might with good reason seek to stimulate two markets, one for specified preventive and therapeutic innovations and one for the delivery of effective treatment packages (i.e. for drugs supply at prices set at as close to the marginal production cost as is sustainable, plus immediate service) to vulnerable populations.

HIV treatment is a special case, where, in the face of a new global pandemic affecting both rich and poor populations, new products were priced at levels affordable in the context of rich world health care delivery (ie to include R&D costs and/or investment returns sufficient to justify continuing highly risked research expenditures). As was obvious from a very early stage in the pandemic, these were unaffordable in the areas of greatest need. Hence special intervention before the normal processes of patent expiry and mass commodity level production had occurred was required, leading to considerable controversy.

It is in essence the experience of HIV drug supply in the poor world which lies behind much of the current argument for de-linking medicines research funding and drug supply costs in the developed world, albeit that conditions such as malaria present to a degree comparable challenges. However, the view taken here is that the prices of commercially supplied patented medicines should in normally functioning markets continue to reflect the levels of incentive needed to drive not only an adequate supply of existing treatments, but also investment in ongoing innovation.

Given that there is already substantial public funding for medicines research to institutions such as universities and public sector hospitals and laboratories, the advantages of continuing 'integrated' private sector pharmaceutical pricing in developed countries, including the UK, relate in essence to the power of market forces to inform (translational) research prioritisation, and maintain an adequate level of urgency in the process of getting new and improved products to their potential consumers, notwithstanding concerns in areas such as safety and cost.

## 5. Implementing VBP in the UK

Based on the above, undue separation of the production, delivery and pricing process ('generic' or commodity supply) from that of innovation, and the removal of direct market incentives from the latter, could well lead to stagnation rather than enhanced welfare. Within the context of the current system of pricing and direct (financial) incentives in the UK, these are best suited together with a view to actively contributing to welfare enhancement.

### Box 5.16

#### Key Observation 14: Prices of patented pharmaceuticals should include R&D contributions in settings such as the UK

From a welfare perspective, separating production and pricing from that of innovation and removing the direct market incentives could have a stagnating rather than a welfare enhancing effect. Continuing to link pricing with investment in innovation through the provision of direct financial incentives imbedded in product prices – as is currently the case under the PPRS – should have a welfare-enhancing effect.

## 6. What incentives to encourage pharmaceutical innovation in the UK?

### 6.1. Providing incentives for pharmaceutical and biomedical research

Within the current context, incentives are provided to pharmaceutical manufacturers to innovate. These are provided by the central government through a variety of schemes and measures. Among them, the DH, through the PPRS agreement, provides incentives for pharmaceutical R&D (DH, 2009). The Office for Life Sciences issued its Life Sciences Blueprint outlining actions to support and transform research in life sciences in the UK (OLS, 2009; OLS 2010). These are unique to the pharmaceutical and life sciences industry. Other government departments provide certain incentives (e.g. tax breaks, tax credits), which are not unique to this industry.

The PPRS provides significant support for R&D through an R&D allowance and restricts allowable expenditure on marketing and information. The 2005 PPRS increased the maximum R&D allowance from 23 per cent to 28 per cent of NHS sales with a new element of up to 3 per cent of NHS sales as an incentive for licensing medicines with paediatric indications and an additional 2 per cent for innovation. These allowances are available only where companies can demonstrate within the provisions of the scheme that the amounts claimed relate to expenditure actually incurred. The 2009 agreement increases support for R&D through allowances for R&D to a maximum of 30 per cent of NHS sales. In 2007, pharmaceutical industry R&D expenditure in the UK increased to over £3.9 million compared with £3.3 million in 2006. This is greater than in any other country in Europe and third behind only the USA and Japan in international terms.

Current observations demonstrate diverse emerging trends in global health and the process of drug discovery, development and diffusion:

- biomedical R&D costs have escalated dramatically in recent years;
- high, middle, and low income nations continue to experience significant and diverse unmet medical needs;
- despite public funding for almost three quarters of all (cancer-related) biomedical research in Western Europe and North America, uptake of research results in the health care systems of these funders frequently is poor;
- moreover, the process of bringing an innovative medicine to market has become increasingly risky because of its complexity and selective risk aversion;
- there is a relative lack of novel treatments for neglected diseases.

