FOCUS ON THE NETHERLANDS

In a healthcare system where insurers wield increasing power, huge pressure is being exerted to cut prices of both branded and generic drugs.

THE NETHERLANDS AT A GLANCE

GDP: €468.1 billion (2009)
GDP growth: -3.4% (2009)
Total healthcare expenditure per capita: €58 billion (2009)
Healthcare expenditure as percentage of GDP: >12% (2009)

Figures from IMS Health
INTRODUCTION

The Netherlands is facing its worst economic crisis for many years. Consumer and business confidence has slumped and credit conditions have deteriorated. Real growth started to decline in mid-2008, although growth for the year was positive at 2.1 per cent, with all components of aggregate demand registering positive results.

The most recent data, from mid-2009, predicted that the outturn was expected to reverse in 2009, with GDP expected to contract by 4.0 per cent. Private consumption, which rose in 2008 on the back of higher employment, was set to contract by 1.2 per cent in 2009 as unemployment rose and credit conditions worsened. Investment was also predicted to fall by 7.2 per cent after several years of strong expansion. Only government consumption increased, albeit slightly. Exports, which drive the economy forward normally, shrank by 8.2 per cent as demand in the developed and developing worlds fell back. Recession is set to characterise the economy in 2010 and real growth will not resume before 2011.

Almost two years into its four-year term, by 2008, the governing coalition of the Christian Democratic Appeal (CDA), the Labour Party (PvdA) and the Christian Union (CU) was suffering voter disaffection, particularly with the PvdA and its leader, Wouter Bos, who is also the minister of finance.

The coalition suffers from regular disagreements between the CDA and PvdA and growing numbers of voters saw it as ineffectual in 2007 and 2008 because of disagreements over tax policy, benefits programmes and the budget. Other causes of voter disaffection may be attributed to economic concerns relating to the global financial crisis, and increasing anti-immigration sentiment.

Their low rates of public approval and the economic slowdown caused the two dominant parties to smooth over their differences and pursue a more unified position towards the end of 2008, especially in drawing up the 2009 budget. The government also took a proactive approach to stabilising the financial system, which boosted the coalition.

HEALTHCARE SYSTEM

Healthcare provision in the Netherlands is universal, and emphasis is on guaranteed access in accordance with the principles of solidarity and equality enshrined in the Dutch constitution. The system is highly regarded and increasingly seen as a model for other countries pursuing healthcare reform. A basic level of private health insurance is mandatory.

Unlike many other European countries, healthcare in the Netherlands has always been privately provided, with primary care doctors and practices, hospitals, nursing homes and so on traditionally having negotiated contracts and budgets with health insurers. The system encourages competition among providers and patient choice in respect of insurers, with the latter obliged to purchase the best care at a reasonable price. Insurers must accept every Dutch resident in their area of activity and a risk-equalisation scheme prevents ‘cherry-picking’ of affiliates.

The government is responsible for health policy but does not play a major role in financing healthcare. In what may be described as a system of regulated competition, funding is through a compulsory basic insurance scheme for curative care – that is, care provided by general practitioners (GPs) and hospital specialists, which also covers pharmaceuticals. The system is run by private insurance companies that may make profits and pay dividends to shareholders. The Health Insurance Board (CVZ) co-ordinates implementation and funding of the insurance schemes, representing an independent position between the government and the insurers.

Health insurers contract with healthcare providers (hospitals, doctors, etc) to provide health services or, in some cases, they deliver care directly through their own facilities. As a result of the move to a more market-based system, relationships among providers, insurers and patients have altered, with providers having to negotiate more extensively with insurers in respect of price and quality of service.

Healthcare in the Netherlands is primary care-led. Patients are registered with a ‘huisarts’ (home doctor/GP), who acts as a gateway to secondary care.

