

Innovative Pricing Agreements to Enhance Access Prospects

IN THE FACE OF RISING DEMAND FOR INCREASINGLY EXPENSIVE HEALTHCARE PRODUCTS AND SERVICES, PAYERS AROUND THE WORLD HAVE RESPONDED WITH A RANGE OF COST-CONTAINMENT MEASURES DESIGNED TO REIN IN ESCALATING EXPENDITURE. PHARMACEUTICALS – IN PARTICULAR EXPENSIVE NEW TREATMENTS – HAVE BEEN KEY TARGETS IN THIS RESPECT. MARKET ACCESS CONDITIONS HAVE BECOME INCREASINGLY HARSH – AND MAY BECOME HARSHER IN WHAT MAY PROVE TO BE A PROTRACTED ECONOMIC DOWNTURN.

In the light of this, strategic approaches are being utilised with increasing frequency, as industry explores alternatives to mainstream pricing and reimbursement applications in an attempt to gain coverage for new products. Such approaches are also proving to be of interest to hard-pressed payers, as means to control costs (and other risks) while facilitating some form of access for innovative treatments. The recent NextLevel Pharma conference, *Pharmaceutical & Medical Device Risk-Sharing and Value-Based Pricing & Reimbursement Schemes*, staged in Brussels, provided a forum for discussion of the role of innovative agreements – and in particular, risk-sharing agreements – in the current climate. *Mick Maroney presents the first of two reports on an event that attracted a high level of interest from industry, payers and other stakeholders.*

THE RISE OF RISK-SHARING

Mel Walker, Director, Global Health Outcomes, Oncology, with GlaxoSmithKline, chaired the conference and provided some initial observations on factors affecting the rise of innovative agreements. “With organisations such as NICE [the National Institute for Health and Clinical Excellence] in the UK and PBAC [the Pharmaceutical Benefits Advisory Committee] in Australia leading the way, payers are becoming increasingly willing to make difficult decisions about drug funding. And they are doing this within a framework of opportunity cost – if they pay for one medicine, it will prevent them paying for another. Pharmaceuticals may offer easier targets for cost-containment than other components of healthcare. However, restricting the use of innovative medicines may have a broader impact on healthcare budgets or outcomes that is often not taken into account,” commented Walker.

“In some countries, risk-sharing is becoming popular because there is a common desire to make sure that patients get access to the medicines they need. As the industry moves forward, into a future where risk-sharing schemes are going to be more common, it’s my belief that we need to make sure that we offer true partnerships in which we genuinely share risk or commit to demonstrate the value of our products. In return there should be mechanisms in place to reward value for genuinely innovative medicines and to reflect the changing value of a medicine throughout its lifecycle.

“It’s becoming very clear that we need to be aware that payers are increasingly unwilling to accept uncertainty. It may be uncertainty about trial efficacy, or around how that translates into effectiveness in the real world. It may be around the safety of the product, around modelling, the methods or the link between surrogate endpoints and long-term outcomes. It may be around cost-effectiveness, or around budget impact or usage.

“One thing that is certain is that willingness to accept uncertainty is absolutely polarised by price. The higher the price, the less willing the payer is to accept that level of uncertainty. Risk-sharing deals try to deal with uncertainty to a level where it becomes acceptable to the payer,” said Walker.

In the view of Gustav Ando, Director, Healthcare Practice, Global Insight, achieving “normal” market access for a new treatment, where regulatory approval is followed immediately by drug pricing and launch, is an increasingly rare phenomenon. Health economics is being used with increasing sophistication by reimbursement authorities, which is in turn requiring increasingly flexible and creative pricing and reimbursement arrangements.

In line with others who spoke at the meeting, Ando observed that there are essentially two approaches to risk-sharing: financial and outcomes-based schemes. “Finance-based schemes are conditioned by a set of pre-specified budget caps, discounts or restrictions that can either be based on a particular patient or on the disease population,” said Ando. These can include price-volume agreements (as in France), expenditure caps (as in Australia and the US), price cuts that are attached to forecasted spend (Japan) and conditional discounts (as in Italy and the UK).

“Outcomes-based agreements are conditioned by a pre-specified endpoint or definition of response that dictates whether the payer will cover the treatment on an *ex post facto* basis. These can include outcomes guarantees



(as in the UK and the US) and form the traditional model of risk-sharing agreements, as payment is weighted entirely against the performance of the drug,” said Ando.

