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This Issue

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LETTER FROM THE EDITOR

The latest IMS Institute for Healthcare Informatics report forecasts global pharmaceuticals spending of US$1.3 trillion (€1.05 trillion) by 2018, up 30% on 2013 (see p28). However, while per capita spending on drugs is forecast to increase in most countries, it notes that France and Spain are expected to see declines in this respect, owing to policies designed to control spending. Indeed in France, the Pricing Committee's latest annual report (pp8-9) shows that value sales of reimbursed drugs fell for the second year running in 2013, partly as a result of the launch of many generics. Notably, under the 2015 social security finance bill (p20), the permitted annual growth rate for reimbursed drug spending in France is to be set at -1.0% for 2015 – the first time that the rate has been set at zero or below. The bill also provides for the further development of the use of biosimilars, as France adopts an increasingly aggressive stance on this front. With the news that the European Medicines Agency (EMA) has revised its overarching guideline on biosimilar products (pp16-17), which is expected to smooth the pathway for the entry of these products into the European market, others may soon be following France's example.

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US EDITORIAL

CMS Proposes to Revise Insurance Marketplace Rules

IN A MOVE THAT COULD HAVE SIGNIFICANT REPERCUSSIONS FOR PRIVATE INSURERS, THE CENTERS FOR MEDICARE AND MEDICAID SERVICES (CMS) HAS ANNOUNCED THAT IT IS SEEKING TO OVERHAUL THE REQUIREMENTS FOR "QUALIFIED HEALTH PLANS" PARTICIPATING IN THE NEW HEALTH INSURANCE MARKETPLACES ESTABLISHED IN OCTOBER 2013 (SEE *PPR* NOVEMBER 2013, P318). NOTABLY, THE CHANGES WOULD OBLIGE HEALTH PLANS TO LOOK AGAIN AT HOW THEY DECIDE WHICH PRESCRIPTION DRUGS TO COVER, FOLLOWING WIDESPREAD DISSATISFACTION AT THE SYSTEMS CURRENTLY IN PLACE. MOREOVER, THE CMS IS LOOKING FOR GREATER TRANSPARENCY FROM DRUG PLANS IN RELATION TO THEIR COST-SHARING STRATEGIES, AND TO PROHIBIT MAIL-ORDER ONLY POLICIES, AS IT LOOKS TO REDUCE FURTHER THE BURDEN ON PATIENTS SEEKING PRIVATE HEALTH INSURANCE COVERAGE.

The proposed reforms would apply to so-called qualified health plans (QHPs) sold via state-based or federally-administered health insurance marketplaces. QHPs are required to provide a minimum level of care, via coverage of 10 "essential health benefits" (EHBs) including out-patient prescription drugs (see *PPR* January 2013, p26), but there have been concerns that the existing rules have proved overly challenging for insurers – concerns that the CMS aims to address in its latest announcement.

Under the proposals, QHPs would no longer be required to cover at least one drug from each drug class or category included in the United States Pharmacopeia (USP) (or the same number of drugs for each USP class/category as covered by the state's benchmark plan [see *PPR* January 2013, p26], whichever provides the greater coverage). Instead, the CMS has proposed two alternative approaches, which would take effect from 2017.

The first approach would require all QHPs to establish a dedicated pharmacy and therapeutics (P&T) committee tasked with developing and maintaining the plan formulary. The committee would be obliged to meet at least quarterly and to make formulary decisions for new drugs (and new indications for existing drugs) based on scientific evidence and standards of clinical practice. Significantly, the CMS has stressed that the P&T committee would also be required to ensure that the formulary covers "a range of drugs across a broad distribution of therapeutic categories and classes and recommended drug treatment regimens that treat all disease states and does not substantially discourage enrollment by any group of enrollees".

Alternatively, the existing USP-based system would be replaced with one based on the American Hospital Formulary Service (AHFS), which is updated and published annually by the American Society of Health-System Pharmacists. The CMS has suggested that, since the AHFS has more classifications than the USP system, such a system would ensure coverage of a broader range of drugs. As is customary, the CMS will seek detailed feedback from manufacturers and other stakeholders before publishing a corresponding final rule.

Patients also stand to benefit from changes designed to make it easier for consumers to choose the health plan that best suits them. To this end, the CMS has proposed that health plans would be required (from 2016) to publish their formularies (including details of any cost-sharing tiers) in an easily accessible manner, and that from 2017 plans would be prohibited from having a mail-order only drug benefit (although they would still be permitted to charge patients higher cost sharing when obtaining a drug at a retail pharmacy than through a mail-order pharmacy).

The CMS hopes that the changes will address some of the concerns that have been raised by both patients and providers in relation to the coverage provided by QHPs. But the proposals cannot hope to address all such issues. There have been reports, for example, that the network of providers covered by many individual QHPs remains excessively restrictive, making it difficult for many patients to access healthcare locally, and even prompting some providers to sue individual health plans. The CMS plans to partially address this by beefing up information requirements for health plans so that more accurate and up-to-date information is made available for patients – but it appears it can do little to tackle the underlying issues surrounding access.

In this context, the proposed shake-up of the rules governing QHP prescription drug benefits may improve things for many beneficiaries; but it's unlikely to be the last such overhaul as the new health insurance marketplaces bed down to become a permanent feature of the American health insurance landscape PPR

EU EDITORIAL

Ireland: Government Seeks to Shore Up Support with Latest Healthcare Overhaul

WITH SUPPORT FOR THE GOVERNMENT FALLING SHARPLY IN THE WAKE OF THE IMPLEMENTATION OF A RAFT OF UNPOPULAR TAXES, HEALTH MINISTER LEO VARADKAR HAS SOUGHT TO ARREST THE DECLINE BY ANNOUNCING A RANGE OF NEW HEALTHCARE INITIATIVES – INCLUDING AN OVERHAUL OF THE GENERAL MEDICAL SERVICES (GMS) SCHEME, WHICH PROMISES TO MAKE IT EASIER FOR PATIENTS TO OBTAIN COMPREHENSIVE STATE-FUNDED COVERAGE FOR THEIR CARE. PATIENTS IN THE PRIVATE SECTOR, TOO, ARE LIKELY TO FEEL SOME BENEFIT AS THE GOVERNMENT PLANS TO CURB COSTS FOR YOUNGER PEOPLE SEEKING PRIVATE COVER. AND WITH THE ROLL-OUT OF A DEDICATED SCHEME TO PROVIDE ACCESS TO EXPENSIVE NEW HEPATITIS C MEDICINES, IT WOULD SEEM THAT THE GOVERNMENT IS DETERMINED TO DEMONSTRATE THAT IT CAN RESPOND TO PATIENTS' CONCERNS IN RELATION TO THE RISING COST OF HEALTHCARE.

The move to overhaul the GMS "medical card" scheme, in particular, represents something of a climbdown by the government. In 2013, in line with measures agreed with the *troika* of international creditors (the International Monetary Fund [IMF], the European Union [EU] and the European Central Bank [ECB]), the administration moved to tighten up the rules governing eligibility for the GMS programme (see *PPR* December 2013, pp374-375), which enables low-income patients to access primary and secondary care services free of charge (and to obtain out-patient prescription drugs subject only to a nominal co-payment – see *PPR* December 2014, p372). As a result, more than 15,000 patients suffering from chronic and/or terminal diseases, who had been granted "discretionary" medical card coverage due to their condition but who did not meet the income criteria, suddenly found that they were no longer entitled to care under the scheme – sparking a political furore that hugely damaged the government's credibility.

Under the health minister's latest proposals, however, patients with "significant" medical needs will be able to access care under the scheme more easily than before. While a patient's income level remains the primary criterion for deciding eligibility, general practitioners (GPs) are to be given much greater freedom to extend GMS coverage for up to 12 months to patients in "difficult circumstances" who would not otherwise qualify for the scheme. Moreover, patients suffering from terminal diseases will not have their eligibility for the scheme reviewed if they have already been granted a medical card.

The government also plans to make it much easier for patients to apply for coverage via the various state-backed medical schemes. To this end, it plans to create a single application process for the GMS scheme and the GP Visit Card programme (which enables patients with low incomes but who do not qualify for a medical card to attend GP consultations free of charge), as well as for the Drugs Payment (DP) scheme – which reimburses out-patient drug costs for non-GMS patients above a monthly threshold (see *PPR* December 2014, p372) – and the Long Term Illness (LTI) scheme, which covers out-patient drug costs for patients suffering from a number of specified illnesses.

It's significant that the proposed changes have come following Ireland's exit from the *troika*'s "bailout" programme in December 2013, a development that gives the government much greater freedom to set budgetary priorities. In this context, the decision to establish an early access scheme for new hepatitis C drugs is another important indicator of the administration's priorities: the scheme will enable hepatitis C patients requiring "urgent" treatment to be treated with medicines that are not (or are not yet) covered by the GMS, DP or LTI schemes, including Sovaldi (sofosbuvir), Daklinza (daclatasvir) and Olysio (simeprevir).

For patients in the private sector, meanwhile, the news that premium rises for younger beneficiaries are to be capped has been welcomed. From 1 May 2015, insurers will be required to stagger premium increases in stages once a beneficiary turns 21, with the full adult rate applying only from the age of 26.

Of course, it's not the first time that the government has sought to reduce medical costs for patients, despite the fiscal and budgetary pressures still facing the country. Most notably, plans to roll out free GP care for children aged five and under remain on the agenda (see *PPR* December 2013, pp374-375). But whether these and other initiatives will be enough collectively to address patients' concerns over healthcare costs remains to be seen PPR

LEADING ARTICLE

Russia: Planning for a Reimbursed

WITH REFORM OF THE HEALTHCARE SYSTEM REMAINING A KEY MEDIUM-TERM GOAL OF THE GOVERNMENT (SEE *PPR* NOVEMBER 2014, PP334-337), THE AUTHORITIES HAVE BEGUN TO TURN THEIR ATTENTION TO ADDRESSING THE PRACTICAL IMPLICATIONS OF THE DRIVE TO DELIVER BETTER HEALTHCARE COVERAGE FOR ALL. CHIEF AMONG THESE IS THE REFORM OF THE EXISTING OUT-PATIENT PRESCRIPTION DRUG REIMBURSEMENT SYSTEM – INCLUDING, POSSIBLY, PLANS TO EXPAND THE SYSTEM TO SECTORS OF THE POPULATION THAT CURRENTLY DO NOT HAVE ACCESS TO REIMBURSED MEDICINES IN THE OUT-PATIENT SETTING. *CONTINUING PPR'S RECENT COVERAGE OF DEVELOPMENTS IN RUSSIA, LARISA POPOVICH AND ELENA POTAPCHIK OF THE NATIONAL RESEARCH UNIVERSITY HIGHER SCHOOL OF ECONOMICS TAKE A CLOSER LOOK AT THE CHALLENGES THAT STILL LIE AHEAD FOR THE COUNTRY'S NASCENT PHARMACEUTICAL REIMBURSEMENT SYSTEM. THIS ARTICLE WAS PREPARED BASED ON RESEARCH CARRIED OUT FOR THE CENTRE OF FUNDAMENTAL RESEARCH OF THE HIGHER SCHOOL OF ECONOMICS.*

INTRODUCTION

It is perhaps fair to say that, in any given country, the key goals of any move towards healthcare reform tend to be similar – if sometimes contradictory. In particular, in recent years governments across the globe have tended to seek:

- control over the rising cost of medical care (as reflected in the growing share of gross domestic product [GDP] represented by healthcare spending, driven by ageing populations and technological progress);
- improvements in access to medical care and a reduction in health and healthcare inequalities;
- improvements in the quality of medical care;
- reduced inefficiencies and the removal of unnecessary and costly duplication in the medical system;
- improved health outcomes (*eg* survival rates, overall life expectancy);
- a reduction in the level of public dissatisfaction with the availability and quality of medical care provided;
- the provision of greater choice for patients in terms of their treatment.