Most prescription drugs – and some over-the-counter (OTC) medicines – are reimbursed under the health insurance system. The Dutch tend to use relatively few medicines in comparison with other Europeans. The lower consumption can be explained to some extent by the ageing of the Dutch population, which is lower than the European average, although the main reason is conservatism on the part of consumers and prescribers in respect of prescription drug use. The government adopts a ‘hands-off’ approach to pharmaceutical provision, leaving this to the insurers.

GOVERNMENT HEALTHCARE POLICY

Government health policy will focus on further development of ‘regulated competition’.

The next stage will be expansion of the negotiable aspect of hospital reimbursement, although this will not go beyond 70 per cent. The health minister has noted that the remaining 30 per cent, comprising ‘acute care and top-end academic care’, will not be negotiable, as it is not suitable for a free market.

As far as prescribing is concerned, the government will look at current guidelines amid criticism that these are updated too slowly, which hinders uptake of new medicines. A more evidence-based approach can be expected with new guidelines.

As insurers are responsible for funding and delivery of most healthcare services, they will play a major role in developing health policy at macro and micro levels. For prescription medicines, they provide major input into prescribing and pricing policies at national level. At the level of individual doctors and pharmacists, they will exert increasing control over both prescribing and dispensing in order to curb costs.

Pharmaceutical reimbursement pricing will remain a focus of interest, especially as the transition pricing agreement expired at the end of 2009 and the government is considering deregulation.

In common with its counterparts in other countries, the Dutch government is planning to introduce electronic medical records.

In February 2009, parliament voted in favour of a bill that would make it compulsory for healthcare providers to be linked to the national electronic medical record system. This is expected to take effect from spring 2010, but will apply only to GPs, pharmacists and specialists. Patients will have to give their permission to be included in the system and will have the right to lodge an objection.
# Expenditure

Total expenditure on health in the Netherlands is running at about €58bn, or over 12 per cent of GDP. The rate of increase in health spending has accelerated to 7-8 per cent per annum over the past two years, up from 4-5 per cent in previous years, in line with demand for new health and medical technologies and the ageing of the population. The government appears fairly relaxed about the increase, perhaps anticipating that pressure on pharmaceutical prices and changes to hospital reimbursement will help reverse this trend. The health ministry has been overspending its allocation, but is expected to balance its budget by 2011, assisted by cost savings from financing reforms in the hospital sector, among other things.

Insurers’ spending on healthcare totalled €27.6bn in the first nine months of 2008, compared with €25.4bn in the same period in 2007 (+8.5 per cent). While the rate of increase in expenditure has risen, it remains below the double-digit figures of 2001 and 2002. The main reasons for the slower growth rate in recent years have been restrictions on reimbursement (removal of OTC-type products), price cuts on off-patent medicines and lower wage costs for health professionals.

Hospital care accounts for about 20 per cent of the healthcare budget, while outpatient pharmaceutical care accounts for around nine per cent.

The Dutch drug bill, at around nine per cent of total healthcare costs, is low in comparison with other countries. However, the ‘preference policy’ adopted by insurers, whereby only the cheapest drugs in a rapidly expanding range are reimbursed, had a major deflating impact on pharmaceutical costs.

Costs were also pushed down by the effects of the maximum price policy as the weaker UK pound hit Dutch prices. Volume growth in terms of defined daily doses (DDDs) was also higher than expected in 2008, growing by 3.8 per cent. The preference policy is helping to offset the growth in spending on expensive medicines (those costing more than €500 per prescription). This element of the drug bill grew by 20 per cent in 2008, to €839m.

Further savings on pharmaceutical expenditure will be realised as a result of the preference policy and maximum pricing, as well as through the transition pricing agreement between industry, government and pharmacy, which imposes price cuts on off-patent products. The brand industry hopes there will be some relief in respect of the maximum price scheme as discussions are being held with the health ministry on the downward pressure on prices caused by the fall in the value of the UK pound. There is some expectation that the rate of growth for pharmaceutical expenditure will begin to rise again.