Unless health care stakeholders world wide change their outlook and behavior to support research and development, to produce socially desirable treatments that address unmet medical need and reward risk-taking behaviour, funding for biomedical R&D and the consequent benefits for patients will almost certainly decline in the years to come.

The above diverse emerging trends in global health and the process of drug discovery, require current incentive structures – where they exist - should be maintained and some coordination of activities and collaboration among stakeholders across jurisdictions should be encouraged in order to maximise benefit, utilise scarce resources optimally and capitalise on knowledge gained.

Based on the above, in addition to the PPRS, the broader directions in pharmaceutical/biomedical R&D and the funding of innovation may need to be coordinated by a cross-departmental, multi-disciplinary "Innovation Commission". The Commission will build on the Office for Life Sciences initiative and will include a wide range of governmental bodies (Business, Innovation & Skills, Health, Education, Science and Technology), key funding agencies (e.g. MRC, WT), industry and NGOs (e.g. Cancer Research UK). The Commission will also set priorities for "socially desirable research", and will experiment and potentially expand on schemes which aim to diffuse new technologies to the NHS. Above all, the Commission will form a long-lasting partnership among

## 6. What incentives to encourage pharmaceutical innovation in the UK?

stakeholders for the benefit of future innovation. Box 6.1 summarises the type of broad actions initiated by the “Innovation Commission” and Box 6.2 outlines some of its strategic directions in this context.

### Box 6.1

#### Key Observation 15: Providing R&D incentives to encourage pharmaceutical and biomedical innovation

It is proposed to strengthen the support and incentives for pharmaceutical and biomedical research in the UK by a series of actions:

- (a) the establishment of a cross-departmental, multi-disciplinary “Innovation Commission” which will build on the Office for Life Sciences initiative and will include a wide range of governmental bodies, funding agencies, industry and NGOs to mastermind and monitor innovation policy, priorities and actual funding of the R&D effort;
- (b) continue the commercialisation of research by transferring knowledge, including the provision of opportunities to extend market exclusivity periods where warranted; and
- (c) set priorities for research in a collaborative manner as well as identify and implement strategies to fulfil these.

### Box 6.2

#### Key Observation 16: Strategic directions for the “Innovation Commission”

The Innovation Commission will develop further and expand the OLS package of actions to support UK pharmaceutical and biomedical R&D:

- (a) create vertical links with the life sciences community to identify research areas and needs, across disciplines (e.g. information technology, biology/stem cell research, chemistry, etc);
- (b) understand the needs of science in terms of numbers of researchers and invest in disciplines to produce a critical mass of appropriately trained scientists;
- (c) help select new treatments diffuse in the NHS by providing some central funding;
- (d) build strategic alliances with overseas bodies and research communities where this is feasible, thereby creating partnerships to create further knowledge and capitalise on likely scale effects;
- (e) support basic research and continue to provide the bridge between research and commercialisation; and
- (f) supplement these initiatives by providing financial and non-financial incentives to manufacturers to continue to invest in R&D and attract further investment.

### 6.2. A methodological taxonomy of incentives for innovation

In order to explore the ways in which the pharmaceutical/biomedical sector can be supported in the most optimal way, a conceptual framework is needed that pulls together the various incentives and views these strategically. This framework supplements the structure outlined in the previous section, whereby some of the incentives for the sector are managed by a cross-departmental commission, which includes interested stakeholders from government, research funding bodies, NGOs, professions and industry.

