No-name heroes can save Europe billions

Anna Wagstaff

European countries struggle to fund new cancer drugs which bring benefits at a high price. Meanwhile billions of euros are wasted, say researchers, because doctors prescribe branded drugs when a generic equivalent is just as good, and because the cost of generics is far too high.

IN late January 2007, two more cancer drugs fell victim to health rationing, when England's National Institute for Health and Clinical Excellence (NICE) decided against making either Avastin (bevacizumab) or Erbitux (cetuximab) available on the National Health Service for metastatic colorectal cancer. The decision followed the rejection last October of the case for public funding of Velcade (bortezomib) in the treatment of multiple myeloma, and a preliminary decision in November against Tarceva (erlotinib) for lung cancer.

At issue was not whether the drugs offered clinical benefit, but whether the cost–benefits represented the best use of limited National Health Service resources. NICE decided they did not.

The decisions sparked protests from patients and doctors alike, but public anger is tempered by a recognition that healthcare expenditure is escalating faster than the country can afford and that some form of rationing is the only answer. NICE – an independent body, taking expert advice from all stakeholders and following transparent procedures – seems the fairest way to achieve this. But is it looking in the wrong direction?

Panos Kanavos is a health economist based at the London School of Economics. He and his colleagues have spent the last few years researching pharmaceutical policies in Europe and the US, and he believes that if the public and politicians were aware of how much money is wasted in the overall drugs bill, they might think again about denying cancer patients drugs that could help them.

Much of his recent work has focused on the market for generics. A generic drug is the chemical and bioequivalent of a drug that has an expired patent (usually after 25 years), and which can therefore be copied by other companies and sold under the generic drug name. Because generic medicines replicate an existing drug, there are no research and development costs and no 'innovation' or 'risk' premium to be reflected in the price. In a free market, the price of generics should therefore be the cost of production plus a reasonable profit margin.

The problem is, says Kanavos, the market is distorted. Price levels are maintained significantly above what the companies would accept. Wholesalers and pharmacies negotiate major discounts from the manufacturers, which are not passed on to the end-payers. A failure to encourage doctors and pharmacists to opt for equally effective lower priced drugs results in inefficient prescribing practices, particularly where there are heavily marketed branded products, which often command a price close to the original patented medicine.

These 'branded generics' may be a continuation of the original product supplied by the same manufacturer at a slightly lower price, or a new brand name produced by a generic company when the original is newly out of patent. The research by Kanavos and colleagues showed that these 'branded generics' tend not to go down significantly in price as new suppliers enter the market, and that prescribers often

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stick with the brand name, despite the price difference.

Taken together, this represents a massive area of potential saving, according to Kanavos. "The situation varies widely from country to country, but speaking very generally, we have shown that in a country that spends about 15 billion euros on medicines, and about 5 or 6 billion of that on generics, we could save about a quarter of that, simply because we are paying too much." That implies savings of 1 to 1.5 billion euros, up to 10% of the entire drug budget.

Evidence for this comes principally from comparing the prices at which a selection of generics retail to health services or health insurance schemes in a number of European countries, the USA and Canada.

A12-FOLD PRICE DIFFERENCE

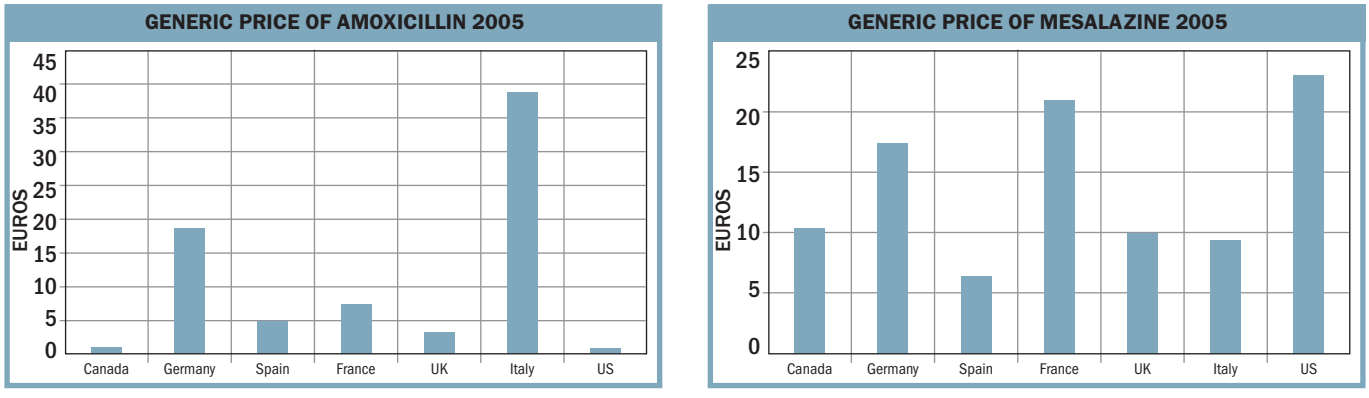
Take mesalazine, used for inflammatory bowel disease, and mooted as a preventive for IBD-related colorectal cancer. In the UK it retails at an average price of 10 euros, in Germany at 17 and in France at around 21 euros. Metformin, a drug widely used to control diabetes, retails for around 0.7 euros in Spain and the UK. In Germany the price is closer to 1.8 euros, in France 3.5 euros and in Italy 4.2. In other words, Italy is paying six times the price paid by their Iberian cousins, for the same product. The story is similar for the antibiotic drug amoxicillin, for which you pay 3 euros in the UK, 5 in Spain, 7 in France, 18 in Germany and 38 in Italy – more than 12 times the UK price.