In Russia, however, one of the main obstacles currently standing in the way of an improvement in the overall health of the population is the existing non-optimal system of medicine provision. Indeed, only a small proportion of the population is currently eligible to receive out-patient medicines free of charge. The majority, by contrast, must pay for such treatment out-of-pocket.

In an effort to improve this situation, a strategy for medicine provision in the Russian Federation until 2025 was adopted in 2013 (see *PPR* March 2013, pp80-82). One of the main objectives of this strategy was to implement mechanisms to manage medicine consumption and to widen drug reimbursement coverage.

BACKGROUND

Reimbursement

At present, in-patients (including patients in day hospitals) and patients to whom emergency care is provided are fully reimbursed for the cost of medicines used as part of their treatment.

In the out-patient setting, however, only certain population groups are eligible to receive either free or partially-subsidised prescription medicines. Eligibility for these benefits is determined by the federal government – although the regional authorities have the right to extend reimbursement to additional groups, provided that such coverage is funded by the regional (rather than federal) budget.

The population groups entitled to free medicines can be divided into two broad groups:

- Those in certain social groups (for example, Russian and USSR war veterans, disabled individuals, children aged up to three years old) (see Box 1).
- Those with certain diseases (for example, cancer, diabetes mellitus, HIV/AIDS) (see Box 1).

Future

Funding

Out-patient pharmaceutical care programmes are financed via a number of different public sources: the federal budget, regional budgets and compulsory health insurance (see Figure 1, over).

Compulsory health insurance (via the Federal Fund for Mandatory Medical Insurance, FFOMS) funds the reimbursement of medicines provided for in-patient and emergency care. The government maintains an essential drugs list (EDL) outlining which drugs should be made available in the in-patient setting, and which is also used as the basis for a number of out-patient reimbursement schemes (see Box 1).

Current Situation

Of a population of around 142 million, it is estimated that in 2013, approximately 78 million people in the Russian Federation received full reimbursement for pharmaceuticals either in the hospital setting – 29.8 million as in-patients and a further 7.6 million in day hospitals – or for emergency care (40.6 million).

By contrast, it is estimated that around 32.8 million people were eligible to receive out-patient medicines free of charge, including 27.7 million via programmes financed by regional budgets and 5.1 million through programmes financed via the federal budget.

It's clear, therefore, that medicine costs as a share of overall healthcare costs are significant. In the three years from 2010, public expenditure on overall healthcare provision increased by 23%, reaching RUB1,976.4 billion (US$36.9 billion; €29.9 billion) – or 3.0% of GDP – in 2013. This expenditure was financed from two public sources: compulsory health insurance (59.1%) and general government revenues (40.9%). Pharmaceutical costs comprised about 19% of total public spending on healthcare provision – with RUB116 billion spent on reimbursement of out-patient prescription drugs.

It is noteworthy, however, that at present not all of those who are eligible to access out-patient drug reimbursement actually exercise that right (see Table 1). The principal reason for the low uptake, relative to the numbers eligible for coverage, is that the lists of covered drugs are strictly regulated, and often do not correspond to the real needs of patients.

Box 1: Eligibility for Out-patient Drug Reimbursement in Russia

The federal budget fully reimburses out-patient prescription drugs for patients meeting the following criteria:

The ONLS programme: This scheme provides coverage to patients who have the right to receive "a set of social services" (including fully reimbursed out-patient prescription medicines). Eligible population groups include: veterans of the Great Patriotic War (World War II) and other wars, Leningrad siege medal-holders, others who worked on specific objectives during World War II, family members of those killed or disabled in action, disabled individuals, and disabled children. The list of medicines provided under the scheme (drawn largely from the Essential Drugs List [EDL]) is maintained by the Ministry of Health (MoH) (see *PPR* October 2014, pp302-305).

The VZN programme: Also referred to as the "Seven Nosologies" scheme, this programme covers patients with high-cost diseases, including haemophilia, mucoviscidosis, multiple sclerosis, and Gaucher's disease. The government maintains the list of medicines covered under the scheme (see *PPR* October 2014, pp302-305).

Other: Coverage is also provided at the federal level to patients with infections considered to be particularly dangerous (such as HIV/AIDS, tuberculosis, hepatitis). Medicines provided free of charge under this provision are regulated according to a list maintained by the federal government.

Together, the ONLS and VZN programmes are referred to as the *Dopolnitel'noe Lekarstevennoe Obespechenie* (DLO) scheme (see *PPR* November 2014, pp334-337; October 2014, pp302-305).

At the regional level, territorial and regional governments are theoretically required to finance out-patient drug reimbursement for the following population groups:

Patients suffering from orphan diseases: There is no specific list of medicines reimbursed for such conditions.

Certain other groups: These include children under three years of age, people exposed to radiation as a result of the Chernobyl nuclear power plant disaster, or as a result of nuclear testing at the Semipalatinsk range, and patients suffering from certain diseases (*eg* diabetes mellitus and cancer). Medicines reimbursed under the scheme are included on a corresponding list approved by the regional administration (see *PPR* October 2014, pp302-305).

However, the guidelines governing such coverage are not clear, and as a result there can be a wide regional variation in the level of care provided.

Source: Larisa Popovich and Elena Potapchik

Table 1: Out-patient Reimbursement: Eligibility vs Uptake

	Number eligible		Number accessing reimbursed out-patient drugs	
	2012	**2013**	**2012**	**2013**
ONLS	4,865,491	5,109,467	3,104,298	2,994,024
Certain social groups/diseases	13,449,399	27,657,100	5,458,550	10,836,210
Orphan diseases	8,967	11,842	2,667	4,403
TOTAL	**18,323,857**	**32,778,409**	**8,565,515**	**13,834,637**

Source: Larisa Popovich and Elena Potapchik

PILOT SCHEMES

In recent years, the government has made a concerted effort to establish a framework for the roll-out of a new reimbursement system for out-patient prescription medicines (see *PPR* November 2014, pp334-337). Under the current plans, a pilot project is scheduled to begin in 2015 in selected regions.

To this end, the Ministry of Health (MoH) has drafted an order establishing the criteria for pilot region selection. In accordance with this draft, to partake in the pilot scheme, a region must:

- Not run a financial deficit in its compulsory health insurance scheme.
- Demonstrate that it has executed an approved regional programme of health system modernisation.
- Have a high number of qualified medical and pharmaceutical staff.
- Possess a sufficient number of pharmacies and pharmaceutical warehouses.
- Have a well-developed IT system.

It is expected that in the near future the MoH will publish the list of approved pilot regions. At present, some 18 regions have already announced their willingness to take part in the pilot, including Moscow, Tatarstan and the Kaluga and Kirov regions.

It is noteworthy also that the government assumes that participating regions will choose from the various proposed reimbursement and organisational models put forward by the MoH for consideration (see below).

Reimbursement Models under Consideration

Currently three reimbursement models are under consideration.

Option 1: The first model envisages changes in reimbursement policy, but does not envisage any changes to the currently "privileged" population groups who are eligible for coverage. Under this proposal, medicines included in the relevant regulatory list (see Box 1) for each of the existing schemes would be assigned a reference price (*ie* a single price for each international non-proprietary name [INN]). If the price of the prescribed medicine exceeds this reference price, the patient would be required to pay the difference out of pocket.

Option 2: The second model envisages the retention of the existing reimbursement model for "privileged" population groups, but supplemented by the addition of new "privileged" groups suffering from certain diseases (*eg* hypertension, peptic stomach ulcers). Like Option 1, the new system would introduce an INN-based reference pricing system for covered drugs, with patients required to pay any difference between the reference price and the actual price of the prescribed medicine.

Option 3: The third model envisages the introduction of a risk-sharing model for orphan disease patients.

Organisational Schemes under Consideration

There are a variety of organisational schemes under consideration, but two have thus far attracted the most attention from the authorities:

Option 1: Under this proposal, the primary responsibility for out-patient drug reimbursement would reside with the

territorial compulsory health insurance funds (TFOMSs), which would directly reimburse pharmacies for the cost of drugs dispensed to beneficiaries (with additional payments to pharmacies coming from patients either through out-of-pocket payment or private insurance plans).

Option 2: Under the alternative scheme, the TFOMSs would distribute funds to patients' insurers, which would then reimburse pharmacies for the cost of medicines dispensed to beneficiaries.

In each case, however, the TFOMSs would be funded via a combination of payments from the Federal Fund for Mandatory Medical Insurance (FFOMS) (around 70%) and the regional governments (around 30%).

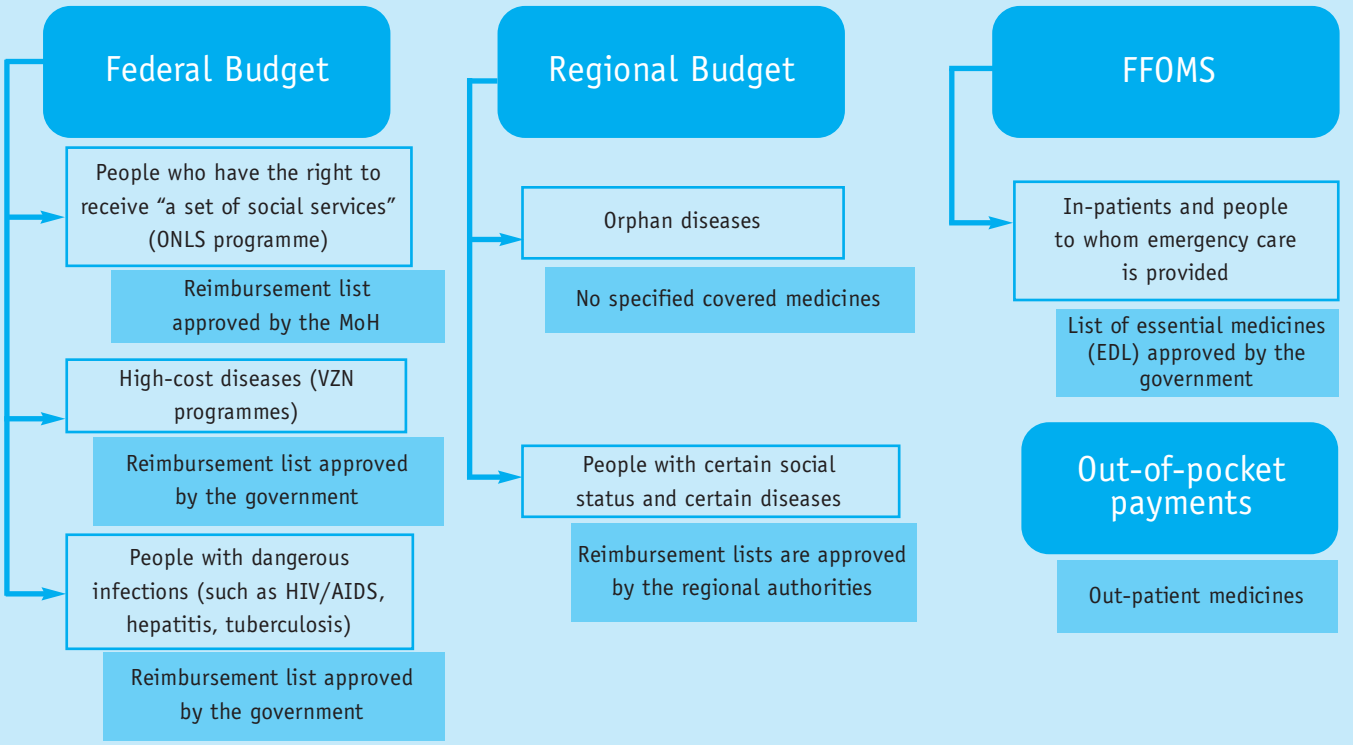
CONCLUSION

Reform of out-patient prescription drug provision is vitally important, both in terms of improving the level of medical care available to the population and increasing the level of satisfaction with the public healthcare system. In addition, reform of the system would contribute toward improving the overall efficiency of the health system.