Methodologically, the incentives for pharmaceutical/biomedical innovation outlined in this section can be divided into financial incentives and non-financial incentives. Financial incentives can be further sub-divided into pull mechanisms and push mechanisms; while the R&D incentive – a direct incentive to manufacturers to locate in the country and conduct R&D activities - is thought to be better linked with the existing agreement (see section 5.5.4, Box 5.16) the latter include both direct funding and general tax incentives; the former address issues such as advanced market commitments and intellectual property. Non-financial incentives comprise a wider gamut of measures, including regulatory mechanisms, product development partnerships and non-financial push mechanisms. The above framework is outlined in Table 6.1. The sections below briefly discuss these incentives in the context of the UK.

**Table 6.1**

**Incentives in pharmaceutical R&D – A methodological taxonomy**

Financial Incentives		Non-financial Incentives		
Pull Mechanisms (PM)	Financial Push Mechanisms (FPM) <ul style="list-style-type: none"> <li>• Direct funding</li> <li>• Tax incentives</li> </ul>	Regulatory Mechanisms (RM)	Product Development Partnerships (PDP)	Non-financial Push Mechanisms (NPM)

Source: The authors, 2010 from a variety of sources, including Kanavos et al (2009) and Mossialos et al (2009).

### 6.3. Financial incentives to encourage pharmaceutical and biomedical R&D

#### 6.3.1. Pull mechanisms

Pull mechanisms can be used to further incentivise R&D and reward innovation. Important in this regard are (a) advanced market commitments (b) market access mechanisms and (c) intellectual property mechanisms.

Advanced market commitments are agreements between payers and industry for the former to purchase a product at a pre-agreed price and volume. Payers can specify the volume to be purchased and agree on a price, thus reducing the risk to the innovator. They could be implemented in selected therapeutic areas including rare cancers, anti-infectives and selected anti-cancer agents.

Market access mechanisms include initiatives such as the recently proposed Innovation Pass, whereby earlier access will be given to patients for promising licensed medicines. Depending on the availability of resources, this type of mechanism can improve uptake and diffusion of new treatments among target patient populations. Finally, the issue of intellectual property is critical in rewarding innovation. The advent of personalised medicine is likely to make a review of the reward system through intellectual property an essential measure to enable new research to take place and new therapies to come on to the market place. Longer protection periods are

## 6. What incentives to encourage pharmaceutical innovation in the UK?

likely to diffuse pressures on prices, particularly in small patient therapeutic areas (see also section 5.4.6, Box 5.12), and could be achieved through extended market exclusivity periods and/or longer Supplementary Protection Certificates (SPCs).

### 6.3.2. Push mechanisms

Push mechanisms relate to the creation of an environment conducive to research, ensuring that scientific personnel is available and that industry R&D funding is supplemented by public funding of R&D. As part of this process, certain types of tax incentives can also be used to attract investment. The recently announced patent box is one such measure (OLS, 2010; OLS, 2009). Differentiation could be made in such incentives to foster the innovative potential of smaller firms. Similarly, access to research results, whether these are technology platforms or novel molecules, is key in enhancing the pool of available knowledge that can create positive spillover effects.

### 6.4. Non-financial incentives to encourage pharmaceutical and biomedical R&D

#### 6.4.1. Regulatory mechanisms

Important regulatory mechanisms relate to (a) clinical trials and (b) accelerated (HTA) reviews.

Further encouraging clinical trials is a particularly acute issue in an environment where clinical trials are globalised in part due to high cost. Whereas the UK situation suggests that significant improvement has been made over the past 5 years, further developments could take place in this regard. For instance, initiation of clinical trials across the UK should be further streamlined. The experience of the Clinical Research Network indicates that its procedures and templates have made a positive difference to the time taken to set up clinical trials. These arrangements should be rolled out across all potential trial sites in the UK. The Office for Life Sciences Blueprint announced that a framework for professional local management of research would be put in place. This is a good step forward but until the details of what this looks like are made clear it is hard to see what contribution it will make to improving the research environment. Improvements can also be made in patient recruitment. There are now many staff involved in the administration of research at network level, but the focus now should be on ensuring that staff in clinics have adequate time to identify and recruit patients. Their capacity to do this properly and not just as an ‘add-on’ has to be addressed. Accountability must be recognised by Trusts which have contracted to undertake clinical research. There should be reported metrics on recruitment targets and where performance falls short, Trusts should be required to put additional resource into supporting recruitment. This is currently a focus for the NIHR Research Support Services External Reference Group. Finally, the costing template should be adopted across all trials with the aim of reducing variability and time spent on negotiations. Initial set-up costs should be clarified and standardised.