“The type of risk-share agreement varies significantly by government – and by company – in terms of what type of arrangements the parties prefer, or indeed are prepared to engage in,” said Ando. “What is not in doubt, however, is that they are on the rise. In Australia, the first official risk-sharing agreement was signed in October 2003, but it has since grown into a regular pricing strategy, and five years later there were 60 such agreements in place or in development.”

In Ando’s view risk-sharing is a “developed world phenomenon”. At the moment, the “hot spots” are in the UK, France, Germany, Italy, the US, Canada, Australia, New Zealand and Japan. However, it is likely that they will be adopted in key emerging markets such as China and Brazil, as well as South Korea.

EUROPEAN PERSPECTIVES

Adrian Towse, Director of the Office of Health Economics in the UK, discussed some of the European findings of work carried out with Professors Sean Sullivan and Lou Garrison of the University of Washington, Seattle.

According to Towse, risk-sharing agreements can be divided into performance guarantee schemes and those offering coverage with evidence development. An example of the former is a scheme in which Parke-Davis (now Pfizer) agreed to rebate a local health authority in the UK if a patient population did not achieve defined targets after using statins (see Table 1). “This is performance-related, but this is an intermediate marker, so we don’t know what impact that is having on the number of patients who have myocardial infarction,” said Towse.

“An example of coverage with evidence development is the case in France where the healthcare authority agreed to cover J&J’s schizophrenia treatment, Risperdal Consta. This is a particularly interesting one, being linked to compliance,” observed Towse. Some schemes can be classified as both performance guarantees and coverage with evidence development. This applies in the case of the well-known multiple sclerosis risk-sharing scheme in the UK, he explained.

Towse noted that there are also schemes based on proven short-term effectiveness. An example is the Alzheimer’s drugs scheme in Italy, under which products are provided

free for the first three months and are then reimbursed in full if they prove to be effective. “This is not a risk share as I would see it, but the short-term evaluation involved effectively means the product is listed once it proves effectiveness,” said Towse.

UK DEVELOPMENTS

The UK has been at the forefront of developments in Europe (see *PPR* April 2009, p95; March 2009, pp73-74 *et al*). Perhaps the most famous (or infamous) scheme in the UK dates back to 2002, when the multiple sclerosis initiative got under way.

“This is a complicated scheme, lasting for 10 years and involving a complex arrangement of contracts with a number of competing companies,” explained Towse. “There are many issues with this scheme. There have been difficulties with recruitment and with monitoring, and we still have an untried reconciliation and adjudication process. The scheme has scarred the Department of Health (DH): for a while, risk share equalled MS equalled nightmare. It has had a very substantial adverse effect on the payer’s view of risk-sharing schemes. I’m sure the Department is advising payers around Europe and elsewhere to be very careful when entering schemes as they can be extremely burdensome in terms of administration and cost. They also pose a considerable political challenge.”

OFT ACKNOWLEDGEMENT

Despite such concerns, acknowledgement of the increasingly important role played by innovative agreements in the UK came in February 2007, when the Office of Fair Trading (OFT) produced a critical study of the Pharmaceutical Price Regulation Scheme (PPRS).

“This was a competition authority discussing the appropriate environment in which a publicly-funded insurer should be buying medicines, and how it is appropriate to regulate that in a way that gives the payer value in a competitive environment,” said Towse. “The OFT had a very clear view of risk-sharing. If the data at time of launch is insufficient to take an informed view of cost-effectiveness, then in a limited number of cases a scheme should be adopted. It said it is particularly appropriate for chronic conditions where final outcomes may only become clear after several years of use.”