These findings are set out in an LSE discussion paper (Kanavos and Costa-Font 2007) which looked at 13 generic molecules. Though none are used primarily in cancer patients, they are all paid for out of the same, overstretched drugs budget. A saving on this would allow for greater flexibility when considering how to pay for new and expensive anti-cancer drugs.

But while the study shows that, overall, prices tend to be significantly lower in the UK and Spain than, for instance, Germany, France or Italy, it would be wrong to conclude that the UK price must therefore be somewhere close to the lowest price companies would agree to sell at. A further piece of research into the UK distribution chain (*Curr Med Res Opin* vol 23, pp105–116) has revealed that pharmacies are able to negotiate substantial discounts from wholesalers or the manufacturer, without passing on the savings. This means that while the National Health Service is paying the prices quoted above, the manufacturer is content to supply the product for far less.

The maximum discounts offered by the manufacturer exceeded 60% of the price paid by the NHS in 20 of the 31 generic products included in the study, while in a further seven the maximum discount ranged between 50% and 60%. It is hard to avoid the conclusion that if European health systems got their act together, they could purchase the same generic drugs for a fraction of the current price.

This situation would not be sustainable in a free market, where in theory



Why pay more? Significant price differences for identical molecules across countries indicate the potential for very substantial savings in Europe's drugs budgets

Source: Generic Competition in Drug Markets and the Impact of Regulation, Kanavos and Costa-Font, LSE discussion paper, 2007

excess profits attract new entrants and competition pushes the price down. But that's not how pricing in most European countries tends to work.

Drug prices in Europe are heavily regulated, and every country has its own system. Prices, including those of generics, tend to be agreed in negotiation between the government and the drugs companies, often with the involvement of health insurance agencies. Kanavos and colleagues have identified a number of practices that tend to result in high generic prices.

Often the price of a generic drug is closely related to the price of the original patented drug. When the drug's patent ends, negotiators look to lop around 20%–30% off the patented price. Very often, this is taken as a 'reference' price, which means that additional generics of the same molecule cannot come onto the market as a higher price. However, unless there is pressure within the system to purchase at the lowest price possible, or incentives for pharmacists to give priority to lower priced products, new manufacturers coming into the market have every reason to keep their prices close to the original reference price, preventing prices from falling.

It seems hard to believe that, while patients are denied drugs that could help them, and health professionals are obliged to tailor decisions to budgets, this inefficiency in the price of generics is allowed to continue. Kanavos puts it down to a combination of inertia and caution. "We are humans, and we are creatures of habit. Some policy makers are convinced that it is much better for them to stick with a particular system that delivers them 30% say, as opposed to a system which, if they dare implement it, could deliver them twice as much. But it takes knowledge, guts and pressure to do all that."

Else Borst Eilers, Minister for Health in the Netherlands between 1994 and 2002, is an interesting case in point. She joined a government under intense pressure to cut back public spending, and she is widely respected for having had the guts to look for savings not where they were easiest but where they would hurt patients least – in her own words: "I always argued that before we set priorities in the sense of withholding treatment from those who need it, we should try to make healthcare much more effective and efficient". One of the areas she targeted was the price of generic medicines. It commenced with an average pricing scheme through legislation introduced in 1996. This was followed up eight years later by an agreement brokered between health insurance funds, pharmacists, generic medicines companies, and the government to reduce prices of generic medicines by a further 40% (including 'claw-back' of discounts).

Price, however, is not the only obstacle to bringing down drugs bills. The other major factor, which has received more attention in recent years, is the extent to which prescribers switch from branded drugs to take advantage of cheaper generics.

Making the switch

Here too the picture varies widely across Europe. Figures from the European Generics Association indicate that generics account for a very high proportion of all drugs prescribed in most central and eastern European countries – more than 85% in Poland. These countries have traditionally relied heavily on generics, many of which they produce themselves. They represent some of the poorer countries in the EU, where cancer patients are fighting to get access to cancer drugs such as Glivec [imatinib] or Herceptin [trastuzumab].

