GENERIC MEDICINES

FOUR YEARS OF UPS AND DOWNS IN THE GENERICS MARKETPLACE

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In this article the author looks at current and future trends in the use of generic medicines in the United Kingdom and at what has changed since he first reviewed the topic in 1997

In my previous article on generic medicines (*PJ*, April 19, 1997, pp554–9) I forecast that generics usage would continue to grow. It has and generics remain a key element in the Government's strategy for the provision of medicines through the National Health Service. Speaking at the British Generic Manufacturers Association's dinner in November, 2000, Lord Hunt (Parliamentary Under-Secretary of State for Health) said: "Generics are crucial to the NHS in two ways. First, as a means to release substantial savings for redeployment in other areas of health care and, secondly, to make a crucial contribution in their own right to the quality of life of patients up and down the country." (*PJ*, December 9, 2000, p845)

Lord Hunt reiterated the target for generic prescribing stated by John Denham (Minister of State for Health) in the House of Commons on March 24, 1999, of achieving an average generic prescribing rate of at least 72 per cent by 2002. Lord Hunt noted that as he spoke the figure had reached almost 70 per cent, and that generics accounted for almost half of all medicines dispensed in the community. Figure 1 gives an update of the official prescribing and dispensing statistics for England. It is interesting to note that the level of generic dispensing has stabilised in recent years, against a background of a rising generic prescribing rate. This can be explained by a combination of increased generic prescribing of products that are still under patent, and by pharmacists continuing to dispense (for commercial reasons) the original brand against generic prescriptions.

Between December, 1996, and December, 2000, the moving annual total market for branded medicines, at NHS purchase prices before clawback, increased by £1,273m to £5,566m, while the cost for generics rose by only £447m to £870m. Total market growth was thus 36 per cent during this period (based on IMS December 2000 figures). It should be noted that the data exclude purchases by hospitals and is gross before deduction of pharmacy contractor clawback.

United Kingdom prices for generics remain the lowest in Europe. Across a sample of commonly used generics, on a pence per tablet basis, prices are two to five times greater in the rest of Europe than in the UK (based on official prices before discounts).

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PRICE EROSION

The market structures for pharmaceuticals across Europe differ greatly. The UK allows free pricing for new chemical entities, leading generally to higher prices than elsewhere in Europe. This is balanced, however, by a rapid penetration of generics following patent expiry, associated with rapid erosion of the Drug Tariff price.

The speed of penetration is helped by the established UK culture of open generic prescribing. This practice is hardly seen in the other major European markets, where prescribing by brand is more common. Price erosion in the UK is driven by competitive activity among suppliers, which in turn applies downward pressure on the Drug Tariff.

Comparing the UK with Germany, if cost price per dosage unit is regarded as the key measure, then the UK market is certainly more effective at delivering lower prices than the German system. Germany is the other major European Union member state with high generics usage. Penetration levels are similar to those in the UK. Pricing lev-