There have been swingeing price cuts on a range of off-patent products as a result of the preference policy. When the price wars began in 2008, the cost of treating osteoporosis, for example, declined by 17 per cent (to €62.6m), mainly as a result of a price cut of 85 per cent on alendronic acid (Fosamax); the number of prescriptions for the drug rose by 6.1 per cent, to 1.2m. Similarly, despite an increase of 3.5 per cent in volume use in terms of DDDs, the cost of antidepressants fell by 28 per cent to €86m, with the decline attributed to price cuts prompted by the preference policy.

# Market Value and Growth, Access and Regulation

The pharmaceutical operating environment has become much harsher in the Netherlands over the past year or so. A sharp slowdown in sales growth reflects price wars on off-patent products and the insurers’ view that generics in some therapeutic classes (notably statins) are therapeutically interchangeable with top-selling patented products. The transition pricing agreement has cut the price of new generics by 50 per cent and insurers’ preference policies have prompted even greater reductions. Brand, as well as generic, manufacturers have been hit by falling maximum prices as the UK pound declined against the euro.

Companies now face a period of uncertainty on pricing, at least until a decision is taken on how the market should be regulated (or not) following the transition agreement expiry at the end of 2009. That uncertainty looks set to stretch through 2010. In the meantime, extension of the preference policy to include therapeutic clusters, if the pilot programme is pursued in 2010, would be bad news for manufacturers of patented brands whose products are already clustered in the reimbursement system.

There is some optimism that the market will begin to recover. With the generic share in value terms on the decline, original brands are taking a larger share, at 76.3 per cent in 2008 versus 73.9 per cent in 2007, according to IMS Health data. Demand will continue for breakthrough medicines, particularly for the hospital market where premium prices can still be obtained, albeit with closer scrutiny of cost-effectiveness and therapeutic advantages, and the likelihood of more restricted usage. Introduction of new medicines will feed through into higher sales, especially in the hospital sector. However, there was a drop in the number of medicines containing a new active substance launched in the Netherlands in 2007 – to 19 from 33 in 2006. This lower number, along with expiry of patents on drugs such as Pantozol (pantoprazole), Efexor (venlafaxine) and Casodex (bicalutamide) will clearly have an impact on pharmaceutical sales growth.

Staff cuts are being made in the Netherlands in line with the worldwide trend. At the end of April 2009, for example, GlaxoSmithKline announced 100 redundancies, or about a quarter of its Dutch workforce. The merger of Schering-Plough into Merck & Co also had particular implications for the Netherlands, as Schering-Plough had previously acquired the Dutch firm Organon.

# Market Forecasts for Audited Sales - Netherlands

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<tr>
<td>Country sales - $ (millions)</td>
<td>6,986</td>
<td>7,324</td>
<td>7,710</td>
<td>8,146</td>
<td>8,610</td>
<td>9,034</td>
<td></td>
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<tr>
<td>Growth - $ (%)</td>
<td>9.00%</td>
<td>4.80%</td>
<td>5.30%</td>
<td>5.70%</td>
<td>5.70%</td>
<td>4.90%</td>
<td>5.30%</td>
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*CAGR = Compound annual growth rate

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MARKETING

Access to doctors is becoming much more difficult for pharmaceutical company sales reps, not least because prescribing now influenced to a large extent by payers, and also by product information from non-industry sources.

Salesforces are being cut back in the Netherlands, as elsewhere, and marketing strategies are being adapted so that sales reps are now taking on the role of account managers, focusing on different decision makers. These will include insurers, with companies now developing special account teams to target payers. Given the relatively small number of insurers and consolidation in the insurance sector, firms will not need large salesforces or significantly increased marketing budgets to address this target group. Companies marketing generics are much less likely than brand companies to target insurers, as the criteria for selecting multisource products tend to focus only on price.