With regards to accelerated (HTA) reviews, there have been positive developments in that NICE actively encourages contact with manufacturers to explore and discuss data and approaches. Nevertheless, consideration could be given to the link between access to treatments and investment in research.

There is concern within the industry that companies may be unable to conduct some trials in the UK because HTA recommendations or local NHS trust formulary decisions restrict access to certain medicines.<sup>11</sup> This affects primarily those medicines being studied for second line use, where initial treatment has been unsuccessful. In some cases the initial treatment is unavailable first line on the NHS but is routinely available in other countries, which consequently become more attractive locations for research as they have patient population with the relevant treatment history. This is most likely to impact priority areas such as cancer and Alzheimer’s disease.

The consequences may be that not only will clinical research not be located in the UK, but that UK-based HTA bodies will not have access to UK specific data on medicines they want to appraise.

11. David Grainger & Helen Llewellyn, personal communication.

## 7. Conclusions

Rather than relying on private companies being able to fund pharmaceutical research and development through charging premiums for innovative (patented) medicines, some critics of current arrangements believe that it would be preferable to develop alternative mechanisms for funding medicines research. They may point to initiatives such as the Gates Foundation, and the fact that there has already been some shift in the UK towards providing enhanced fiscal incentives for research investment. In future there could also be additional movements in the direction of offering ‘prizes’ for successful therapeutic ‘inventions’, coupled with more reliance on directly taxpayer funded research markets.

Taken to the extreme, developments in this direction could ultimately mean that the funding of all private sector medicines research will be de-linked from selling medicines per se, and that all drugs will be supplied at a generic (i.e. commodity competitive) price from the time of their initial launch. Models of this sort may seem to be an attractive proposition to people or institutions wishing to cut the cost new medicines. Yet there is little or no evidence that they would in reality benefit the public, if members of these institutions wish to combine continuing innovation with ensuring affordable prices for licensed drugs.

The use of ‘value-based’ techniques for the pricing of patented pharmaceuticals may therefore appear to offer a more secure way of balancing these competing goals in a sustainable manner, depending where the affordability threshold is set. The higher the latter, the greater the likelihood of investors being prepared to accept the risks and uncertainties inherent in funding pharmaceutical research and development. The lower it is, the lower the amount of money the NHS will have to find for delivering treatments.

However, people in countries such as the UK also have interests in issues like the indirect benefits that conducting pharmaceutical research and producing high quality medicines can bring to their communities. They may also be seeking assurances in contexts such as balancing NHS contributions to promotional as opposed to medicines research costs. The view suggested in this paper is therefore that the linked health and wealth creating objectives of the ‘traditional’ PPRS should not be abandoned, but rather that future UK pharmaceutical pricing approaches should seek to combine the appropriate use of VBP methodologies with desirable elements of the former, in a collaborative spirit between government and industry.

Care should be taken to ensure that the overall approach to medicine pricing in the UK does not become unduly dominated by the (in some respects) limited calculus that VBP alone embodies. HTA, as currently implemented in the UK (and elsewhere) may need to be “reformed” to comply with the principles of VBP as defined in this paper. This may result in a unique UK approach, which may be necessary, considering the current interests of the country and its leadership as a knowledge-based economy in pharmaceutical and biomedical research.

The main body of this paper explores in technical detail issues relating to the further implementation of value-based pricing for medicines within the NHS, via its existing or new institutions. But a key point to finish on here is that it is in common sense terms unlikely that a more coherent set of twenty first century national health, industrial development and medicines related policies and controls will be achieved if the process of deciding what the NHS is prepared to spend on individual medicines becomes functionally split from that of protecting the UK’s longer term interests in the pharmaceutical sector as a whole.