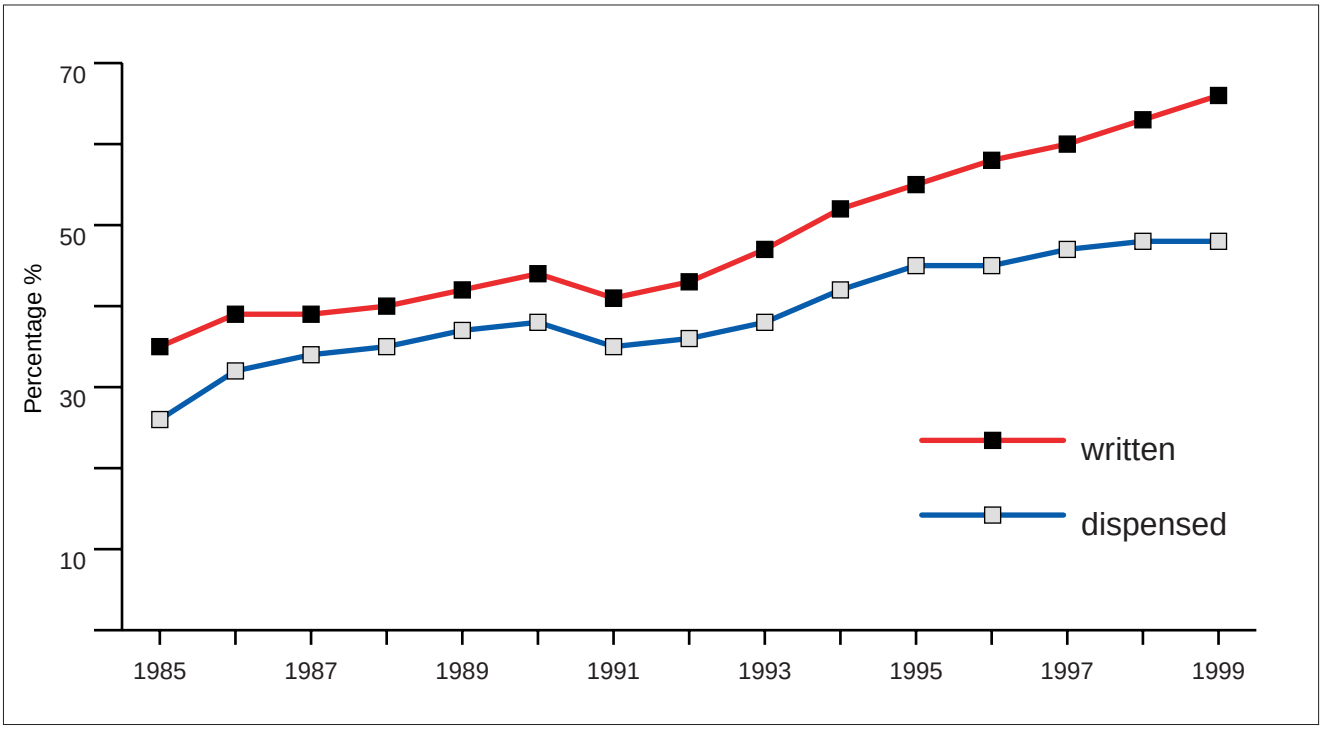

Figure 1: Proportions of prescriptions written and dispensed generically in England since 1985. Source, Department of Health

els, however, are dramatically higher in Germany. Germany is a conventional branded market, where branded generic products are promoted to doctors as a lower cost alternative to the innovator product. Price reductions are seen, but not to the extent in the UK. Table 1 gives an impression of the implications of this for German medicines expenditure, and also shows the limited penetration of generics in other major markets.

All health care providers are aware of the potential role that generics can fulfil in the management of medicines expenditure. Italy and Spain are in the process of introducing measures to stimulate their generics markets, and France introduced generic substitution at pharmacy level in September, 1999.

The evidence of the past four years has supported the view that the UK generics market is expanding, but it is highly competitive and low priced.

MARKET MOVERS

So, during the past four years, has the composition of the suppliers to the market changed? The answer is, that at face value, little has changed. There remain four leading players in the unbranded generics segment — APS/Berk, Cox Pharmaceuticals, Merck Generics and Norton Healthcare. I estimate that each of the companies has a similar position in the market, although Norton is the largest in absolute terms by virtue of its respiratory products portfolio, though many of these cannot be regarded as generics. The other major suppliers remain Lagap Pharmaceuticals and Sterwin Medicines.

So, at face value, little change, but behind the scenes there has been dramatic change, all of it consistent with the forecasts made in 1997. Following the acquisition of Cox Pharmaceuticals by Alpharma in 1998, and the recent acquisition of Lagap by Novartis, all of the major generics suppliers are now part of multinational groups with substantial international generics interests.

Broadly speaking, the companies controlling the majority (at least 80 per cent) of the generics supplies into the UK fall into two categories; global companies with major activity in research based products but with an international presence in generics, and major global generics companies.

The four leading global players now hold a significant position in the UK market (Table 2). The next three companies that follow in the global league table (Mylan Laboratories, Watson/Schein and Barr Laboratories) are either wholly or mainly active in the United States generics market alone.

At a global level, the generics industry is consolidating, driven vigorously by Novartis and Teva. The impact on the local customers is not obvious, apart from when a name change takes place. Such an event in the UK has been Cox changing its name to Alpharma as part of a strategy for establishing an international brand identity.

CONSOLIDATION

What is the rationale behind this consolidation? Company acquisition provides an obvious route to growth, either as a means of boosting market share in a territory where a company is already active or as an entry strategy to a new territory. The profitability of such acquisitions can be significantly enhanced if the acquiring company can liberate synergies in any or all of the cost areas of a generics business; manufacturing, purchasing, product development, sales and marketing or administration. Such synergies have been significant for five of the top six companies and will in time be relevant for Lagap within the Novartis family.