Table 1: Examples of European Risk-Sharing Agreements

Country	Disease area	Manufacturer	Payer	Agreement	Type
UK	High cholesterol	Parke-Davis (Pfizer)	North Staffordshire Health Authority	Parke-Davis (Pfizer) agreed to rebate the local payer if a defined patient population did not achieve a low density lipoprotein cholesterol concentration target after using statins.	Performance guarantee
UK	Colorectal cancer	Merck	Primary Care Trust	Rebate direct to primary care trust on the cost of any vials of Erbitux (cetuximab) used for patients who do not achieve a pre-agreed clinical outcome at up to 6 weeks.	Performance guarantee
Germany	Kidney transplant	Novartis	Deutsche Angestellten-Krankenkasse (DAK)	Novartis and DAK (a German insurance company) have agreement to fund money for Sandimmun Optoral (cyclosporin), Myfortic (mycophenol acid) or Certican (everolimus) if a patient loses his/her donor kidney.	Performance guarantee
Germany	Osteoporosis	Novartis	DAK and Barmer	DAK and Barmer (a German insurance company) have a money back guarantee for Aclasta (zoledronat) if an osteoporosis-related fracture occurs.	Performance guarantee
UK	Multiple myeloma	Johnson & Johnson	National Health Service	J&J agreed to reimburse the NHS in either cash or product for patients who do not respond after four cycles of treatment with Velcade. Responding patients receive additional four cycles.	Performance guarantee
UK	Multiple sclerosis	Biogen, Schering, Teva/Aventis, Sero	National Health Service	Patients using interferon beta or glatiramer acetate are followed for 10 years with treatment effects determined every two years. Drug price reduced to maintain cost effectiveness at £36,000/QALY.	Performance guarantee/coverage with evidence development
France	Schizophrenia	Johnson & Johnson	French Health Authority	France's health care authority agreed to cover Risperdal Consta at the asking price if J&J performed studies to show that the product helps patients stay on medication. Otherwise, J&J will reimburse a proportion of the money spent on the drug.	Coverage with evidence development

Source: Adrian Towse, based on *Pharmaceutical Outcomes Research & Policy*, University of Washington

The OFT also addressed non-linear pricing – different prices for different indications or different patient groups, in the same marketplace, for the same product. “This is not risk-sharing, but it is another example of a competition authority putting forward innovative ideas about ways in which European payers should be thinking about paying appropriately for medicines.”

THE NEW PPRS

As discussed by Jim Furniss, Director of Market Access Solutions with Bridgehead International, the 2009 PPRS addresses issues raised by the OFT on both risk-sharing and flexible pricing (see *PPR* January 2009, pp4-7 *et al*). “The new 2009 PPRS scheme provides a framework for these schemes in the UK. It may not offer guidelines as such, but at least is going some way forward,” said Furniss.

The patient access schemes discussed in the PPRS need to be clinically robust, plausible, appropriate and monitorable, he added. “They need to be monitorable by the NHS without involving undue complex monitoring, costs or bureaucracy,” said Furniss, reflecting Towse’s observation on the impact of the MS scheme, as well as other experience in Italy, for example.

“The PPRS makes a very simple distinction on patient access schemes between those that are essentially a financial arrangement, whether through restrictions on the number of patients treated, the response or the number of doses required, and outcome-based schemes. The critical point is that the financially-based schemes are financial arrangements – not risk-sharing,” said Towse. “The outcome-based schemes, where we are essentially talking about the company and the NHS having to agree the sort of data that is going to be collected in some form and which will be revisited, are rather different.”

“The provisions for ‘proven value’ can lead to a price increase and in the case of ‘expected value’ can result in a rebate. These have some similarities with what we see in France,” said Towse. However, in Furniss’ view, the fact that the patient access schemes are to be consistent with existing financial flows in the NHS means that this will not be possible.

PRACTICAL APPLICATION

Furniss noted that the risk-sharing aspects of the PPRS are already being used in practice. “Revlimid (lenalidomide) is an example. This was a small offer by a pharmaceutical company

to obtain market access,” observed Furniss. NICE recommended coverage of the product as a treatment for multiple myeloma on the basis of a two-year cap on treatment costs, after which the company, Celgene, will pay (see *PPR* June 2009, p184 *et al*). The recommendation was also based on NICE’s new end-of-life criteria (see *PPR* March 2009, p89 *et al*).

Another example discussed by Furniss was that of Sutent (sunitinib) for the first-line treatment of advanced and/or metastatic renal cell carcinoma. “In this case, Sutent was in effect extracted from the MTA [Multiple Technology Appraisal] process and treated as if it was an STA [Single Technology Appraisal],” said Furniss. The outcome was that in one indication, for a specific patient group, a risk share was agreed, despite a cost per QALY of more than £54,000 (US\$88,000; €63,000).