Steps towards the end of establishing a better integrated system than that currently in place could include redefining and broadening the health related benefits included in cost effectiveness calculations, and recalibrating the ‘cost per incremental QALY’ affordability thresholds applied within the overall pharmaceutical price regulation framework employed in this country. It might also be worthwhile considering whether or not a ‘cost per average QALY’ measure should be introduced as a check against unwisely judging beneficial treatments that are unaffordable for NHS service users.

## 7. Conclusions

The paper puts forward 16 key issues for consideration by UK decision-makers (see Box 7.1) relating to the implementation of VBP and the expansion of the knowledge and research base in pharmaceutical R&D in the UK.

A fundamental stepping stone towards creating a stable 21st century financial environment for medicines research could be provided by re-evaluating the appropriate duration of intellectual property protection for new medicines. Without provisions in place to assure appropriate levels of intellectual property protection in changing scientific and commercial environments, the implementation of ‘value-based pricing’ can only have limited utility.

### Box 7.1

#### Key Observations for the implementation of VBP in the UK

1. Considering the PPRS in the context of UK pharmaceutical policy
2. Pricing options for medicines
3. The limitations of the current VBP
4. Variable affordability thresholds
5. Ex-ante vs. ex-post assessment
6. Varying medicine prices – post-launch or ex-post price?
7. VBP should PPRS cease to exist
8. Who will be subjected to VBP assessments?
9. Role of NICE, SMC and AWMSG in a devolved setting
10. UK HTA agencies and their role in VBP
11. Varying patent terms in relation to VB prices
12. Risk sharing and improving access to patients
13. Dynamic efficiency
14. Prices of patented pharmaceuticals should include R&D contributions in settings such as the UK
15. Providing R&D incentives to encourage pharmaceutical and biomedical innovation
16. Strategic directions for the “Innovation Commission”

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## Appendix

### Risk Sharing and Innovative Payer Schemes

Innovative payer schemes are uncommon or novel negotiated contracts between institutional health system payers and pharmaceutical companies. These innovative schemes respond to specific needs, or in some cases gaps, in the prevailing national health systems purchasing schemes. Five types of innovative payer schemes have been identified in pharmaceutical purchasing: (a) portfolio deals, (b) one price per patient, (c) targeting out of pocket burden, (d) disease management schemes and (e) risk sharing schemes.

Portfolio deals involve tradeoffs within pharmaceutical company portfolios. A new drug price is negotiated including concessions on prices for other drugs in the company's portfolio. The portfolio deal scheme is exemplified by Roche's deal with NeoRecormon and the rest of its oncology products. One price per patient deals involve payments based on the sum of individual patient consumption. One price per patient deals are exemplified by the Johnson and Johnson deals with Eprex, through Janssen-Cilag, and the urinary incontinence medication deals made by ConvaTec, of Bristol Meyer Squibb. Disease management schemes characterize deals where the drug company doesn't just provide medication, the company is paid to take over all aspects of care for a disease, the nurses, training, and supplies. Disease management deals are exemplified by Pfizer's treatment of diabetes, Bristol Meyer Squibb's CareConnex modules, and Johnson and Johnson's Risperdal. Out of pocket burden schemes will not be covered in this assessment. This assessment will characterize the remaining innovative payer schemes and reveal their backgrounds, mechanisms, where they are used, and how widely they have been studied or reported on.