The biggest revolution has been in manufacturing and product development. Of the top six companies, only two (Cox and Sterwin) still manufacture to a significant extent in the UK. Even for these companies, their production is drawn from substantial manufacturing units which are not totally dedicated to the production of generics destined for the UK market.

All the major suppliers have sought to consolidate manufacturing into the smallest number of units positioned in the most

TABLE 1: MARKET SIZE AND GENERIC PENETRATION IN MAJOR EUROPEAN MARKETS

Market	Market size (Ebn)	Generic value (%)	Generic volume (%)
Germany	15.7	39	51
France	14.4	2.2	4.3
UK	10.5	16	53
Italy	9.8	0.4	0.6
Spain	5.8	2.4	2.7

TABLE 2: GLOBAL RANKING OF INTERNATIONAL GENERIC COMPANIES

Parent company	UK trading name
Teva	APS/Berk
Novartis	Lagap
Merck KG & A	Merck Generics
Ivax	Norton Healthcare

favourable locations. Many factors contribute to the selection of an ideal location, and no two companies will select identical criteria. In general terms, the criteria will be cost of labour, investment support and other local incentives, patent climate and the presence of existing facilities.

PATENTS

The patent climate has been a major factor driving first generic product development and then manufacturing out of the UK. A key factor for a successful generics company is its ability to launch new products. Where this involves a patent expiry, it clearly makes sense to aim for a launch on the first day after patent expiry in order to gain competitive advantage. In the UK, in common with other EU countries (apart currently from Italy), it is legal to make a submission of data in support of a marketing authorisation application in advance of a patent expiring. It is not legal to conduct the actual development work, ie, handling or processing the patented active material.

Some countries either have weak patent climates or have specific legislation in place to allow generics companies to conduct development work during the patent term. Countries with specific early working provisions include the US, Israel and Hungary. Global patent and intellectual property rights are subject to global agreements administrated through the World Trade Organisation. The Trade Related Intellectual Property Scheme (TRIPS) regulates conventions and standards for protection of intellectual property rights for pharmaceuticals. A recent dispute instigated by the EU against Canada was resolved by a WTO panel that ruled that early working provisions are consistent with TRIPS, and are thus allowable.

The lack of such an early working provision in the UK, although it has no impact on the ability of a generics company to make available generic products immediately following patent expiry, has driven the majority of generic product development overseas with obvious loss to the UK economy. This has a knock-on effect for manufacturing given that it makes good technical sense to develop and manufacture a product at the same site. Unless there is a change in the attitude of the UK Government towards early working, and provision of incentives to encourage manufacturing in the UK, the trend for the generics industry to move its manufacturing overseas will continue. Since 1996, APS/Berk and Norton have moved such facilities to Hungary and Ireland, respectively.

GENERICS CRISIS

What impact do these structural changes in the industry have for the NHS and for patients? When everything works well, the answer is nothing. Companies adapt to the competitive environment by increasing efficiency and reducing costs. Quality standards are maintained wherever the site of manufacture is under the supervision of the Medicines Control Agency. But what happens when something in the supply chain goes wrong? The events of 1999 are worthy of consideration in this context. I do not intend to cover this in detail, but will focus on the unresolved issues.

The withdrawal from the market of Regent Laboratories immediately before Christmas, 1998, reduced generic supply by volume into the market by some 10 per cent. The majority of Regent's stock in trade continued to be sold, but commercial production at the company did not start again for well over a year. By the end of the first quarter of 1999 it became apparent that the supply chain did not have sufficient spare capacity available to make up the shortfall. The supply chain as a whole (pharmacists, distributors and manufacturers) managed to ensure that patients did not go without medicines, but at significant inconvenience and expense to all concerned. It took until the early part of 2000 for the supply chain to return to normal supply levels.

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MAXIMUM PRICES

Prices did increase in 1999 in line with the market operating as a number of smaller commodity markets. As supply levels normalised going into 2000, the Government was keen to see prices fall back to historical levels. Rather than waiting for the result of its own fundamental review (see below), the Government announced in April, 2000, proposed regulations aimed at limiting the maximum price that could be charged by a supplier to a pharmacist for the vast majority of generic medicines (*PJ*, April 29, 2000, p642). The stated target level for maximum prices was the Drug Tariff for the period of October, 1998, to January, 1999.