Firms still spend most of their promotional budget on salesforce activities, although this declined from 80.6 per cent in 2004 to 75.4 per cent in 2008. The number of rep visits per doctor continues to decline – from 5.3 per month in 2006 to 4.5 in 2008, according to IMS Health data.

Sales and marketing efforts will concentrate on unique and non-interchangeable products, especially those aimed at specialists.

The Netherlands is more advanced than many other European countries in terms of using new promotional tools and approaches. More stringent rules on pharmaceutical promotion, especially relating to company-sponsored hospitality for doctors, have been welcomed by smaller companies with much lower promotional budgets, to the extent that tighter rules result in a more level playing field in relation to expenditure.

There are no plans to change the current system of regulating pharmaceutical promotion, although a close eye will be kept on the influence of companies on continuous medical education for health professionals and on sponsorship of research and of patients’ organisations. Also, companies will have to be wary of using phase IV studies for promotional purposes.

While there will be new decision makers in respect of prescribing, the overall number of promotional targets is likely to reduce over the prognosis period, particularly as insurers gain more influence over the prescribing practice of contracted doctors. Also, new treatment guidelines and protocols will lead to more standardised prescribing. These developments imply a need for fewer company sales reps, but for more reps experienced in putting across the pharmaco-economic, as well as the clinical, message.

PRICING AND REIMBURSEMENT

The Pricing & Reimbursement (P&R) system is relatively advanced in terms of structure, assessment criteria and implementation and has influenced the design of other European P&R systems. In 2009 it covered €5.2bn, which is about nine per cent of all health care expenditure. After 19 years of the outpatient reimbursement system (1991) and eight years of the in-hospital reimbursement system (2002), there is room for improvement.

A dual system finances medicinal products. Products for outpatient care are covered by the “Dutch Price Reference System” (GVS), which contains either clusters of substitutable products with a reimbursement limit or unique individual products without one. The in-hospital system is broadly similar, but lacks reimbursement limits. Both use three market access assessment criteria: therapeutic value, budget impact and cost-effectiveness. If products pass these criteria, they are accepted in the outpatient system and acquire preliminary reimbursement status in the in-hospital system, to be reassessed after four years.

Pharmaceutical companies are finding it increasingly difficult to get their innovative products passed through these criteria. Budgetary constraints represent an important complication in the system. The budget system is continuously challenged by the entrance of newer, often more expensive, innovative products. However, this process is not balanced by a societal discussion about which products could be removed from the insured package and paid for by patients themselves. Political and societal perspectives often prevent politicians and health insurers from having this debate. The system seems congested and high-volume, expensive products face long reimbursement procedures, restricting indications and obstruction by health insurers at the level of doctor’s prescription and pharmacy delivery.

In addition, there are complications at the level of the assessment criteria therapeutic value, budget impact and cost-effectiveness. Therapeutic added value is a relative measure; it is the sum of the added characteristics of the product versus current treatment standards. If no alternative product exists, added value criteria seem more easily met than when alternative products exist. In particular, new versions of existing products that increase ease of use and compliance face this problem. Indications with a high burden of disease, like oncology, also appear more likely to be considered as adding therapeutic value than indications for large patient populations. Authorities sometimes question the value, shown by significant differences in efficacy and side-effects, by stating that the ‘clinical relevance’ of the differences is not known. Here lies an important task for health care professionals.

Today, the authorities are the first to consider new medicinal products in terms of therapeutic added value and position in the therapy. However, it would be more appropriate if experts in that particular field, and therefore able to gauge clinical relevance, judged the preliminary added value and position in the therapy directly after market authorisation was given. This would stop the Ministry of Health and health insurers deciding clinical issues and restrict their role to financial concerns like setting cost-effectiveness thresholds for reimbursement.