At present, not all patients have the right to access reimbursed (or subsidised) medicines in the out-patient sector. Moreover, for those "privileged" groups that do have access to reimbursed out-patient prescription drugs, the list of drugs covered is often not satisfactory. As a result, it is important to reform out-patient medicine provision in order to make the system more patient-oriented.

Russia will have to solve this problem in the next few years, despite the present economic difficulties. Indeed, the government has declared that there will be no reduction in "social guarantees", and it actually plans to increase health expenditure over coming years. The main task now, therefore, is to effectively manage the resources that have been allocated to the healthcare system and to establish a rational and efficient system of medicine provision for out-patients PPR

Figure 1: Medicine Provision in Russia by Source of Financing



Source: Larisa Popovich and Elena Potapchik

FOCUS

France: Reimbursed Drug Sales Con

TOTAL SALES (RETAIL AND HOSPITAL SECTOR) OF REIMBURSED DRUGS FELL BY 1.8% IN 2013, ACCORDING TO THE PRICING COMMITTEE (*COMITÉ ECONOMIQUE DES PRODUITS DE SANTÉ*, CEPS) – THE SECOND SUCCESSIVE ANNUAL DROP IN OVERALL SPENDING, FOLLOWING A 2.2% DECLINE IN 2012 (SEE *PPR* DECEMBER 2013, PP358-361). THE FINDINGS, PUBLISHED BY CEPS IN ITS LATEST ANNUAL REPORT, MAKE CLEAR THAT EFFORTS TO CONTAIN OVERALL DRUG EXPENDITURE APPEAR TO BE HAVING AN EFFECT, ALTHOUGH SIGNIFICANT SALES GROWTH FOR CERTAIN PRODUCTS – NOTABLY ONCOLOGY DRUGS – CONTINUES TO BE OBSERVED. *EOIN JENNINGS TAKES A CLOSER LOOK*.

ROLE OF CEPS

The Pricing Committee is responsible for regulating the manufacturer's selling prices (MSPs) of all reimbursed drugs. CEPS is an inter-ministerial committee operating under the joint authority of the Ministry for Economy and the Ministry for Social Affairs, Health and Women's Rights.

CEPS negotiates prices for new drugs with manufacturers, taking into account a range of factors including the drug's improvement in medial benefit (*Amélioration du Service Médical Rendu*, ASMR) rating versus therapeutic equivalents, the price of the drug in the rest of Europe and sales volume forecasts. In addition, as of October 2013, CEPS considers health economic evaluations of certain drugs when setting prices (see *PPR* November 2014, pp320-321). And, once the MSP of a drug has been established, a (confidential) pricing agreement (known as a *convention*) may be signed between the manufacturer and CEPS, which may include additional pricing conditions (*eg* payback clauses).

Furthermore, certain drugs used in hospitals have their prices regulated by CEPS under the terms of the *Accord Cadre* negotiated between the Committee and the research-based industry association (LEEM) in late 2012 (see *PPR* February 2013, p54). This applies to:

- Specified high-cost drugs (including cancer drugs and orphan drugs), which are excluded from the diagnosis-related group (T2A) tariffs.
- Drugs included in the *liste rétrocession* (hospital drugs suitable for dispensing to out-patients and charged to the ambulatory sector, rather than the hospital). Hospital-only (*réserve hospitalier*, RH) drugs are not eligible for inclusion on the list.

As part of CEPS' remit, it is required to monitor reimbursed drug sales, and to publish an annual report detailing its activities (and the impact on the pharmaceutical market in France).

KEY FINDINGS

According to CEPS' latest annual report, published in October 2014, sales of reimbursed drugs fell in 2013 for the second year in a row. This has been attributed to a range of factors – including the impact of price cuts imposed in 2013. It is noteworthy, too, that the Committee processed a total of 1,345 drug pricing applications in 2013, although the average duration of the pricing procedure fell when compared to 2012.

Reimbursed Drug Sales

Total (retail plus hospital) sales of reimbursed drugs fell by 1.8% in 2013 (at MSP), to €24,720 million (US$30,530 million). This represents the second successive annual fall in overall spending, following a 2.2% drop in 2012 (see *PPR* December 2013, pp358-361).

In particular, the report notes that:

- Reimbursed retail pharmacy sales (including dual circuit retail drugs – see below) fell by 2.2% to €18,440 million in 2013, largely as a result of the impact of the launch of generic versions of a number of top-selling branded medicines.
- Sales of reimbursed hospital sector medicines fell by 0.6% in 2013, to €6,280 million.
- Furthermore, sales of medicines included on the *liste rétrocession* (see above) fell by 2.7%, to €1,400 million.

tinue to Fall

- Hospital and retail pharmacy sales of dual circuit drugs (HIV and hepatitis B *liste rétrocession* drugs which can be dispensed to out-patients through either hospitals or retail pharmacies) fell by 5.7% in 2013.

However, while overall sales of reimbursed prescription drugs fell, sales of oncology drugs increased by €115 million in 2013. Similarly, sales of anticoagulants increased by €97 million, and sales of antirheumatics rose by €58 million.

By contrast, sales of proton pump inhibitors (PPIs) fell by €161 million in 2013, with anticholesterol drugs seeing a fall of €158 million and sales of renin-angiotensin system medicines dropping by €156 million.

Price Reductions

CEPS estimates that as a result of price cuts (*eg* following patent expiry) and other measures, total economies of €844.6 million were generated on reimbursed prescription drugs in 2013. Of this, €784.6 million was accounted for by price reductions and other cost-saving measures on reimbursed retail sector medicines. The remaining €60.0 million was accounted for by price cuts for hospital sector drugs.

Pricing Applications

According to the report, CEPS processed a total of 1,345 drug pricing applications (corresponding to 7,579 presentations) in 2013, of which 415 were first applications for new drugs and 10 were price increase applications. Of the remainder, 666 applications related to pricing modifications for existing drugs and 25 to indication extensions; there were also 229 re-submissions.

The average duration of the pricing procedure for (retail and hospital) original branded medicines was 249 days, while for generics it was 77 days. In 2012, by contrast, the average duration was 298 days for branded drugs and 71 days for generics.

For hospital drugs alone, the average time from submission of the price notification dossier to publication of the price in the *Journal Officiel* was 95 days in 2013, according to CEPS (86 days for *liste rétrocession* drugs and 118 days for T2A-excluded medicines).

It is noteworthy that certain innovative drugs are eligible to use an accelerated pricing procedure, known as the price notification (*dépôt de prix*) system. However, in 2013 just two products used the accelerated procedure (the same number as in 2012), according to CEPS.

Reimbursement Rates

The standard rates of reimbursement in France are 65%, 35%, 15% (and 0%), although certain products (*eg* HIV/AIDS medications) are 100% reimbursed. Reimbursement rates are decided by the National Union of Health Insurers (UNCAM), based on the drug's perceived medical benefit (*Service Médical Rendu*, SMR) rating, as assessed by the Transparency Commission.

According to the CEPS report, however, the average reimbursement rate for retail sector drugs in 2013 was 67.5% (67.0% in 2012). Taking into account the 100% reimbursement rate granted to patients suffering from chronic diseases (*Affections de Longue Durée*, ALDs), the effective average reimbursement rate in 2013 was 78.4% (compared to 77.8% in 2012).

Industry Paybacks

A national target growth rate for reimbursed drug spending is established each year. If the target is exceeded, a payback clause (*clause de sauvegarde*) kicks in, with manufacturers liable for repayments.

According to CEPS, however, no repayments were due from manufacturers under the payback system, as the permitted annual growth rate for reimbursed drug expenditure was not exceeded. This target (referred to as *taux K* in 2013) was set at 0.4% for 2013 (and indeed for 2014, down from 0.5% in 2012 and 2011).

Notably, however, under the 2015 social security finance bill (2015 PLFSS, a parliamentary vote on which was scheduled to take place as this issue of *PPR* went to press – see p20), the *taux K* is to be renamed *taux L* in 2015. Moreover, the annual growth rate for 2015 is to be set at -1.0% – the first time that the target growth rate has been set at zero or below PPR

CONFERENCE REPORT

Brazil: A Complex Market Demanding

AT THE RECENT CONFERENCE ON *PHARMACEUTICAL & MEDICAL DEVICE MARKET & PATIENT ACCESS IN LATIN AMERICA* STAGED BY NEXTLEVEL PHARMA IN RIO DE JANEIRO, ALESSANDRO CIRRINCIONE, GLOBAL DIRECTOR, PRICING AND GOVERNMENT AFFAIRS, VIFOR PHARMA, DISCUSSED THE UNIQUE CHARACTER OF THE BRAZILIAN MARKET AND ADDRESSED THE CHALLENGES FACED BY MARKETERS SEEKING TO GAIN ACCESS TO IT WITH NEW PRODUCTS. *FOLLOWING THE MEETING, HE SPOKE TO MICK MARONEY FOR PPR.*

The Market

"All eyes are on Brazil, and for a very good reason," noted Cirrincione. "It's the eighth-largest pharmaceutical market in the world, so in the headquarters of multinational companies there is always a drive to gain access to it. It's one of the largest public healthcare systems in the world – almost 200 million people. There's also a private healthcare system that covers 48 million people: this alone is equivalent in size to the Spanish market," he observed.

Healthcare System

"Brazil has a unique healthcare system setup," said Cirrincione. "The *Sistema Único de Saúde* (SUS, see *PPR* December 2014, pp359-363), the public healthcare system, offers universal coverage: based on the Constitution, all Brazilians have the right to be treated. This offers a mix of national programmes and decentralised funding through states and municipalities and diverse third-party payers.

"The private system, regulated by the ANS (*Agência Nacional de Saúde Suplementar*, the National Supplementary Health Care system, see *PPR* December 2014, pp359-363 *et al*), is complementary to the public system. Normally, treatments not covered by the public system can be covered by healthcare plans or insurance companies," he advised.