Following representations from the industry, supported by others in the supply chain, the proposals were significantly modified and a list of maximum prices for generics was introduced in August, 2000. The modifications reflected the fact that if prices were set too low then the industry might not be prepared to continue to supply. This was particularly true for products such as frusemide (furosemide) which had moved from bulk to patient packs in the intervening period.

The future of the maximum pricing scheme is not clear. It must be reviewed later this year and Lord Hunt confirmed at the BGMA's annual dinner in November, 2000, that the measure was a short-term one.

FUNDEMENTAL REVIEW

A fundamental review of the provision of procurement and supply of generic medicines to the NHS was instigated in late 1999. At the same time the House of Commons Health Select Committee held an inquiry into cost and availability of generics. The fundemental review, being carried out by Oxford Economic Research Associates (OXERA) is still underway. The report, or its conclusions, have yet to see the light of day, although a commitment has been given to place a summary in the House of Commons library in due course. It is known that the report has been presented to Ministers. In any event, the maximum pricing scheme referred to above must be reviewed by November to comply with European law and thus it can be expected that more will be heard of the OXERA report after the general election.

The Department of Health has indicated that a number of options have been identified for the future ranging from a modified version of the existing system to a radical overhaul.

Whichever solution is implemented, to be robust it must strike a fair balance between the price paid by the NHS for each product and the need to maintain adequate depth of supply. Any system must ensure an adequate level of return for all elements of the supply chain — manufacturer, distributor and pharmacist.

For manufacturers, the BGMA seeks an environment where it is possible for them to obtain a fair and predictable return on shareholders' investments. The current arrangements make the former difficult and the latter impossible. The UK generics industry is not highly profitable. In 1999, the total pre-tax profits of the top five suppliers (those publishing statutory accounts that can be readily interpreted) were approximately £45m from a turnover of £420m.

Of course, generics companies choose to be in the UK market, and develop their own strategies to succeed. Surplus capacity is something that cannot be afforded and was shown in 1999 not to exist. At all times, in a market where price is critical, suppliers will make choices among internal and external suppliers on cost and quality. This is a driver of consolidation which can be a danger to integrity of supply in the event of disruption.

Lord Hunt has acknowledged this issue and has requested a specific study to investigate the effects of concentration of supply and propose solutions.

PATIENT PACKS

A major development forecast in my 1997 article was the move of generics from bulk to patient packs. The background to this was European Directive 92/97/ECC, which laid down the requirement that patients should receive detailed product information in the form of a patient information leaflet and that the dispensing label should contain significant quantities of technical information. The only realistic and safe means to

implement the directive identified by industry was a co-ordinated plan to move dispensing in pharmacies to use unsplit patient packs, either plastic pot or strip and blister. In early 1997, a general agreement existed between the pharmaceutical industry, Ministers, the Department of Health and the professions that a phased introduction of patient packs, with rationally selected pack sizes and dispensing rounding rules was the way forward.

The change of Government in 1997 ended the initiative. In a letter to the Association of the British Pharmaceutical Industry dated November 6, 1997, the then head of the Department's international and industry division revealed that the then Minister of State for Health (Alan Milburn) was "now considering alternative means of implementing the directive". To this day these are still awaited.

CONSEQUENCES

The resulting vacuum was to have unfortunate consequences. The majority of manufacturers remained convinced that the move to patient packs was the only safe means of implementing the directive and proceeded with the switch from bulk to patient packs, albeit at their own pace and in a unco-ordinated manner.

In the absence of rounding in the pharmacy, cutting and snipping of blisters remains necessary other than for special containers and calendar packs. This is a highly unsatisfactory situation for pharmacists and patients, as well as for the industry. All parties are left trying to resolve issues surrounding handling split packs, a situation that was never envisaged at the launch of the original patient pack initiative.

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The unco-ordinated move to patient packs was an unwitting contributor to the market turbulence of 1999. The Drug Tariff was too slow in responding to the introduction of the new pack sizes. Consequently, shortages of medicines in the pack size stated in the Tariff were widespread. These enhanced the impression of shortages.