Budget impact is focusing on added costs solely within the pharmaceutical cost section. This criterion could be skipped if the third criterion, cost-effectiveness, were implemented correctly. Indeed, if a product is cost-effective, which means that the costs of all medical and non-medical effects are in balance with all clinical effects and the costs per effect are below a predetermined threshold, then the budget impact is irrelevant from the societal perspective. Although several thresholds exist in the Netherlands, the authorities do not apply them. It is assumed that applying a certain threshold leaves too much room for the entrance of innovative products for a large patient population which have cost-effectiveness levels below the threshold, or leaves too little room for very expensive oncology or orphan products which have cost-effectiveness levels often far above the threshold.

The structure and criteria must change to cope with future challenges like advanced cell therapies and more individualised pharmaceutical solutions.

The Author

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DOMESTIC PHARMACEUTICAL PRODUCTION

Pharmaceutical companies in the Netherlands spend around ten per cent of their sales on research and development (R&D). Considering its small market size, the Netherlands remains a popular location for pharmaceutical R&D. The pharmaceutical industry is the third largest spender on R&D in the Netherlands (after the electronic and chemical industries), accounting for ten per cent of all R&D in the country. The majority of R&D spending is on clinical trials.

The government encourages pharmaceutical research through, for example, the Top Institute Pharma (TI Pharma), a collaboration between academic institutions and companies, aimed at fostering co-operation in pharmaceutical R&D. Companies collaborate with each other as well as with academic institutions on many of the projects, with funding provided by all parties involved. Public/private partnerships will also be encouraged by the establishment recently of a Life Sciences and Health programme backed by government and industry. A key aim of this programme is to help the Netherlands boost its life science sector.

The Netherlands, in common with other western European countries, is likely to lose international pharmaceutical R&D investment as companies look to India, China and other countries in Asia and consolidation continues in the global pharma industry.

Animal rights activism remains an issue of concern for the pharmaceutical industry in the Netherlands, with homes of company staff as well as company facilities having been targeted by activists. The animal rights party won two seats in parliament in the last elections. The prospect of harassment by animal rights activists will inevitably be a factor when companies are considering investing in pharmaceutical R&D in the Netherlands.

The Netherlands has a tradition in biotechnology that began many years ago with the local company Gist-Brocades/DSM, and the infrastructure for the industry is now well developed. Around 150-160 life sciences companies invest in the sector – from start-ups to multinational ones such as Biogen Idec, Amgen and Centocor. The Netherlands ranks fourth in Europe (after the UK, Germany and France) in respect of number of companies and number of patents in the field. In R&D, oncology is the main focus of research by member companies of the Biofarmind industry association, followed by infectious diseases and coronary disease.

There are several biotech clusters, centred around leading universities. Leiden’s BioScience Park, for example, hosts several biomedical research companies, including Centocor, Gene Pharming and Crucell. Amsterdam is developing its own biotech cluster, which includes the Dutch Cancer Research Institute.

Initiatives by the government to boost the sector include the BioPartner Programme, set up in 2000 to assist new start-ups; the 2004 ‘Action Plan (for) Life Sciences’ which has a five-point action plan to encourage biotechnology; ‘BioConnection’, offering start-up biopharmaceutical companies production facilities through one central site; and the Netherlands Genomics Initiative, backed by government funding of €360m, and the same amount from other sources. More recently, creation of the Life Sciences and Health programme will help the Netherlands boost its life sciences sector – the aim is to double the sector over the next ten years. The programme will help small and medium-sized companies bring early-stage research towards commercialisation. Fledgling biotech companies in the area of human pharmaceuticals include ProteoNic, which has raised funding to develop a technology for optimising translation of messenger ribonucleic acid into proteins.

In the current economic climate, the biotech industry in the Netherlands faces the same problems as its counterparts elsewhere, particularly for companies yet to bring products to market.

The government has indicated that there could be some room for fiscal manoeuvre to help biotech companies but, so far, nothing concrete has emerged.