The Private Sector

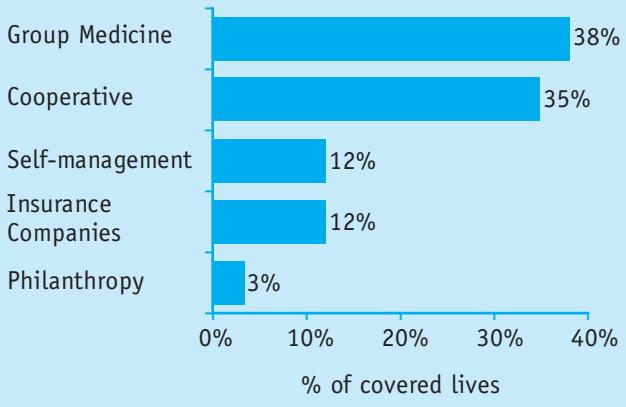
As discussed by Cirrincione, around half of the people who have a private plan are covered by the 30 largest companies. "Seven of them have more than one million beneficiaries: another way of looking at this is to say that these seven companies between them are as big as the Swiss market. Some 30% of this population are distributed among 150 health insurance companies and 20% are covered by more than 800 health insurance companies. So if you want to reach all of this population you need to visit a lot of healthcare plans and insurance companies," he told *PPR*.

"The private (supplementary) sector is a universe of third-party payers, with different business models [see Figure 1]. Group Medicine companies are similar to managed care organisations: they can have their own hospitals or can have contracts with providers. There are also cooperatives (medical societies) – non-profit organisations where the physicians are shareholders. There is also the self-management sector – large employers which have their own healthcare plans. And there are the insurance companies managed mainly by Brazilian banks," he advised.

The Public Sector

There are three main funding systems for pharmaceuticals in the public sector. According to Cirrincione, the Basic component includes low-complexity products, such as asthma and hypertension treatments and analgesics. Funding for this is provided by the Ministry of Health (around 50%), the states (some 30%) and the municipalities (around 20%). The municipalities oversee the purchasing and dispensing of medicines.

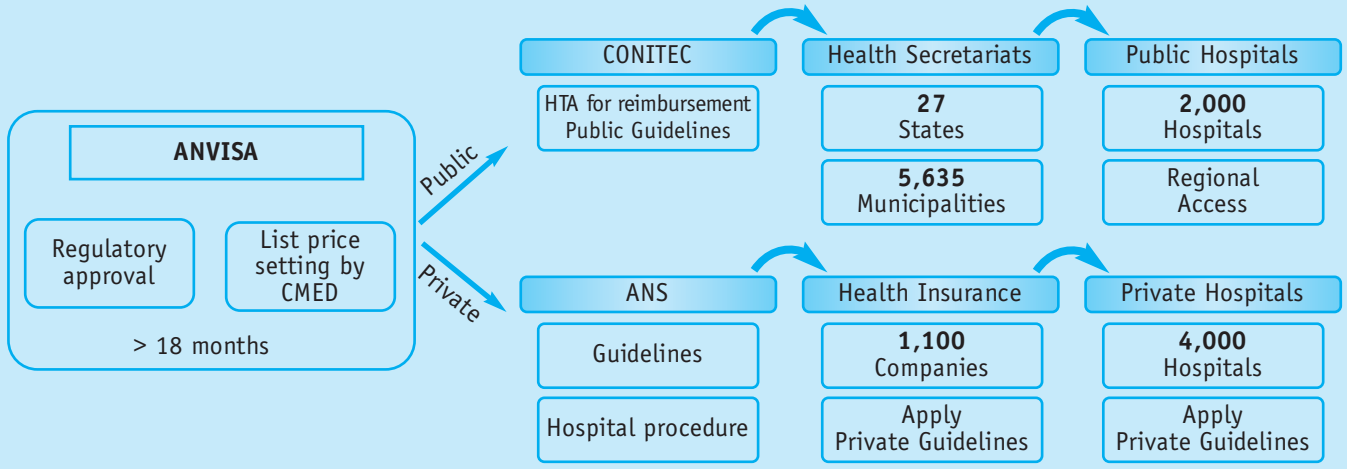
Figure 1: Supplementary Healthcare Plans Market, 2012



Source: Alessandro Cirrincione (with thanks to Andre Vicente, Takeda Brazil)

Substantial Commitment

Figure 2: Steps to Market Access in Brazil



Source: Alessandro Cirrincione (with thanks to Andre Vicente, Takeda Brazil)

The Strategic or national health priority system is completely funded by the federal government and managed by centralised tenders. This includes programmes such as hepatitis C and HIV. Meanwhile the funding and management of the high-cost, high-complexity products in the Specialised system is in the hands of the states (although 80% of the funding comes from the Ministry of Health).

Gaining Market Access

"Many steps are required to gain market access", commented Cirrincione. "The first step is of course the regulatory process, managed by ANVISA [*Agência Nacional de Vigilância Sanitária*, the National Health Surveillance Agency, see *PPR* December 2014, pp359-363, 378]. This can take 18 months, or probably longer. Price setting is central to this process: you cannot start to commercialise a product until the pricing process is completed [see below].

"Then you have to think whether your product fits into the public system or the private sector. There are several steps. In the public sector you put in an application to CONITEC [*Comissão Nacional de Incorporação de Tecnologias*, the National Commission for Health Technology Incorporation, see *PPR* December 2014, pp359-363] and apply for an HTA [health technology assessment]. Following that, the product goes to the health secretariats of the states and municipalities. And then there's the question of all the procurement that you have to manage in the states.

"If you go into the private sector, the ANS handles the regulation, but then you have to go to all the individual health insurance companies – though I don't believe any company is visiting all 1,000 of them. However, the amount of work required is substantial," he noted.

Price Setting

Cirrincione moved on to discuss the pricing procedure. "Under the criteria used by the Pharmaceutical Market Regulatory Agency (*Câmara de Regulação do Mercado de Medicamentos*, CMED, see *PPR* May 2014, p156; November 2011, pp334-338 *et al*) for setting the price of a product, if you have a new molecular entity (NME) you can either score I or II," he advised. "A score of I means your product is patent-protected in Brazil and that you have scientific evidence that it offers better efficacy than established products, or fewer side effects – or perhaps the same efficacy with reduced costs (in terms of global treatment costs). If you get category I, the product is subject to international reference pricing – and you get the lowest price in a basket of countries: Australia, Canada, France, Greece, Italy, New Zealand, Portugal, Spain, the US and the country of origin.

Box 1: Public vs Private Sales of Leading Products

Cirrincione reviewed IMS Health data from 2012, to illustrate the differing sales profiles of leading brands in the public and private sector. "If we take Humira [adalimumab], we can see that this is paid 99% by the public system (see below), because it's in the high-complexity funding system. In the case of Herceptin we see a roughly 50/50 split. Several years ago, when I was working for Roche, Herceptin was funded mainly by the private sector. For those who didn't have any private insurance, lawsuits were the only option. Finally, it came through CONITEC, which approved funding for adjuvant breast cancer: this is probably what we see here in the public sector. The private sector is probably patients with metastatic breast cancer or gastric cancer," he told *PPR*.

Public/Private Sector Value Sales of Leading Hospital Products, 2012

Product	Private	Public
Humira (adalimumab)	1%	99%
Herceptin (trastuzumab)	47%	53%
Enbrel (etanercept)	1%	99%
Mabthera (rituximab)	57%	43%
Glivec (imatinib)	4%	96%
Clexane (enoxaparin)	54%	46%
Avastin (bevacizumab)	70%	30%
Remicade (infliximab)	20%	80%
Pegasys (peginterferon alfa-2a)	1%	99%
Betaferon (interferon beta-1b)	0%	100%

Source: Alessandro Cirrincione, based on IMS Health data

"If you are not able to demonstrate such, you are automatically classified in category II, which means you get the price of the local comparator. So it's really important that you understand what the local comparator is and what CMED's understanding of the local comparator will be," he told *PPR*.

"The meaning of better efficacy is also debatable in Brazil, because it's rather black and white. The discussion isn't about how great the effect of the treatment is – it's about the clinical relevance of the data compared with the local standard of care. And of course the pricing regulation (CMED Resolution 02/04) doesn't mention which costs we need to consider – whether direct or indirect costs, for the public or the private system," said Cirrincione.

Scorecard

According to Cirrincione, in 2013 CMED published a report on the outcome of applications between 2004 and 2011: during this time only 14 products were judged to be innovative and were granted category I status.

"I compared the scores in Brazil with those achieved under the French ASMR system [*Amélioration du Service Médical Rendu*, improvement in medical benefit, see *PPR* September 2012, p277], which I think is the closest model to that used in Brazil [see Table 1]. Under the ASMR system, category I is a breakthrough treatment, a cure. Category II is a breakthrough, but it's not a cure. Category III is a major clinical improvement, and if you get I, II or III you can have free pricing.

"Category IV means a minor improvement in safety or efficacy, and category V means it's a me-too product. If a product is judged to be category IV or V you get the price of the local comparator. Indeed sometimes for category V you get a lower price than the comparator," he observed.

"So Nexavar, for example, was given category I in Brazil and category II in France. I would say that this is aligned.

Table 1: Comparison of Brazilian and French Benefit Ratings for Selected Products

Product	CMED Category	ASMR
Nexavar (sorafenib)	I	II
Firazyr (icatibant)	I	IV
Tygacil (tigecycline)	I	V
Sutent (sunitinib)	I	II/III
Kuvan (sapropterin)	II	III
Sprycel (dasatinib)	II	II
Tasigna (nilotinib)	II	I/II
Yondelis (trabectedin)	II	V
Tykerb (lapatinib)	II	III

Source: Alessandro Cirrincione

But when we look at Tygacil, we can see that CMED gave a score of I (an innovation), but the French said it's not an innovation, so they are not in agreement here. In the case of Yondelis, in Brazil it was given category II, but in France category V, while for Kuvan, it was II in Brazil and III in France.

"So the Brazilian system is black and white – there is no recognition of the difference between true innovation and minor innovation," commented Cirrincione.

Perspectives on the CMED Process

According to Cirrincione, "CMED's approach is an evidence-based pricing appraisal, looking for phase III studies, and looking at the most appropriate local comparator. In France, a minor improvement in a disease area that hasn't seen a new product for 30 years is not the same as a disease area where there is a new product every six months. But in Brazil the pricing process doesn't take into account unmet medical need, the incremental benefit or the size of the effect – whether it's 30%, 40% or 80% more effective, for example. There are no discussions on epidemiology.

"I know some companies that didn't want to launch their products in Brazil because if you get the category II you can get the local comparator's price – and if the local comparator is a generic or a 50-year-old product then probably it does not make business sense to launch. But the issue is not about the local comparator, the challenge is that you cannot really negotiate a price," he told *PPR*.

"I think the standard of care is the most important consideration in Brazil – that we understand how CMED will select this. If your main value argument is about cost, you can still get category I, but you have to really think through what kind of data you need to collect. The exchange rate is also a risk of course. There is always the opportunity to have discussions with CMED – you need to ask for a hearing, to meet the technical people in CMED, and to try to answer all their questions. Be prepared for very good questions: if you need to, do some more analysis of your studies and try to provide them with the information they want, if you can."

Gaining Access to the Private Sector

"Once you've done the price setting it's normal to go for the private market first," noted Cirrincione. "The providers – the hospitals or clinics – are paid by fee for service. And this is regulated by the ANS. Any prescriptions outside the internal formulary may be rejected and there is no obligation to cover out-patient drugs and lifestyle treatments.