The situation could and should have been avoided. Manufacturers notified the Department well in advance of launching new patient packs and had the Department responded by dual-listing bulk and patient packs during the changeover phase, the number of products officially classed as in short supply at the Tariff price would have been less.

The changeover to patient packs has had implications for all elements of the supply chain, from manufacturer to patient. In the pharmacy, procedures are required to address the issue that product identification has changed radically in that the packaging itself now plays the major role rather than the actual dosage form itself. This is also true in the patient's home but to a lesser extent where of course the product is removed from the packaging before consumption.

There are no easy solutions to such a major change in practice. Blister packaging is the norm throughout Europe. The UK up until the change to patient packs was almost unique in dispensing from bulk. Manufacturers are acutely aware of the need to monitor and respond to feedback from users where pack design and layout and use of colour are concerned. It is a fact that there is not a perfect design, nor can any design remove the need for diligence in the storage and selection of products at the point of dispensing, though suppliers have and will continue to introduce refinements. The BGMA is in talks with the Royal Pharmaceutical Society on this topic.

THE FUTURE

Turning now to the future for generics. As has been stated, use of generics is a key element in the medicine strategy of the NHS. Generic prescribing and dispensing are rising over time and will continue to do so.

Over the next five years over 100 molecules lose patent protection and as of December, 2000, these accounted for in excess of £3bn sales from the innovator original products. This is clearly a major opportunity for both the industry and the NHS. At the time of writing the previous article, however, innovators were starting to implement strategies to prolong the period of their monopoly on molecules as they approached patent expiry. Since then, such activities have become more commonplace.

It is appropriate to set the originator/generic context. There is no dispute that genuine innovation merits a full period of patent protection, in order to provide the innovator with a return on its investment. At the end of the patent period, generic competition should immediately commence, in order that the next round of genuine innovation can be afforded by the NHS and that the rapid loss of business endured by the innovator becomes itself a stimulus to further innovation.

PSEUDO-INNOVATION

Worrying trends are emerging with the appearance of pseudo-innovation, where minor changes are made to existing formulations or molecules with the objective of prolonging monopoly through blocking generic competition, but without associated significant therapeutic advance.

Examples include replacing a conventional release formulation with a modified or sustained release before patent expiry. Discontinuation of the original formulation before patent expiry and switching patients to the new one could extend the monopoly (under existing European law) by 10 years. This introduce, switch and discontinue strategy is now being applied to different isomers of previously established molecules. If such a change results in a new patent, then the monopoly could be increased up to 20 years.

Different salts and esters are a further dimension, and arguments continue over whether these can be viewed as essentially similar. This is a key test under EU and UK law to determine whether a product can be authorised and offered as a substitutable generic. If these arguments are lost, and switch strategies successfully applied, monopolies will continue.

With large sums of money at stake, it is no surprise that innovators probe deeply into the laws and regulations that govern the protection of data and intellectual property in the hope of obtaining further protection for their existing products. If new generics are to remain a key part of medicines strategy it is important that the UK Government and its EU partners find the right balance between rewarding genuine innovation and allowing free generic competition immediately on expiry of the basic molecular patent.

EUROPEAN LEGISLATION

The 2001 review of European pharmaceutical legislation is currently underway with member states deciding the positions they are to take. In the UK the Government, against a background of a long history of a successful and vibrant innovative pharmaceutical industry, is maintaining a high profile following the publication of the report of the Pharmaceutical Industry Competitiveness Task Force. However, what we have seen of the UK Government's position in the European review negotiations appears to fail to strike a fair balance between reward for genuine innovation and open generic product market access.

In particular, it appears to offer rewards for pseudo-innovation and to reintroduce into legislation the sort of opportunities for seeking ill-deserved extensions of monopoly positions by the innovative sector that I have commented on above. The continued growth of the generics industry, producing downward pressure on the drugs bill and encouraging true innovation, will be at risk unless the Government's proposals are modified in the forthcoming negotiations.

In summary, the past four years have seen the use of generics expand. Generics remain firmly part of Government policy with respect to supply of medicine through the NHS. Major structural changes have taken place among suppliers to the market, driven by the need to boost efficiency in response to competitive pressures.

Major reviews are under way on future supply arrangements to the NHS and on EU pharmaceutical legislation. If handled well, these reviews will afford the NHS continued access to new innovative medicines and high quality generics provided by a pharmaceutical industry that receives a fair return for its efforts, operating in a competitive environment.