At the other end of the scale eight countries, including Italy, Spain and France, prescribe only between 3% and 13% of drugs as generics. In the middle come those western European countries that are actively pursuing policies to encourage the use of generic medicines. Denmark leads the way, with almost 65% of all prescriptions made out as generics, followed by the UK and the Netherlands, at close to 50%, and Germany and Sweden at around 40%.

A hypothetical exercise conducted by the Research Centre for Pharmaceutical Care and Pharmaco-economics at Leuven's Katholieke Universiteit in the Netherlands (Simoens and De Coster, 2006) tried to quantify the savings different countries could make by increased use of generics. For each country, they selected the ten branded originator medicines that accounted for the highest expenditure, and looked at what would happen if 95% of prescriptions for those active substances were made out to generics.

They estimated that, even at the current price of generics, there are savings to be made ranging from 21% in Poland to 48% in Denmark (47% in

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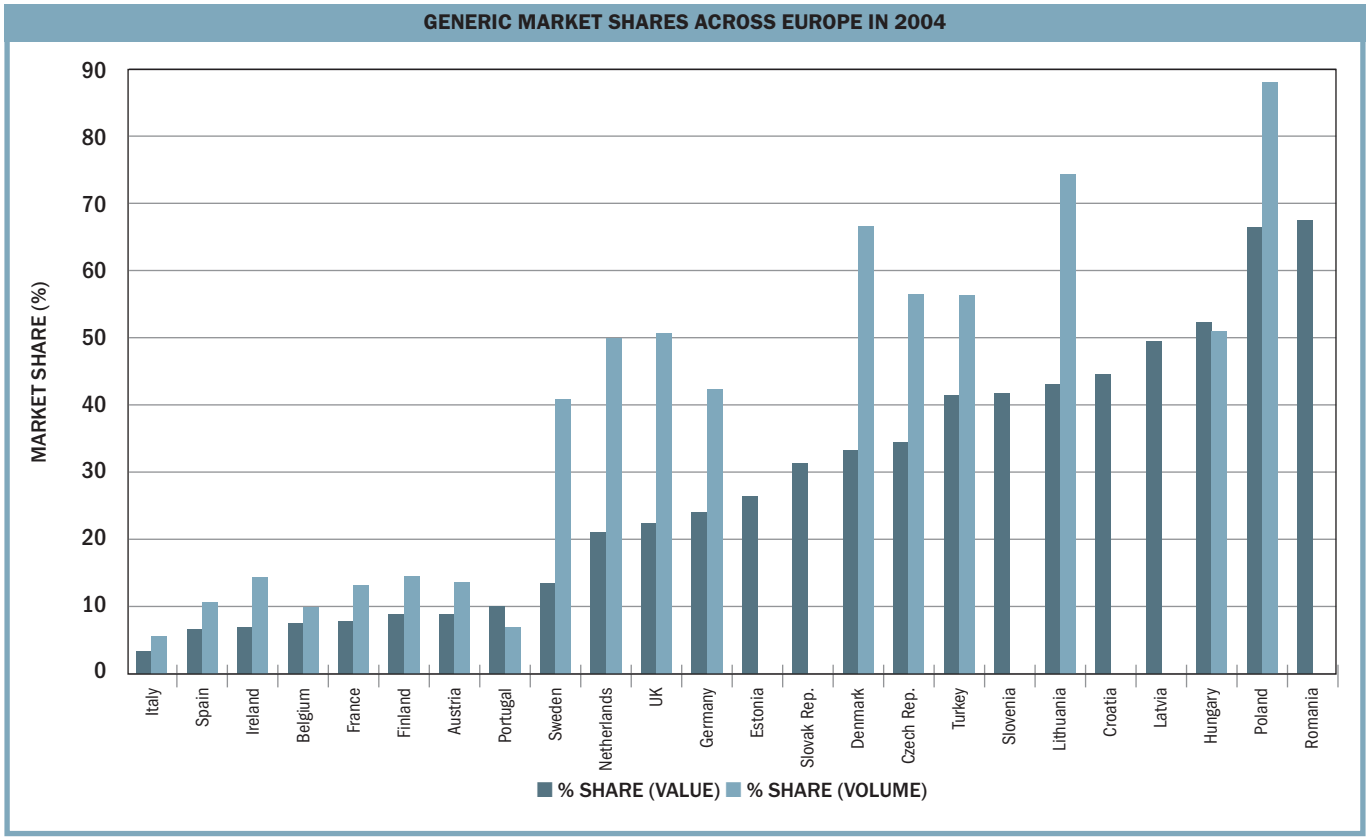
Germany, 42% in Portugal and Belgium, 41% in the Netherlands, 35% in France, 33% in Spain and the UK, 31% in Italy, 27% in Austria). Though the authors stress that the exercise was done for illustrative purposes only and failed to take into account many relevant factors including possible differences in form, strength or package size, it nonetheless indicates that substantial sums could be saved from national drugs bills by encouraging greater use of generics.