"If you want to do a commercial deal on pricing, you have to work with each of the payers/providers – there isn't a national pricing scheme. So even if you only want to cover the top 100 of the 1,000 payers, you need a 'pricing system' for each one of them – it's quite a challenge," he observed.

"Inside each of these companies there are several stakeholders. There are auditors, medical directors, prescribers and providers, all of whom play a role in the formulary listing decisions. Many companies struggle with their key account managers to handle interaction with these stakeholders because you need to have the right profile of people, who can communicate in a different way to the way that sales reps do.

"For example, over a decade ago, a few companies (along with people who believe in the benefits of the drugs) began to work with stakeholders in the private sector on the value of oral cancer treatments. Now, since 2013, all private insurance companies have to offer cover for such products. This took 10 years of work to achieve," he noted.

Accessing the Public Sector

Cirrincione moved on to consider the challenges presented in the public sector. "Once you've got into the private sector, you may consider going into the public system, via CONITEC. Once again it comes back to the value argument, to HTA," he observed.

Prior to 2012, HTA applications in the public sector were handled by the Commission of Health Technology Incorporation (*Comissão de Incorporação de Technologias do Ministério da Saúde*, CITEC, see *PPR* November 2011, pp334-338). According to Cirrincione, between 2006 and 2011, of the applications reviewed by CITEC:

- A total of 88 were accepted for reimbursement
- Some 65 were rejected
- The majority (185) were not analysed.

There were also a limited number of stakeholders involved in the process, noted Cirrincione.

"SUS decided that there was a need to speed up the process and increase its transparency. So CONITEC was created in 2012, which has proved a major step forward and a good signal of the desire to increase access in Brazil, using HTA. I think it's really good news.

"It's now very clear which stakeholders are involved and there are many of them: The Ministry of Health, ANVISA, the ANS, the CNS (*Conselho Nacional de Saúde*, the National Health Council), CONASS (*Conselho Nacional de Secretários de Saúde*, the National Council of Health Secretaries) and CONASEMS (*Conselho Nacional de Secretarias Municipais de Saúde*, the National Council of Municipal Health Secretaries). There is public consultation which is also a major step forward. You can have public hearings, which is important because it's an opportunity to exchange information, to try to understand the other party and their concerns. You can also appeal a decision. I think they have done a really good job," he told *PPR*.

"Since CONITEC's inception there have been 56 positive recommendations and 46 negative. It's also interesting that they are looking at excluding technologies that are no longer cost-effective – four so far. I think that's also important in order to free up some resources.

"It's interesting that CONITEC can give recommendations on virtually anything. This includes pricing anomalies on top of the CAP [*Coeficiente de Adequação de Preços*, the minimum compulsory discount that applies to drugs sold to public hospitals], for instance. They can also give recommendations on pathways, presentations, one sku [stock keeping unit] vs another, or different dosages," he advised.

Lessons for a Company Seeking to Enter the Market

Cirrincione wrapped up by summarising the key considerations that companies entering the Brazilian market need to bear in mind. "Local expertise support is the key to business development. There are experts in the private system and those in the public system.

"Never underestimate the pricing process. Before launch and before going to CMED it is important to think about developing the necessary data, because price setting is really the moment of truth. It's all or nothing – you might end up not launching your product if you don't go through it. So it's important to have an open dialogue with the CMED team, to try to understand and address their concerns," he advised.

"If you go to the private sector it requires a lot of time because there are so many payers in the market that you need a network of resources on a key account type of basis.

"Finally in the public sector the funding is limited, so even if you have a cost-effective drug it doesn't mean you're going to have public funding. The probability of success will depend on the political will to cover a product, to what extent it is seen as a national health priority. And of course there is the key question about the budget impact that it will have on the healthcare system," he concluded PPR

Future Meetings

World Pharma Pricing & Market Access Congress,
24-26 February 2015, London
contact: Health Network Communications
tel: +44 207 608 7057
email: bstansfield@healthnetworkcommunications.com
www.healthnetworkcommunications.com/conference/pharma-pricing

4th Annual Pharma Pricing & Reimbursement Forum,
29-30 January 2015, Frankfurt
contact: Global Leading Conferences
tel: +36 1 848 0532
email: glc@glceurope.com
www.globalleadingconferences.com/conferences/pharmaceutical-pricing-and-reimbursement-forum

Parallel Trade, 9-10 February 2015, London
contact: The SMi Group
tel: +44 207 827 6000; fax +44 207 827 6001
email: events@smi-online.co.uk
www.smi-online.co.uk/pharmaceuticals/uk/conference/parallel-trade

UPDATE

UK: CDF Drugs List to be Reviewed

CHANGES TO THE CANCER DRUGS FUND IN ENGLAND, FIRST FLAGGED BACK IN AUGUST 2014 (SEE *PPR* OCTOBER 2014, P286), HAVE BEEN APPROVED BY NHS ENGLAND FOLLOWING A FOUR-WEEK CONSULTATION WITH STAKEHOLDERS (SEE *PPR* DECEMBER 2014, PP352-354). THE OVERHAUL MEANS THAT, WITH IMMEDIATE EFFECT, CANCER DRUGS WILL ONLY BE ROUTINELY COVERED BY THE SCHEME IF THEY MEET CERTAIN CLINICAL AND COST-RELATED CRITERIA – A MOVE THAT HAS SPARKED ALARM AMONG PATIENT GROUPS. *EOIN JENNINGS REPORTS*.

Key Changes

The cancer drugs fund (CDF) enables patients in England (but not in Scotland, Wales or Northern Ireland) to access cancer medicines that have not (or not yet) been approved for routine use in the National Health Service (NHS) by the National Institute for Health and Care Excellence (NICE). Following a recent cash injection by the government, the scheme makes funding of up to £260 million (US$407 million; €330 million) per annum available to fund these treatments for patients (see *PPR* October 2014, p286).

However, in an effort to ensure that this budget is respected, NHS England has announced that the inclusion of a new drug in the list of treatments routinely covered by the CDF will henceforth take into account an assessment of both the clinical benefit of a drug and the median cost of that drug per patient.

Moreover, as part of these changes, existing drugs/indications listed in the CDF will be re-evaluated to determine whether or not they should continue to be funded. As a result, 42 drugs/indications are to be re-evaluated at the forthcoming (as this issue of *PPR* went to press) meeting of the national CDF panel, scheduled for December 2014 (with final decisions to be announced in 2015). The re-evaluation list covers 25 separate active ingredients, although some are to be re-assessed for the treatment of multiple indications (see Table 1).

However, NHS England has confirmed that where a patient has begun treatment with a drug that subsequently is removed from the CDF, they will be permitted to continue treatment with that product. In addition, individual funding requests for drugs removed from the list (or that have been rejected for listing) will also still be permitted. Furthermore, no drug will be removed from the list if it is the only proven systemic therapy for a specific type of cancer.

Responses

Cancer charities have raised concerns about the changes, with Head of Policy at Breakthrough Breast Cancer Caitlin Palframan noting that the charity was "deeply concerned that several very effective breast cancer drugs appear on the list of drugs at risk of delisting due to their high price". The Association of the British Pharmaceutical Industry (ABPI), meanwhile, has expressed its disappointment with the changes, and has described the method of evaluating new and existing medicines as "crude" PPR

Table 1: CDF-Listed Drugs to be Subject to Re-evaluation in December 2014

Abraxane (paclitaxel)	Erbitux (cetuximab)	Revlimid (lenalidomide)
Adcetris (brentuximab)	Halaven (eribulin)	**Sprycel (dasatanib)**
Afinitor (everolimus)	Imnovid (pomalidomide)	Stivarga (regorafenib)
Alimta (pemetrexed)	Inlyta (axitinib)	Tyverb (lapatinib)
Arzerra (ofatumumab)	Jevtana (cabazitaxel)	**Velcade (bortezomib)**
Avastin (bevacizumab)	Kadcyla (trastuzumab emtansine)	Votrient (pazopanib)
Bosulif (bosutinib)	Levact (bendamustine)	Xalkori (crizotinib)
Caelyx (doxorubicin)	Perjeta (pertuzumab)	Zaltrap (aflibercept)
		Zydelig (idelalisib)

Bold = to be re-assessed for multiple indications

Source: NHS England

NEW DEVELOPMENT

Europe: EMA Revises its Guideline

RESPONDING TO THE NEED TO REFINE THE EXISTING REGULATIONS SURROUNDING BIOSIMILARS IN EUROPE (SEE *PPR* JANUARY 2011, PP15-17), THE EUROPEAN MEDICINES AGENCY (EMA) HAS REVISED ITS OVERARCHING *GUIDELINE ON SIMILAR BIOLOGICAL MEDICINAL PRODUCTS*, THUS SMOOTHING THE PATHWAY FOR THE ENTRY OF THESE PRODUCTS INTO THE EUROPEAN MARKET (SEE *PPR* JULY 2014, PP208-210 *ET AL*). *ROSEMARY PROCTOR REPORTS*.

BACKGROUND

The first version of the EMA's *Guideline on similar biological medicinal products* (EMEA/CHMP/437/04) was adopted in September 2005. The *Guideline*, which was developed by the EMA's Committee for Medicinal Products for Human Use (CHMP), established a regulatory framework for biosimilars, supported by legislation adopted in 2003 and 2004 (Directives 2003/63/EC and 2004/27/EC – see *PPR* December 2004, p357-361). Two complementary guidelines were also published in 2005: the first addressing the quality issues surrounding biosimilar development and the second addressing the clinical and non-clinical aspects of biosimilar development. Together, the three overarching guidelines and the Directives adopted in 2003 and 2004 form the regulatory backdrop against which 22 biosimilar products have thus far received EMA approval (see Table 1).

In November 2011, the EMA released a concept paper on proposed revisions to the *Guideline on similar biological medicinal products*. A draft version of the revised *Guideline* was subsequently put out to consultation on 26 April 2013, and on 29 October 2014 the final version of the revised *Guideline* was published. Its provisions can be applied at any point from this date, but will officially come into effect on 30 April 2015.

Meanwhile, both complementary guidelines have recently been subject to revision – an updated version of the guideline addressing quality issues is scheduled to come into effect in December 2014, while an updated version of the guideline on clinical and non-clinical factors in the development of biosimilars is in its draft stages.

KEY REVISIONS

The revisions to the *Guideline* clarify the terminology for biosimilars and further define the principles of biosimilarity. In addition, the *Guideline* is intended to facilitate the process of bringing biosimilars to market in the European Union (EU) and the European Economic Area (EEA, *ie* the EU28 plus Iceland, Liechtenstein and Norway).

Terminology

According to the revised *Guideline*, a biosimilar drug is "a biological medicinal product that contains a version of the active substance of an already authorised original biological medicinal product (reference medicinal product) in the EEA". By contrast, the previous version of the *Guideline* contained no clear definition, noting only that "in principle, the concept of a 'similar biological medicinal product' is applicable to any biological medicinal product".

In addition, the revised *Guideline* states that before a product can be classified as a biosimilar, "similarity to the reference medicinal product in terms of quality characteristics, biological activity, safety and efficacy based on a comprehensive comparability exercise needs to be established."

