NO CURE NO COST

A drug company is set to refund the NHS if its new drug doesn't work. As healthcare costs grow, **Andrew Jack** investigates the worldwide movement towards value based pricing

Pressure to perform: the NHS will pay for multiple myeloma medicine, Velcade, only if patients respond to the drug

The UK's medicines watchdog caused a stir last month when it announced a groundbreaking payment by results plan with the drug company Janssen-Cilag. In draft proposals on which final guidance is due in October, Janssen-Cilag will charge the NHS for bortezomib (Velcade), its new drug for multiple myeloma, only if the patients show a complete or partial response.

It will rebate the full £25 000 (€37 000; \$50 000) cost of bortezomib for those who do not respond when treated in line with the drug's indication—progressive multiple myeloma in patients who have received at least one previous drug and had, or are unsuitable for, bone marrow transplantation. This risk sharing approach is part of a broader effort by healthcare systems around the world to introduce value based pricing, in an attempt to clamp down on rising medicine costs.

Unveiling the proposal, Andrew Dillon, chief executive of the National Institute for Health and Clinical Excellence (NICE), said: "If the drug's manufacturer accepts the proposals . . . it will mean that when the drug works well the NHS pays but when it doesn't the manufacturer should bear the cost. All patients suitable for treatment will get the chance to see if the drug works well for them."

The announcement was a sobering reminder that most medicines do not work in all patients. If that is the case in carefully controlled clinical trials, it is even truer in the real world, where complications and poor compliance in taking drugs correctly lower efficacy still further.

The deal was one of the most striking examples of a tougher attitude to reimbursement around the world. NICE, set up to scrutinise cost and clinical effectiveness of treatments for England and Wales in 1999, is in the vanguard of the movement. Janssen-Cilag had originally sought blanket approval for the NHS to reimburse bortezomib. When that was rejected on grounds of excessive cost relative to the benefits, it appealed unsuccessfully before proposing conditional payment as a last resort. Even then, the company suggested offering a rebate in vouchers for other Janssen-Cilag drugs. NICE held out for straight cash reimbursement.

Other countries are using similar approaches in the face of rising prices for new medicines. Iqwig (the Institute for Quality and Efficiency in Healthcare),

NICE's counterpart in Germany, ruled in 2005 that Pfizer's anticholesterol drug atorvastatin offered insignificant clinical benefits compared with its off-patent rivals. It ordered reimbursement only at the cost of generic statins, effectively killing the drug in Germany.

Since the early 1990s, Australia's Pharmaceutical Benefits Advisory Committee has taken a similarly tough approach, with the result that its medicine prices are lower than those in much of the rest of the developed world. Other countries are also considering introducing systems to assess health technology—an idea taken up by the European Union's High Level Pharmaceutical Forum, convened last year between patients, payers, regulators, and companies to discuss issues including drug pricing.

In the US, the drug companies have lobbied hard against price negotiations by government funded medicine purchasing schemes. But private insurers are becoming tougher. United Healthcare, for instance, last year removed AstraZeneca's esomeprazole, a proton pump inhibitor, from its formulary, effectively rejecting claims that the drug offered better value for money than the cheaper alternatives.

The tensions are only likely to grow, with drug companies charging ever more for medicines—notably those to treat rare "orphan" diseases in small patient groups and in cancer, where the costs can easily exceed \$50 000 a year for each patient.

Market forces

In theory, a free market for drugs ought to provide value based pricing automatically: the more medicines that exist with similar therapeutic effect, the greater the competition and the lower the price. If a new drug provides additional efficacy and saves health

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costs overall (such as by providing an alternative to expensive surgery), the more its manufacturer can justifiably charge.

In practice, the relation between value and cost is far less clear, partly because drug pricing is not freely determined but set by government. The UK and Germany come closest to free pricing in Europe, but even in these countries after an initial price has been set—and later scrutinised by NICE or Iqwig—it cannot rise and rarely falls until the patent expires and competition drives down the cost.