Disease management is the most prolific scheme based on published materials and news interest. Disease management was started in the 1990's. Pfizer and Medicaid in Florida are one example of disease management schemes. Florida's Medicaid system, which desired to reduce costs in treating multiple types of diseases including diabetes, Alzheimer's, AIDS and congestive heart failure, among others offered disease management deals (Florida Medicaid Website). Pfizer responded to the offer by negotiating a deal where their medications for diabetes were given preferred status in the Medicaid system ensuring near exclusive use of their medication. In return, Pfizer offered additional resources such as patient management services and nursing care that were subcontracted through a separate health care provider (Posey, 2001). Additionally, Pfizer guaranteed Florida's Medicaid services savings of US\$33 million. If these savings were not met penalties would be assessed, so in this regard there was an element of risk sharing in this agreement (Posey, 2001). However, this was very different from a risk sharing agreement because the key (and novel) elements of this deal was Pfizer subcontracting the care of the patients on their treatment and thus assuming full responsibility for these patients and full management of the disease within the health system. This management and care responsibility assumed by the pharmaceutical company distinguishes disease management as an innovative payer scheme. Since this deal Florida's Medicaid has negotiated many disease management deals with other pharmaceutical companies and private providers for numerous other diseases (Florida Medicaid Website). Disease management schemes have proliferated through the Medicaid system to other states such as California and Colorado (Pharma Business Week 2007, Colorado Department of Health Care Policy and Financing 2004). There has been a great deal published about disease management schemes as a general topic. One study distinguishes two models, a primary care based model and a carve-out model (Bodenheimer 1999). These models differ in the level of control the management aspect of care entails. In the carve-out model the companies have total control and may look to their profits, rather than the needs of patients. In the primary care model the companies use existing primary care facilities and employees ideally preserving partiality in the health care system. Many other articles comment on the topic of disease management (Geyman 2007, Sidorov et al. 2002, Bodenheimer 2000, DeBusk 1999).

One price per patient schemes and portfolio deals are far less prolific in the literature and current events. Regarding the Roche NeoRecormon portfolio deal the only prominent literature was a Danish Ministry of Health and Prevention (Danish Ministry of Health and Prevention, 2009). This report did not discuss a portfolio deal, but it addressed a part of the negotiations and the use of add on value. In the add-on value deal Roche agreed to offer research money and training to settle the price of NeoRecormon. No information was found specifically regarding one price per patient as a scheme, or even in less specific terms addressing the agreements

## Appendix

of ConvaTec and Eprex as a price per patient schemes. The lack of strong literature coverage of these schemes may be an indicator that less attention has been paid to these mechanisms.

Disease management is the clear leader in public interest and in academic evaluation among the innovative payer schemes. Portfolio deals and one price per patient schemes have not been widely studied or reported on as individual topics. More academic investigation is needed on the subject of one price per patient and portfolio deals. Thus far, it appears payers and researchers have chosen to invest their resources in exploring the possibilities and future of disease management schemes.

Consensus on risk-sharing agreements in pharmaceutical deals is nearly complete: risk sharing agreements will become increasingly popular in the future. Risk-sharing in general terms involves a pharmaceutical company agreeing to take financial responsibility for lower than anticipated (and agreed upon) results. In uncertain situations, where the outcomes of new drug treatments are unknown, this method allows a government to limit its financial exposure and still gain access to potentially effective medications. There are four types of risk sharing agreements currently in use: (a) coverage with evidence development, (b) conditional coverage, (c) outcome guarantee, and (d) price volume agreements.

Coverage with evidence development is a scheme where the full effectiveness of a drug is not known, and so an agreement is reached that involves continued trials and evaluation of the medication but also reimbursement and use (which will be reevaluated once the data is collected). This scheme is exemplified by the Centers for Medicare & Medicaid Services coverage of chemotherapy costs in the National Cancer Institute trials of Colorectal Cancer treatment.

Conditional coverage is a scheme where failure to meet targets results in price changes or rebates. Conditional coverage was the scheme covering Pfizer and statins in the UK, the UK NICE MS scheme, and France with Acomplia.

Outcome guarantee is a scheme where pharmaceutical companies pay (or refund) the price for medications that do not produce a therapeutic benefit for a patient. Outcome guarantee was used with Velcade in the UK. Price volume arrangements will not be analyzed in this assessment; however the other schemes will be evaluated based on material found in journals and news sources.