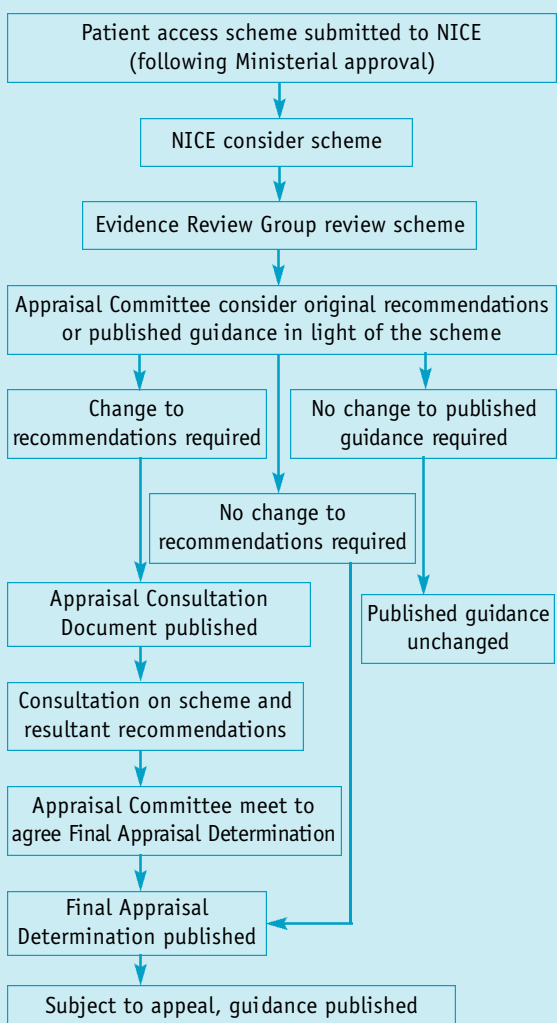
The risk share was based on the first cycle of treatment being free to the NHS. Along with the application once again of NICE’s end-of-life criteria, the patient access provision resulted in a recommendation for coverage. However, NICE did not recommend other renal cell carcinoma drugs for treatment: Avastin (bevacizumab) and Nexavar (sorafenib) proved unacceptable at respective costs-per QALY of £82,700 and £65,900, even taking into account end-of-life criteria. “This would suggest,” said Furniss, “that for products going through risk share, for which end-of-life criteria also apply, the threshold is somewhere above £55,000.”

In Furniss’ view, risk-sharing schemes will remain the exception, rather than the rule, in the UK. However, they may become the preferred pricing mechanism for high-priced products with limited evidence of efficacy or cost-effectiveness. “Transparency, however, is a major issue,” said Furniss. Unlike in most markets, the terms of the deals will be publicly available. “This may have implications for other markets.”

Adrian Towse was upbeat about the opportunities stemming from the new approach under the PPRS. “The patient access schemes introduce a fast-track route back to the NHS. The approaches offer the opportunity to introduce schemes on a more regular, systematic basis, superseding the current *ad hoc* approach. Companies will maintain control of price setting, but NICE will still be advising on whether or not products are affordable. While the DH has set up a group to manage these schemes, the critical issue remains the procedures that will be followed by NICE.”

NICE has now issued draft process guidance for consultation (see Figure 1). “This reflects the intent of the PPRS,

Figure 1: NICE Process for Considering a Patient Access Scheme



Source: *Guide to the Single Technology Appraisal Process: Patient Access and Flexible Pricing Schemes, Draft for External Consultation, June 2009 (NICE)*

although could make clearer that this is a fast-track route back to NICE at the end of the current appraisal process and that schemes are not intended to be proposed during the appraisal process, which risks gaming on both sides," Towse told *PPR*. "It also needs to be clear how the outcomes-based schemes will be reviewed."

THE TIMING OF AGREEMENTS

Whether in the UK or elsewhere, risk-sharing is something that companies should consider as they prepare for market access, continued Furniss. While it may not be appropriate for all markets, companies may from phase III onwards consider the possibility of an agreement. Ando agreed that phase III – or sooner – is an appropriate time to look at a scheme. But he cautioned: "I would favour letting the normal reimbursement process run its course, and then look at the possibility. There is a danger that this could be seen as a substitute for the reimbursement process." In Furniss' view, there can be value in taking the initiative rather than, in the UK for example, waiting until NICE has carried out its appraisal (and possibly issued a negative recommendation).

Neil Palmer, Vice-President, Pricing & Reimbursement with RTI Health Solutions, advised that early communication is already established in Canada. "Payers will speak with manufacturers about risk-sharing agreements before they make their assessment. If it is understood that listing could be based on such an agreement, it helps put pricing into context and informs the payer that the manufacturer is prepared to accept measures to limit the budget impact. At early-stage meetings, payers will often offer parameters on the types of agreements they may consider. Such meetings offer the chance to propose some initial concepts, and receive feedback that can be taken into account when preparing the formal submission and for negotiations of the listing agreement at subsequent meetings."