German regulators priced out anticholesterol drug, Lipitor, by offering only generic prices

Many countries' governments regularly impose crude price cuts after launch, with little regard to the efficacy of particular drugs. The most recent renegotiation of the UK's long running pharmaceutical price regulation scheme in 2005 demanded an average reduction of 7% across all drugs, for example.

In a report published earlier this year, the Office of Fair Trading highlighted important weaknesses with the system and called for reforms in order to introduce value based pricing for medicines in the UK.

One idea it endorsed was a risk sharing scheme that GlaxoSmithKline recently began discussing with several European healthcare systems. The company argues that it should be allowed to set an initial price at launch but then be able to raise or lower the price after 1-2 years once meaningful data on its true benefits and costs have been collected.

The Office of Fair Trading also highlighted the possibility of price-volume agreements—a way to deal with the fact that companies launching a drug at a high price for a small group do not then cut the price when it is

approved for other indications and used by far larger numbers of patients.

Finally, the office recommended introducing a cap on the price of new drugs that offer only a marginal benefit over existing treatments. However, that raises one of the drug companies' greatest concerns with value based pricing. They argue that most innovative medicines are developed in stages, with each new drug providing modest improvements that lead to breakthrough medicines over time. Removing the financial incentives for incremental research risks killing off long term progress.

More generally, Arthur Higgins, head of Bayer HealthCare and the newly elected president of the European Federation of Pharmaceutical Industries and Associations, the trade body, says he is open to discussing value based pricing but the industry fears that the approach is being used as a pretext by politicians simply to add additional hurdles to the approval of medicines and save costs.

Link between research and price

The industry also argues that many countries that have rejected or aggressively pushed down the price of new medicines have also failed to build—or undermined—a domestic drug industry. Their health systems are free-riding on research funded by more generous payers elsewhere.

There are certainly few research based drug companies in lower priced markets such as Australia or southern Europe, and many more in the US, the UK, and Switzerland, which have paid higher prices and launched other policies to encourage research.

Furthermore, in many European countries the price of generic drugs is only slightly below the patent price. The US, by contrast, stimulates more aggressive competition and much lower generic prices, saving costs and allowing healthcare providers to reward newer patented drugs with higher prices.

Value based pricing offers a separate set of challenges for regulators and advisory bodies such as NICE. Health economics remains a relatively undeveloped and poorly resourced discipline, and there are fierce intellectual debates over how to measure the additional efficacy and cost savings of new drugs. NICE's own resources would need to

be significantly increased to undertake such scrutiny.

Tracking the true costs and benefits of drugs after launch is also likely to be expensive and not always easy to do. It may be feasible for bortezomib, given the infrastructure already in place to monitor patients with myeloma closely. It will prove more difficult for many other treatments.

After NICE rejected NHS reimbursement of interferon beta and glatiramer acetate to treat multiple sclerosis in 2002 as not cost effective, the Department of Health approved the medicines in any case. In a model for bortezomib, it established a pioneering risk sharing system with the manufacturers, who could face price cuts if the treatment results are disappointing.

So far an estimated 10 000 patients are being treated at annual cost of £50m,¹ of whom half are being regularly monitored over a decade by researchers. The Multiple Sclerosis Trust, which helps administer the schemes, estimates the system is likely to cost a further £5m. The first assessment is due to be completed this summer, so no price changes have yet been introduced.

Risk sharing offers advantages to companies that can show their medicines provide important extra value to patients. But they will need to be able to prove it with data, and any price reductions implemented in one country are likely to be rapidly imposed in other countries.

More broadly, value based pricing is a tempting objective for policy makers but far from a universal cure. They have to trade price reductions against the need to continue to stimulate future medical innovation.

Above all, drugs typically represent 10-15% of total healthcare expenses in most countries. Value based pricing will probably make only a marginal difference to that proportion. If healthcare providers' real concern is capping a growth in health spending, they will also need to tackle the more difficult task of limiting salaries, infrastructure, and other far greater drains on their budgets.

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1 Department of Health. *HSC 2002/004—Cost effective provision of disease modifying therapies for people with multiple sclerosis*. www.dh.gov.uk/en/Publicationsandstatistics/Lettersandcirculars/Healthservicecirculars/DH_4004332.