Conditional coverage and conditional coverage with evidence development are subtly different. The key difference is that evidence development involves an ongoing formal study, and conditional coverage involves potential rebates due to underperformance (requiring analysis similar to those in formal trials but not as rigorous). Conditional coverage is not well reported as an individual entity. Most of the reporting on conditional coverage, is more accurately describing conditional coverage with evidence development or outcome guarantee. This could be the consequence of language that has not been standardized, but examining the deals described in the literature reveals that the literature is correct in the instances I saw (and these examples are included in the correct places in this assessment). The confusion also appears to involve both schemes using an evaluation while in use. The distinction is whether that is an ongoing study in formal trials, evidence development, or merely an effectiveness analysis to assess targets, conditional coverage. The Centers for Medicare & Medicaid Services coverage of chemotherapy costs in the National Cancer Institute trials of Colorectal Cancer treatment is an archetypal example of conditional coverage with evidence development. The key features of this evidence development schemes are that they are most useful in only certain circumstances, when the need to be met is large, the costs are high, and the outcome is uncertain (Cancer Drug News Pharmaceuticals 2008). The use of this scheme for high cost unproven cancer medication fits the description well. There is also coverage of Medicare and Medicaid's use of coverage with evidence development with respect to positron emission tomography (PET) scans and implantable cardioverter defibrillators (ICDs) (Pharmaceutical Executive 2006). The tone of these articles appears to be a bit more critical, raising doubts as to whether treatments without proven value should be used in trials in a clinical setting. In contrast to the worries over the practical issues, the

outlook on conditional coverage with evidence development is being praised as the compromise that will allow doctors to keep pushing technology forward, but responsibly (The New York Times 1992). Coverage with evidence development also gained attention as a main topic in the Health Technology Assessment International meeting in Montreal, Quebec in 2008 (Canada NewsWire 2008). Despite a number of examples of this risk-sharing schemes and their potential impact, little comparative or evaluative research has been published on this scheme to rate its success or failure. This is potentially due to the fact that these agreements are made when the data is not available, and the studies and use may still be ongoing, or the difficulty of evaluating futuristic and expensive technologies.

Outcome guarantees are a separate scheme from the conditional schemes distinct by requiring pharmaceutical companies to cover the costs, partially or in full, when a patient does not respond to treatment at the individual level. This eliminates the need to do trials or target setting at an aggregate level. After negotiating patient goals and indicators the company refunds all, or some, patient costs for those patients that fall short of the determined outcome. Most of the articles fail to investigate the issue thoroughly, but many pick up on the refunds without positive responses to treatment (Moss 2009, Pollack 2009, Pulse 2004, Business Wire 2007). The literature praises these agreements, even if possibly being too strong against industry, for being a compromise where companies can bring their product to market, helping patients, and helping the companies also who would not go to market otherwise. Velcade as a treatment for MS in the UK is an example. This case brings several aspects of risk-sharing to light. Risk-sharing is not a way to avoid drug licensing, and unless risk-sharing is the only way to get a drug on market, it is unlikely that risk-sharing will be the choice for pharmaceuticals. This is because if the drug exceeds expectations, it may be tough to raise the price, while if the drug fails to meet expectation the pharmaceutical company is left with the loss. This stresses that risk sharing is only to be used in certain situations when the traditional mechanisms of drug purchasing break down.

A general concern of risk-sharing schemes relates to their legal implications. Often complicated contracts can give rise to tough legal questions and a few articles were based on this concern or a response to specific legal actions taken regarding risk-sharing. These problems appear manageable, and even though a few cases have been reported on, no significant problems with the scheme have emerged (McDermott Will & Emery, Business Briefing, 2004; Presswire, 1998).

Overall risk-sharing is a very prominent feature of pharmaceutical schemes in the news especially. Momentum is building for risk-sharing to the area where the most progress is made in the near future, along with value based pricing. Some instances even seem to suggest that risk-sharing and innovative schemes can be linked: for example disease management with outcome guarantee (Barnett, 1995). Outcome guarantee and conditional coverage schemes appear to be prominent arrangements in risk-sharing, but new novel risk-sharing arrangement schemes will also likely emerge as this idea is pushed further.

## Appendix

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