Reference Product

In order for a biosimilar to receive EMA approval, manufacturers must demonstrate that its quality, safety and efficacy are similar to those of a comparator (*ie* a reference product) identified by the manufacturer. Under the previous version of the *Guideline*, manufacturers' choice of comparator was restricted to products authorised in the EEA. But according to the revised *Guideline*, "it may be possible for an Applicant to compare the biosimilar in certain clinical studies and in *in vivo* non-clinical studies (where needed) with a non-EEA authorised comparator (*ie* a non-EEA authorised version of the reference medicinal product)".

This revision, the *Guideline* states, was made "with the aim of facilitating the global development of biosimilars and to avoid unnecessary repetition of clinical trials". Opening up the choice of reference product is likely therefore to result in significant savings for biosimilars manufacturers.

Nevertheless, it is noteworthy that the reference product must have received marketing authorisation in a country with similar standards to the EMA (*eg* member countries of the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use [ICH]).

on Biosimilars

Table 1: Biosimilars Approved by the EMA, January 2006-November 2014*

Brand Name	Active Ingredient	Authorisation Date	Manufacturer
Abseamed	epoetin alfa	28 August 2007	Medice Arzneimittel Pütter
Binocrit	epoetin alfa	28 August 2007	Sandoz
Epoetin alfa Hexal	epoetin alfa	28 August 2007	Hexal
Retacrit	epoetin zeta	18 December 2007	Hospira
Silapo	epoetin zeta	18 December 2007	STADA R&D
Inflectra	infliximab	10 September 2013	Hospira
Remsima	infliximab	10 September 2013	Celltrion
Abasria	insulin glargine	9 September 2014	Eli Lilly/Boehringer Ingelheim
Accofil	filgrastim	18 September 2014	Accord Healthcare
Biograstim	filgrastim	15 September 2008	CT Arzneimittel
Filgrastim Hexal	filgrastim	6 February 2009	Hexal
Filgrastim ratiopharm	filgrastim	15 September 2008[1]	Ratiopharm
Grastofil	filgrastim	18 October 2013	Apotex
Nivestim	filgrastim	8 June 2010	Hospira
Ratiograstim	filgrastim	15 September 2008	Ratiopharm
Tevagrastim	filgrastim	15 September 2008	Teva Generics
Zarzio	filgrastim	6 February 2009	Sandoz
Bemfola	follitropin alfa	24 March 2014	Finox Biotech
Ovaleap	follitropin alfa	27 September 2013	Teva Pharma
Omnitrope	somatropin	12 April 2006	Sandoz
Somatropin Biopartners	somatropin	5 August 2013	Biopartners
Valtropin	somatropin	24 April 2006[2]	BioPartners

Notes
[1]Withdrawn on 20 April 2011
[2]Withdrawn on 10 May 2012

*Listed alphabetically by active ingredient. Each colour block represents a group of products with the same active ingredient, listed alphabetically by brand name.

Sources: www.ema.europa.eu, "Biosimilar medicines authorised via the Agency"; http://gabionline.net (Generics and Biosimilars Initiative), "Biosimilars approved in Europe"

REACTION

The European Generic medicines Association (EGA), along with its affiliate the European Biosimilars Group [EBG], have commended the revised *Guideline* as "a new milestone in the EU biosimilar medicines regulatory framework". Commenting on the *Guideline*, EGA Director General Adrian van den Hoven concluded that "the revised regulatory framework for biosimilar medicines is crucial to support the development of the biosimilar medicines industry, to bring healthy competition to the biopharmaceutical market in Europe and to accelerate patient access to effective modern biological therapeutic alternatives" PPR

UPDATE

Portugal: Compromise Reached over Payback Agreement

AFTER CONSIDERABLE DEBATE – AND ONE FAILED ROUND OF TALKS – THE PORTUGUESE HEALTH MINISTRY AND THE PHARMACEUTICAL INDUSTRY ASSOCIATION (APIFARMA) HAVE REACHED AN AGREEMENT ON A REVISED INDUSTRY PAYBACK SCHEME. COMING IN THE WAKE OF GOVERNMENT PLANS, ANNOUNCED IN OCTOBER 2014, TO ESTABLISH A NEW DIRECT TAX ON SALES FROM 2015 (SEE *PPR* DECEMBER 2014, P374), THE REVISED PAYBACK SCHEME OFFERS DRUG MANUFACTURERS A WAY OF AVOIDING THE NEW LEVY. *JULIA TROCMÉ-LATTER BRINGS READERS UP TO DATE ON THIS AND OTHER RECENT DEVELOPMENTS.*

BACKGROUND

In June 2014, APIFARMA signed an agreement requiring manufacturers collectively to contribute a total of €160 million (US$218 million) to help reduce government expenditure on pharmaceuticals for 2014 (see *PPR* August 2014, p246). Such agreements have been a standard cost-containment tool in Portugal for some years – a similar accord was signed back in 2012, for example (see *PPR* July 2012, p215).

In October 2014, however, the government announced that it was formulating plans to replace the industry payback system with a direct tax on sales. The tax would be levied on sales at the public price (*Preço de Venda ao Público*, PVP) (excluding sales tax) of reimbursed drugs, orphan drugs, medicinal gases, drugs used in elective treatments, restricted prescription drugs and drugs made from blood and human plasma (see *PPR* December 2014, p374). The tax would also vary between 0.5% and 15% depending on the product, with the highest rate being applied to restricted prescription drugs, hospital drugs and drugs used in elective treatments.

PAYBACK AGREEMENT

It would appear that the primary motivation behind the government's decision to announce the new tax was to encourage pharmaceutical manufacturers to negotiate with the government a new payback agreement for 2015.

Consequently, in November 2014, talks between the Ministry of Health and APIFARMA got underway. However, the initial round of negotiations failed – reportedly due to the €200 million in savings being sought by the government under the agreement. Nonetheless, negotiations continued, partly due to the necessity of reaching agreement prior to 25 November 2014, in time for the scheduled parliamentary vote on the 2015 budget.

As a result, on 21 November 2014, the parties announced that they had reached agreement on a new payback scheme for 2015. Notably, the agreement stipulates that drug manufacturers will collectively be required to pay a total of €180 million to the government in 2015 to limit pharmaceutical expenditure. The figure represents a €20 million increase on the amount agreed under the 2014 accord (see above), but is €20 million less than the figure sought by the government in the first round of negotiations (see above).

Furthermore, it has been reported that although participation in the new payback scheme is voluntary, firms that choose not to participate will instead be obliged to pay the new direct tax on sales in 2015.

REFERENCE COUNTRIES

In other developments, the government has announced that the basket of reference countries used to set the maximum manufacturer's selling prices (MSPs) of new drugs and to calculate annual price revisions for existing branded products will not be updated in 2015. As a result, prices of branded drugs in Portugal will continue to be measured against those in France, Slovenia and Spain (see *PPR* January 2014, p3), which all have a similar per capita gross domestic product (GDP) to Portugal's. It is estimated that 2015 price revisions will produce total savings of €22 million for the healthcare system: €15 million for the government and €7 million for patients.

It is noteworthy that annual price revisions for generics, based on the price of the corresponding branded original, were suspended in 2014 (see *PPR* February 2014, p55). The government confirmed in November 2014 that no annual price revisions for generics will take place in 2015 PPR

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- Will the genericisation of this key competitor impact my brand's price?

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EUROPEAN ROUND-UP

France: Update on Progress of PLFSS

At the time of going to press, local news reports suggested that the lower chamber of parliament (*Assemblée Nationale*) was set to definitively adopt the 2015 social security finance bill (*Projet de Loi de Financement de la Sécurité Sociale*, PLFSS) (see *PPR* December 2014, pp356-358) in a vote scheduled to take place on 1 December 2014. The final version of the legislation is understood to reinstate a number of measures removed from the bill by the upper chamber (*Sénat*), including the abolition of certain co-payments for patients who receive financial assistance for the purchase of health coverage (*aide à l'acquisition d'une complémentaire santé*).

The final version of the bill is also reported to include measures to enable the implementation (with effect from 1 July 2015) of a third-party (*tiers payant*) payer system for all ACS beneficiaries. Furthermore, the final legislation reportedly confirms that the annual target growth rate for healthcare spending (*Objectif National de Dépenses d'Assurance Maladie*, ONDAM) will be set at 2.1% in 2015. Measures to encourage generic uptake and reduce prescription drug prices have also been retained, including a controversial cap on reimbursed spending on high-cost drugs for the treatment of hepatitis C.

Germany: Early Benefit Assessments from IQWiG

On 17 November 2014, the Institute for Quality and Efficiency in Health Care (*Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen*, IQWiG) published early benefit assessments of the type 2 diabetes drugs Jardiance (empagliflozin) and Vokanamet (fixed dose combination of canagliflozin and metformin). Neither Jardiance nor Vokanamet was found by IQWiG to exhibit additional therapeutic benefit versus the relevant comparator therapies set by the G-BA.

In addition, on 3 November 2014, IQWiG published its early benefit reassessment of the breast cancer drug Halaven (eribulin) (see *PPR* June 2014, p182). According IQWiG, Halaven demonstrates a "proof" of minor additional therapeutic benefit in a particular patient sub-group, and a "hint" or "indication" (depending on how many organs are affected by the cancer) of lesser therapeutic benefit in a second sub-group.

Early Benefit Assessments from the G-BA

The G-BA has issued early benefit assessment decisions for seven drugs, as follows:

No additional therapeutic benefit:

- the overactive bladder medicine Betmiga (mirabegron) (see *PPR* November 2014, p340)
- the wound therapy treatment Larvae of Lucilia sericata.

Indication of minor therapeutic benefit:

- the chronic hepatitis C drug Olysio (simeprevir) (see *PPR* November 2014, p340) (in certain patients with the hepatitis C virus [HCV] of genotype 4, and in certain HCV genotype 1 and genotype 4 patients who are also infected with human immunodeficiency virus [HIV]).
- the orphan drug Vimizim (elosulfase alfa), which is approved for the treatment of patients with mucopolysaccharidosis type IVA (MPS IVA, also known as Morquio A syndrome).

Indication of considerable additional therapeutic benefit:

- the orphan drug Jakavi (ruxolitinib) (see *PPR* October 2014, p308; May 2013, p149).
- the orphan drug Orphacol (cholic acid), which is approved for the treatment of patients who suffer from a genetic abnormality that makes them unable to produce bile. It is noteworthy that while Orphacol's marketing authorisation is deemed to offer sufficient proof of its additional therapeutic benefit, the G-BA concludes that this benefit is "non-quantifiable".
- Olysio (in patients with HCV of genotype 1).

Furthermore, according to the G-BA's reassessment of Fycompa (perampanel), the anti-epileptic drug continues to exhibit no additional therapeutic benefit versus the relevant comparator therapies (see *PPR* October 2014, p308; September 2013, p277).

Health Ministry Approves First Tranche of Generic Substitution Prohibition List

The Ministry of Health (*Bundesministerium für Gesundheit*, BMG) has approved the *Gemeinsamer Bundesausschuss* (G-BA)'s September 2014 decision on the first tranche of the list of drugs (and associated pharmaceutical forms) for which generic substitution would never be allowed (see *PPR* November 2014, p341. The decision provides for a general generic substitution ban on:

- beta-acetyldigoxin (tablet)
- cyclosporine (soft capsule and solution for intake)
- digitoxin (tablet)
- digoxin (tablet)
- levothyroxine sodium (tablet) alone and together with potassium iodide (fixed combination, tablet)
- phenytoin (tablet)
- tacrolimus (hard capsule).