However, doctors are likely to stick with the drugs they know, and the ones that are most effectively marketed, unless they have sufficient information and incentives to persuade them to switch.

A variety of approaches are used to promote the use of generics. The first step is to make doctors aware of the cost implications of their decisions and of the generic alternatives. Some countries use prescribing software that substitutes the generic (international non-proprietary name – INN) of the drug for the branded name, with various rules on whether and when the doctor can insist on a particular brand.

Some countries set prescribing budgets at the level of the individual general practitioner (as in Ireland) or at the level of a family doctor practice or at local or regional levels (as in Germany, the UK and some counties in Sweden). These provide an incentive for GPs to bear costs in mind when making out a prescription, but only work if they are enforced. They can be unresponsive to changing circumstances and result in sudden alter-



Missed opportunities. Increasing the proportion of prescriptions made out to generic medicines could relieve the pressure on many of Europe's overstretched drugs budgets

Source: Internal survey, European Generic Medicines Association, 2004

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ations in prescribing as the financial year ends and the budget runs low.

In reimbursement systems that include some element of patient co-payment, variations in charges are sometimes used to encourage patients to opt for a cheaper generic version.

Another option is to allow pharmacies to substitute generic versions when presented with a prescription for a branded product. In Denmark and Germany, for instance, this is mandatory and widely practised, although in Germany doctors have the power of veto. In the UK, the pharmacist only has discretion when a prescription has been made out for an INN. In Greece and Ireland, generic substitution is not permitted at all. Policy makers have to bear in mind how the dispensing fee to the pharmacist is calculated. If the fee is a percentage of the cost of the drug supplied, the pharmacist has an incentive to use a higher priced drug.

One approach being introduced increasingly in Europe is the promotion of prescribing guidelines, which encourage doctors to prescribe rationally and consistently according to a medicine's indications and the therapeutic needs of their patients. This should increase value for money, by cutting expenditure on drugs for which there is scant evidence of effectiveness. It also offers an opportunity to promote cheaper drugs among those that are medically interchangeable.

These measures do not always go down well with doctors. In Hungary, a recent law obliges all physicians to use a free downloadable software package when prescribing, showing the various options for each type of drug. Mihály Kökény, chair of the health committee of the Hungarian Parliament, says that this is part of a major overhaul of the Hungarian health system, which also includes a novel system for conducting negotiations about the price of generics over a publicly accessible Internet system.

"The minimum requirement is that the patient should always be informed that there are various options, 'I would like to offer you this and this, but there are other versions of that molecule'. The doctor must also put in writing in the patient notes that this information was given to the patient. If the doctors do not use the available generics they need to give a reason for this in the documentation, and this can be checked by the insurance.

Sanctions

"If the insurance can see that a doctor in most cases prescribes more expensive drugs, without giving an appropriate reason, the insurance has the right to introduce certain types of sanction, such as a fine for the doctor.

"The doctors are not happy. But everybody should understand, if a doctor makes a prescription, he is spending public money, and it is a must to obtain the maximum health gain available."

Kökény blames heavy drug marketing for some of the resistance, but he believes that raising awareness about the reasons for these changes and reassuring doctors about the strict quality control measures now applied to generics will help overcome it. The sanctions, he says, will not come into force for many months, which should give time for doctors to get used to the system.

There are, however, good reasons for doctors – and patients – to be suspicious of prescribing guidelines, which are sometimes used not to ensure the best value for money, but to ration healthcare. When a doctor is asked to prescribe a non-branded version of mesalazine or amoxycillin, they are being asked to choose a cheaper version of an identical molecule. However, guidelines increasingly consider classes of drugs as a whole, (e.g. anticoagulants or cholesterol-lowering drugs) and pressure doctors to use a cheaper drug, which may be similar but not identical.

In this case there may be a number of reasons why a doctor will argue that a more expensive drug is required – maybe the side-effect profile is different, or the mode of administration means the patient is more likely to comply with one drug rather than another. If doctors are prevented from prescribing a drug that they have good reason to believe is the most appropriate for their patient, this constitutes rationing. It is important to be transparent about the distinction between this and promoting generic prescribing.

Kanavos and his colleagues argue that significant savings can be made by changes to pricing, distribution and use of generics, without affecting patient care. Some form of rationing is also likely prove necessary. But if governments seek to deny clinically effective innovative drugs to patients in need, without taking every step they can to save money in ways that don't affect patient care, they should expect resistance from doctors, patients and the public.