In Mel Walker's view: "Risk-sharing is not and should not be seen as a quick fix for a poor clinical development programme. We need to be thinking about payers' needs very early and we need to build those needs and requirements very early into our clinical development programme. Risk-sharing offers the opportunity to bridge the gap between the varying value recognitions that different markets have."

THE RISKS OF RISK-SHARING

It is clear that risk-sharing offers potential benefits to payers and providers, as well as manufacturers. For the manufacturer, an agreement may open up market access for a product that may otherwise have been denied coverage on the grounds of expense or uncertainty about its relative

effectiveness when weighed against a relatively high price. As noted by Mel Walker, an agreement may also allow a company to start recouping the costs of its research investment, while speeding up patient access.

For payers, aside from the obvious opportunity to reduce the cost associated with the introduction of an expensive new product, the benefits of risk-sharing are “all about covering a product with reduced uncertainty. They also want to minimise the cost of non-response, and minimise inappropriate use,” said Walker.

“Although payers are motivated to make new medicines rapidly available for the benefit of patients, there can also be a lot of political pressure around such decisions – it can reflect positively on a payer when they are able to reimburse a new drug for a particular disease,” commented Walker. “There may be some shared benefits in developing a risk-share agreement when clinical efficacy is accepted but there is some disagreement on costs. Such schemes offer faster access for patients suffering from conditions with high unmet needs such as cancer – particularly where there are no other treatment options,” he observed. “And we should remember that payers are hungry for data. This is a good opportunity to generate that.”

These potential benefits of course need to be set against the risks which by definition characterise such schemes. In most cases, it is clear that manufacturers are taking on board an element of financial risk: in the view of Gustav Ando, there is the danger that the risk is transferred to the pharmaceutical company, which in effect is transformed into a payer. Ando also suggested that there is the risk that a company may call into question the clinical effectiveness of a product, and its status, relative to others – particularly if other countries reference an agreement in their own evaluations. Walker noted related concerns: “There may be a concern that we are setting a precedent – that a payer may expect the same approach on other products, or indications.”

Payers, too, are open to risks. If a drug proves to be highly effective, it may result in greater long-term costs than had been envisaged. On the other hand, if a drug is ineffective, shorter-term costs may be wasted. Walker noted a number of risks on the payer side: “For payers there are risks around budgets, outcomes and evidence. There are risks that other companies may expect similar agreements, and that some may start to try and use such schemes as a way to get around normal reimbursement processes, and established cost-containment techniques.”

For Walker, there are also common risks to take into account. “A huge amount of resource needs to go into these schemes, from the company and the payer. Data systems need to be implemented to collect information and to measure compliance with the agreement. A payer in the UK observed that if such schemes become common, pharmacy departments in hospitals may have to start employing people to monitor them.

“Stakeholder involvement is also an issue. Once a scheme has been agreed, physicians will be the ones who bear the burden of implementation. You need to talk to them. If you don’t involve them, you could be upsetting a very important customer group,” said Walker.

BUILDING RELATIONSHIPS

Such considerations will play an important role in expanding the uptake and coverage of innovative agreements. As discussed by Gustav Ando, public pressure may play a significant role in this respect: calls for patient access led to the MS scheme, as well as others in the UK. “Several of these had an element of public backlash associated with them, following an initial rejection,” commented Ando, “so relationships with patient access groups could be influential.”

As noted by Jim Furniss, the preference will always be to try to gain access without such an agreement. However, if it seems appropriate to consider one in therapy areas or markets in which such agreements have yet to be implemented, it may pay companies to explore at national, but also local levels, whether there are arrangements that may be possible, and that may address payers’ needs at those levels.

As Mel Walker observed: “Many people in the industry remain concerned about the sharing of risk in such schemes – that they may be based simply on the payer’s perspective of driving down costs. However, while some payers may be focused very much on cost, others are focused on efficiency and on improving standards of care.

“A key consideration is the relationship with payers. There is a need to establish and maintain good relations; to build trust and work with them on ways of demonstrating the value of new treatments, before we introduce the idea of risk-sharing. Such relationships will stand us in good stead, should we find that we need to develop an agreement,” concluded Walker PPR