Greece: Pharmaceutical Sector Strategy for the Coming Years

Speaking at a conference organised by Greek pharmaceutical companies, Minister for Health Makis Voridis has outlined the government's strategy for the pharmaceutical sector in 2015 and beyond. According to the Minister, the government will continue to follow a two-pronged approach to containing pharmaceutical expenditure:

- curbing unnecessary spending through prescribing controls (see *PPR* December 2014, p372 *et al*) and exacting greater punishments for fraudulent behaviour;
- while increasing the uptake of generics to 60% by volume (see *PPR* December 2014, p372).

Meanwhile, a number of existing policies will remain in place, including:

- the controversial clawback system for manufacturers (see *PPR* July 2014, pp206-207; June 2012, pp160-163). The system will only be abolished if it is evident that pharmaceutical expenditure can remain within budget.
- the achievement of higher volume-based savings through centralised hospital sector tenders (see *PPR* April 2014, pp98-99 *et al*).

In addition, the government will pursue its long-term goal of revising the way in which maximum supply chain discounts from manufacturers and wholesalers are calculated. The government wishes to see discounts become volume-based, rather than independent of the drug's sales or price, as is currently the case (see *PPR* March 2014, pp64-67).

Temporary Parallel Export Ban

The National Organisation for Medicines (EOF) has issued a temporary parallel export ban, with effect from 14 November 2014, on 26 drug presentations (11 active ingredients and combinations). Introduction of the ban follows warnings from pharmacists about drug shortages. The ban will be revoked once the EOF is satisfied that adequate supply of the listed drugs has been restored.

Ireland: Early Access Scheme for New Hepatitis C Drugs

The Health Service Executive (HSE) is to establish an early access programme to treat patients with new hepatitis C therapies not yet reimbursed by state-funded drug programmes. *For more on this development, turn to p3*.

Overhaul of Private Health Insurance System and Medical Card Scheme

Minister for Health Leo Varadkar has unveiled a package of measures intended to address the rising cost of private health insurance premiums. Meanwhile, the minister has also announced that the HSE is to take a number of steps to overhaul the General Medical Services (GMS) medical card scheme. *For further details, turn to p3*.

Italy: Review of Pharmaceutical Expenditure Ceiling Mechanism

Minister for Health Beatrice Lorenzin is reported to have announced that she intends to review the pharmaceutical expenditure ceiling mechanism (see *PPR* September 2012, p257) (and the associated payback system – see *PPR* December 2014, p373) under which manufacturers, pharmacies and wholesalers, along with the regions, are

responsible for covering any deficits. The announcement was made at a forum on the future of healthcare and pharmaceutical provision in Italy, staged in Rome on 10 November 2014.

In related news, Federfarma (the pharmacists' association) has filed an appeal with the Administrative Court of Lazio (TAR Lazio) against the payback mechanism requirements for 2013 recently published in the Official Gazette. According to the association, the repayment requirements are "against basic juridical principles" and include "illegitimate" operational elements.

P&R Developments Relating to New Hepatitis C Drugs

It is understood that in a recent debate in the lower house of parliament (*Camera*), the Minister for Health stated that the government has prepared a plan for the prevention and treatment of viral hepatitis. According to press reports, Beatrice Lorenzin advised that the government is currently trying to find the resources to support the implementation of the plan, including an *ad hoc* fund that will provide for the extension of reimbursement for the new hepatitis C treatment Sovaldi (sofosbuvir) to cover all affected patients (*ie* not only those covered under the terms of the agreement between the Medicines Agency [*Agenzia Italiana del Farmaco*, AIFA] and the drug's manufacturer, Gilead Sciences – see *PPR* November 2014, p331).

Meanwhile, AIFA Director General Luca Pani is reported to have revealed that Gilead is to be paid €37,000 (US$45,650) for a course of treatment with Sovaldi (for patients covered by the agreement). This figure is understood to represent a 17% discount to the national healthcare system (*Servizio Sanitario Nazionale*, SSN). In addition, AIFA has announced that it has reached an agreement with Janssen-Cilag for the pricing and reimbursement of the hepatitis C drug Olysio (simeprevir). As a result of the agreement, Incivo (telaprevir), a drug authorised for the same therapeutic indication and manufactured by the same company, has been removed from reimbursement.

Netherlands: Reimbursement for Sovaldi

In the Netherlands, Sovaldi has been granted reimbursement with effect from 1 November 2014, under the terms of a confidential price discount agreement. "This is a preliminary reimbursement decision until the end of 2015, and the drug will only be reimbursed for patients with more advanced hepatitis C," the Ministry of Health, Welfare and Sport (*Ministerie van Volksgezondheid, Welzijn en Sport*, VWS) clarified.

Norway: Changes to Reimbursement Conditions for New Hepatitis C Drugs

Meanwhile in Norway, changes to the reimbursement conditions for new hepatitis C drugs were implemented on 1 November 2014 (rather than on 1 October 2014, as originally planned – see *PPR* September 2014, p279). Under the new rules:

- physicians must apply to the Health Economics Administration (*Helseøkonomiforvaltningen*, HELFO) in order to secure the reimbursement of a new hepatitis C drug for an individual patient. However, the older hepatitis C medicines ribavirin and peginterferon are exempt from this rule.
- the authority to prescribe hepatitis C drugs is restricted to specialists in infectious diseases, digestive diseases or paediatrics, and doctors at hospitals specialising in the treatment of such conditions.
- the Norwegian Medicines Agency (NoMA) (*Statens Legemiddelverk*) will undertake cost-effectiveness assessments of all hepatitis C drugs in order to determine reimbursement status and conditions attached to reimbursement.

Poland: Updated Reimbursement List

Updates to the reimbursement list took effect from 1 November 2014, in line with the requirement that the list be revised at least every two months (see *PPR* November 2014, p342 *et al*). The updated list includes three new combination products: amlodipine + indapamide, amlodipine + ramipril

and oxycodone + naloxone. In addition, a total of 20 presentations have been delisted, and the prices of 43 presentations (24 active ingredients or medical devices) have been reduced.

Amendments to the drug programmes scheme (which provides for the treatment of otherwise non-reimbursed high-cost drugs on a named-patient basis) were also made on 1 November 2014.

Portugal: P&R Developments

There have been a number of recent pricing and reimbursement (P&R) developments in Portugal. *For further details, turn to p18*.

Spain: Update on Developments in the CAs

Recent developments impacting the pharmaceutical market in the autonomous communities (*Comunidades Autónomas*, CAs) include the following:

- The local press reports that the central government has allocated additional credit line funding to Cataluña and Valencia to pay outstanding pharmacy invoices (see *PPR* November 2014, p343). The reports do not discuss the amount of funding involved, or whether other CAs have also benefited.
- The Ministry of Health, Social Services and Equality (*Ministerio de Sanidad, Servicios Sociales e Igualdad*, MSSSI) reports that all CAs except Andalucía and País Vasco have agreed to take part in a new centralised national tender for vaccines. In addition to reducing costs, the initiative is designed to harmonise the provision of vaccines via regional programmes (see *PPR* November 2012, p344). According to the ministry, a total of 23 vaccines will be purchased in three clusters: paediatrics (13 vaccines); vaccines for adults (5); 'travel' vaccines (five of which have been classified in a separate cluster). Contracts will be valid for a two-year period, from 1 January 2015, although this may be extended for a further year. The MSSSI says that it expects to realise total savings of €37.4 million in 2015-16 as a result of the tender.
- It has been reported that a total of 10 companies have been selected by Andalucía to supply products included in the fifth retail sector tender (which will commence on 1 January 2015 – see *PPR* November 2014, p342). Only 37 presentations (of a total of 467 tendered) will be covered by the two-year contracts. Furthermore, the savings that are expected to be made have been reduced from €200 million to €15 million for the contract period.
- According to the local press, a group of 30 pharmacists in Madrid have formally objected to the agreement between the regional government and the region's council of pharmacists to introduce a mandatory 10% discount for reimbursed drugs dispensed directly to care homes (see *PPR* December 2014, p374). In response, the regional council of pharmacists is reported to have stated that, contrary to earlier reports, the whole agreement between itself and the CA (including the discounts) remains under discussion.

Sweden: Latest TLV Decisions

The Dental and Pharmaceutical Benefits Agency (*Tandvårds- och läkemedelsförmånsverket*, TLV) has recently made a number of decisions affecting the pharmaceutical sector in Sweden, including the following:

- The Agency has confirmed that changes to the additional fixed fee of SKr13.00 (€1.40; US$1.74) paid to pharmacists for dispensing a generic or off-patent original drug will take effect from 1 January 2015. Instead of reverting back to the original level of SKr10.00 as planned, the fee will be set at SKr11.50, but will be applicable only to drugs within the generic substitution system.
- In addition, the TLV has released an updated list of drugs that will be subject to a 7.5% (at pharmacy purchase price) price cut from 1 January 2015. The price cuts affect drugs that have been on the market for 15 years or more but, due to weak or no generic competition, have not had their prices cut according to the ceiling price regulations (see *PPR* November 2014, p343 *et al*).

Switzerland: Price Cuts for 836 Products

Price reductions of up to 60% were applied to 836 presentations on 1 November 2014, under the third round of cuts (see *PPR* January 2014, p11 *et al*) to take place in line with revised international price referencing rules introduced in March 2012 (see *PPR* May 2012, p153).

UK: Clarification on Statutory Branded Drug Price Controls

After reviewing the impact of European and UK procurement law on the regulations governing the statutory drug price controls for branded drugs (see *PPR* January 2014, pp4-6), the Department of Health (DH) has decided that the mandatory 15% price cut (versus the NHS list price as at 1 December 2013) does not apply to any presentation that meets the following criteria:

- "Procured under one or more framework agreements under the Public Contracts Regulations 2006 (as amended) that were entered into on or before 31 December 2013 and/or that were entered into following a tender which closed on or before 31 December 2013".
- "Where the price specified under such framework agreement is more than the price at which that presentation was on sale for health service purposes on 1 December 2013 less 15% (without regard to any discount or other variation of the price which did not have general application on that date)".

According to the DH, affected products may have their prices increased, and affected companies may be provided with compensation for the period during which the price of an affected presentation was reduced.

Update on Changes to Cancer Drugs Fund

NHS England has announced that its Board has approved the proposed changes to the operation of the cancer drugs fund (CDF) in England. *For further details on this development, turn to p15*.

Latest NICE Decisions

The National Institute for Health and Care Excellence (NICE) has issued preliminary draft guidance rejecting the Dupuytren's disease drug Xiapex (collagenase clostridium histolyticum) for use in the National Health Service (NHS). NICE has also issued preliminary draft guidance approving the NHS use of the chronic lymphocytic leukaemia (CLL) drug Azerra (ofatumumab), subject to a number of conditions.

Furthermore, NICE has issued final guidance approving the following drugs for use in the NHS:

- The gastro-intestinal stromal tumour (GIST) drug Glivec (imatinib) (see *PPR* December 2014, p375). It is noteworthy that this guidance reverses a negative NICE recommendation for the drug, issued in 2010.
- The alcohol dependence drug Selincro (nalmefene) (see *PPR* November 2014, p344).