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MARKET FORECASTS FOR AUDITED SALES - NETHERLANDS

<table>
<thead>
<tr>
<th>Product Name</th>
<th>Active Ingredient(s)</th>
<th>Country Sales, 12 months to Q3 2009, $(millions)</th>
<th>Growth, 12 months to Q3 2009/2008, $(%)</th>
<th>Growth, 12 months to Q3 2009/2008, Fixed Rate $(%)</th>
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<td>ADALIMUAB</td>
<td>160</td>
<td>16</td>
<td>28</td>
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<td>SERETIDE</td>
<td>FLUTICASONE + SALMETEROL</td>
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<td>Total Others</td>
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<td>3,357</td>
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The dynamics of the Dutch generics market have changed significantly with introduction and expansion of the preference policy, which now affects over half of the generics market.

The Netherlands has traditionally had a strong generics culture (most generics are unbranded). Even before introduction of the preference policy and other incentives by insurers to make generics the drugs of choice, generics were widely used instead of brands. Almost 60 per cent of prescriptions are written generically. Use of generics is also encouraged by GP prescribing software, which ensures that doctors prescribe by international non-proprietary name (INN).

However, while volume use continues to expand, price competition will curb sales growth in this market segment. After remaining static for several years, the value share of the pharmaceutical market held by generics declined from 18.4 per cent in 2007 to 15.6 per cent in 2008, according to IMS Health data, testifying to the severity of price competition and price-cutting in response to expansion of the preference policy and the mandatory price reductions under the transition agreement. The volume share, on the other hand, has risen from 45.6 per cent to 47.0 per cent.

While insurers look set to pursue the preference policy approach, it remains to be seen whether generic companies can sustain the level of price cuts so far, especially as prices have sometimes been cut below the cost (of production) price.

Moreover, generic suppliers of preferred products could run into difficulties meeting the entire market demand for the product. Local reports suggest generic firms are supplying each other with preferred ingredients.

Concern is growing about the availability of counterfeit medicines, especially through internet purchases.

The health ministry has launched a website warning patients that they risk buying counterfeit drugs when they order medicines over the internet. The campaign, ‘The Danger of Internet Pills’, is in response to the growing number of counterfeit drugs being trafficked through the internet, according to the health ministry. The problem is thought to relate mostly to lifestyle drugs, like Viagra. The ministry is conducting research to assess the extent of the problem and to determine whether it needs to change its policy on counterfeits.

EU proposals for new anti-counterfeiting legislation would: extend the rules governing wholesale dealers to everyone who trades in medicines; assume powers to require features that allow identity, authenticity and traceability of certain prescription medicines to be established, such as a serialisation number and seal, but also allow parallel traders to open packs to insert leaflets in the national language and replace the security features in a way that maintains security of the product; commit to clarifying in future legislation the status of and rules applying to products held in free zones and free ports within the EU; introduce new rules governing imports of active pharmaceutical ingredients (APIs) into the EU, providing public health protection at least equivalent to that applying within the EU, and auditing of API manufacturers; strengthen rules governing inspection of manufacturers and wholesale distributors of medicines and APIs.

Given the lower average multi-source drug prices and higher generic penetration rates for insurers actively participating in the Netherlands’ preference policy, non-participating insurers are re-evaluating their options. In late 2009, the largest insurer, Achmea/Agis, announced it would abolish for multi-source products. Here, the pharmacy bears the risk of prescribers with prescribers

The IDEA model is attractive when patients are already on cheap multi-source products and the pharmacy is well positioned to manage, in consultation with prescribers, the prescribing of low-cost medicines. Furthermore, by increasing the generic substitution rate, pharmacists can increase their profits. IDEA contracts will last for two years.

Where pharmacies choose not to sign the IDEA contract, Achmea will take the role of purchaser and implement a preference policy for around 70-80 per cent of multi-source products. This policy will be executed via private tenders with undisclosed prices in five major product portfolio batches.

Either choice will result in a substantial reduction in the pharmacy margin.

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