In addition, NICE has recommended (in final draft guidance) that Soliris (eculizumab) be used in the NHS for the treatment of atypical haemolytic uraemic syndrome (aHUS), (see *PPR* November 2014, p344) provided that a number of conditions are met.

Meanwhile, NICE has published guidance extending the use in the NHS of five erythropoiesis-stimulating agents (ESAs) as possible treatments for anaemia in people having chemotherapy to treat cancer (see *PPR* June 2014, p184). The five recommended ESAs are: Eprex/Binocrit (epoetin alfa), NeoRecormon (epoetin beta), Eporatio (epoetin theta), Retacrit (epoetin zeta) and Aranesp (darbepoetin alfa) PPR

Future Meetings

6th International CIS Pharmaceutical Forum,

10-12 February 2015, Moscow

contact: Adam Smith Conferences

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email: nataliapr@adamsmithconferences.com

www.cispharmaforum.com

NORTH AMERICAN ROUND-UP

USA: Proposed Changes to Health Insurance Marketplace Plans

The Centers for Medicare and Medicaid Services (CMS) has proposed a number of changes to the rules governing "qualified health plans" participating in the health insurance marketplaces. *For further details of this development, turn to p2*.

Supreme Court to Hear Healthcare Reform Challenge

The Supreme Court has agreed to hear a lawsuit challenging the legality of the provision of health insurance subsidies to people who have purchased health insurance coverage via the federally-facilitated health insurance marketplace (rather than through a state-based marketplace) (see *PPR* November 2013, p318). Currently, under the 2010 Affordable Care Act (ACA – see *PPR* May 2010, pp126-127), subsidies are provided regardless of whether a plan is purchased via a health insurance marketplace run by the state or federal government. However, litigants have cited wording in the law which, they argue, infers that subsidies should only be provided to individuals that purchase health insurance via "an Exchange established by the State".

Notably, the Fourth US Circuit Court of Appeals in Richmond, Virginia had previously ruled on 22 July 2014 (on the case that will be heard by the Supreme Court – referred to as *King v Burwell*) that the subsidies for the federally-run health insurance marketplace should be upheld. However, this ruling contrasted with a decision delivered on the same day by a panel of the US Court of Appeals for the District of Columbia (DC) Circuit which, in a separate but similar case (*Halbig v Burwell*), ruled against the provision of subsidies via the federal marketplace (overturning a lower court judge's decision) (see *PPR* March 2014, p91). The full DC Circuit Court had been due to hear the case, but has now reportedly suspended proceedings until after the Supreme Court has delivered its judgment.

According to press reports, the ACA healthcare reforms are at risk of being destabilised if the Supreme Court should rule against the provision of health insurance subsidies for plans purchased via federal health insurance marketplaces.

FDA Revokes Tentative Approval of Ranbaxy's Generic Nexium and Valcyte

The Food and Drug Administration (FDA) has revoked the tentative approval granted to Ranbaxy Laboratories for its generic versions of AstraZeneca's heartburn drug Nexium (esomeprazole) and Roche's antiviral medicine Valcyte (valganciclovir). The FDA has also reportedly rescinded the 180-days' marketing exclusivity granted to Ranbaxy for its generic version of Valcyte.

According to press reports, the company was granted tentative approval to market generic versions of Nexium and Valcyte in 2008, but has been unable to begin producing them owing to FDA bans placed on the export of its drugs from its manufacturing plants in India, due to safety concerns.

In response, Ranbaxy has filed a lawsuit against the FDA. According to the manufacturer, the suit (filed in the District of Columbia federal court) also calls upon the court to issue a temporary restraining order "to prevent any further action by the FDA until Ranbaxy's case is decided".

Update on Implementation of Final AMP-based FULs

The CMS has announced that it expects to finalise Average Manufacturer Price (AMP)-based Federal Upper Limits (FULs, *ie* maximum reimbursement prices) for multisource Medicaid drugs at (or around) the same time as publication of the agency's Medicaid Covered Outpatient Drug final rule (see *PPR* August 2014, p222 *et al*). Concurrently, the CMS also plans to issue detailed guidance to states on implementing the AMP-based FULs.

As work continues on implementing AMP-based FULs, the CMS states that it will continue to analyse the draft monthly AMP-based FULs data, including the relationship between these FULs and the National Average Drug Acquisition Cost (NADAC) data (see *PPR* September 2013, p254). It will also continue to publish the draft monthly AMP-based FULs files.

AARP Reports on Drug Prices Increases

According to a new report by the seniors' association, the AARP, retail prices for 227 widely-used brand name prescription drugs increased by an average of 12.9% in

2013. Notably, the increase is higher than in any of the seven years 2006-2012 (during which the average increase ranged from +5.7% to +12.3%) and is significantly higher than the general inflation rate in 2013 (+1.5%).

Furthermore, retail prices increased in 2013 for 97% of the 227 widely-used brand name prescription drugs – while price increases for all but two of the products studied exceeded the rate of general inflation in 2013.

The average annual cost for a branded prescription drug used for a chronic condition was US$2,960 (€2,360) in 2013, more than double the average annual cost of a branded prescription drug for treating a chronic condition in 2006. In addition, retail prices for 140 branded prescription drugs for chronic conditions that had been on the market since 2006 increased cumulatively over eight years by an average of 113.0%, compared to a cumulative general inflation rate of +18.4% during the same eight-year period.

Investigation and Proposed Legislation to Deal with Medicaid Drug Prices

Senator Bernie Sanders (Independent, Vermont) has announced that a hearing will be held on 20 November 2014 by the Senate Subcommittee on Primary Health and Aging to "explore why the costs of certain generic drugs are skyrocketing". Representative Elijah Cummings (Democrat, Maryland), who has supported Sanders' probe into price increases for generic drugs, will also participate in the hearing (see *PPR* December 2014, pp376-377).

Sanders and Cummings have also introduced similar proposed bills in the Senate and the House of Representatives, which aim to reduce the impact of price increases for Medicaid generics that rise in price at a greater rate than inflation. The proposed legislation, titled the "Medicaid Generic Drug Price Fairness Act", would extend to generic drugs a provision that currently applies only to branded Medicaid drugs, requiring manufacturers to pay an additional rebate to Medicaid (on top of the statutory Medicaid rebate – see *PPR* April 2012, pp104-107) if the price of their drug rises faster than the rate of inflation.

Separately, the Department of Justice has reportedly begun investigating two generics companies, Lannett and Impax Laboratories, over recent price increases for some of their drugs. According to separate filings with the US Securities and Exchange Commission (SEC), senior figures at both companies have received grand jury subpoenas requiring them to answer questions relating to price hikes for their products.

Canada: New Powers for Pharmacists in N&L and Saskatchewan

The provincial governments of Newfoundland & Labrador (N&L) and Saskatchewan have passed legislation that will enable pharmacists to administer injections, including influenza vaccinations. In addition, pharmacists in Saskatchewan will be able to order, access and interpret laboratory tests. In Newfoundland & Labrador, the changes will take effect once pharmacists have received the appropriate training from the province's Pharmacy Board, while in Saskatchewan the revised rules are expected to come into force in 2015.

It is noteworthy that patients covered by the Newfoundland & Labrador Prescription Drug Program (NLPDP) will be able to receive influenza vaccinations at their pharmacy for free. However, those not covered by the NLPDP will be charged a fee (to be determined by the pharmacy) PPR

Future Meetings

Orphan Drugs, 24-25 February 2015, London
contact: Informa Life Sciences
tel: +44 207 017 7481; fax +44 207 017 7823
email: LifeSciPTIBookings@tfinforma.com
www.informa-ls.com/event/orphandrugs15

Evidence, 24-26 February 2015, London
contact: Health Network Communications
tel: +44 207 092 1000; fax +44 207 242 1508
email: nathan.allen@terrapinn.com
www.healthnetworkcommunications.com/conference/evidence-eu

INTERNATIONAL ROUND-UP

India: Proposed Amendments to NLEM

In a notice dated 13 November 2014, the National Pharmaceutical Pricing Authority (NPPA) advised that it had undertaken a study of the drugs included in the National List of Essential Medicines 2011 (NLEM 2011), "with a view to ensuring that all Life Saving and Essential drugs of mass consumption are included in the NLEM for safeguarding the public interest" (see *PPR* December 2014, p378 *et al*). Based on its research, the Authority has proposed that corrections/modifications (in terms of the specified route of administration/strength) be made to more than 80 drug formulations found in the NLEM.

Furthermore, on 21 November 2014, the NPPA published a notice inviting stakeholders to offer feedback on recommendations it has received from the Tata Memorial Centre (Mumbai) concerning the addition/removal of oncology drugs to/from the NLEM.

The Authority has invited comments/suggestions from all stakeholders (including pharmaceutical industry and consumer organisations) on the above proposal to amend the entries of more than 80 drug formulations in the NLEM, and separately, on the recommendations received from the Tata Memorial Centre (which falls within the remit of the Department of Atomic Energy). The NPPA will take stakeholder input into consideration when it finalises its own recommendations concerning amendments to the NLEM, before passing these on to the Department of Pharmaceuticals, and a committee established by the Ministry of Health and Family Welfare (MOHFW).

Japan: Government Postpones Annual NHI Price Revisions

Following the publication of poor economic data in mid-November 2014, the cabinet has decided that a planned sales tax increase scheduled to take effect in October 2015 will be postponed until April 2017, in order to facilitate Japan's emergence from recession in 2015.

As a result, no revision of National Health Insurance (NHI) reimbursement prices for prescription drugs will take place in 2015 (a revision of prices had been planned in order to take into account the effect of the sales tax increase – see *PPR* June 2014, p159 *et al*). Instead, the next revision of NHI prices will take place in April 2016, in line with the usual biennial revision cycle. However, it is likely that NHI price revisions will be reinstated in April 2017, to coincide with the delayed sales tax increase.

South Korea: Pricing and Reimbursement Reform Proposals

According to the local press, the government has developed proposals for a range of amendments to the pricing and reimbursement system. The proposals are reported to include the following measures:

- the implementation of a modified procedure for manufacturers of new products willing to accept a weighted average price from a basket of international reference markets. The Ministry of Health and Welfare (MOHW) is reported to have announced that, as part of the modified procedure, it is considering exempting from pricing negotiations new products for which manufacturers are prepared to accept a price equivalent to 90% of the weighted average price seen in the reference markets. In the case of orphan drugs and biopharmaceuticals, the Ministry is proposing to offer 100% of the weighted average international reference price.
- the implementation of a pricing mechanism that would more accurately reflect the value of new drugs. It is understood that the MOHW plans to study the current use of pharmacoeconomics in the pricing and reimbursement process, with a view to improving its application to the evaluation of drugs for National Health Insurance (NHI) coverage.
- the simplification of the application procedures applying to orphan drugs, including the possible exemption of such medicines from pharmacoeconomic analysis.
- the implementation of procedures for the post-market monitoring of new drugs that have been subject to pricing negotiations.

In a separate development, a representative of the MOHW is reported to have announced reform proposals (for implementation in 2015) under which cancer treatments would be reimbursed without the need for a pharmacoeconomic assessment. The reforms would also include the introduction of differentiated patient co-payments for oncology products, and the possible off-label use of paediatric treatments PPR

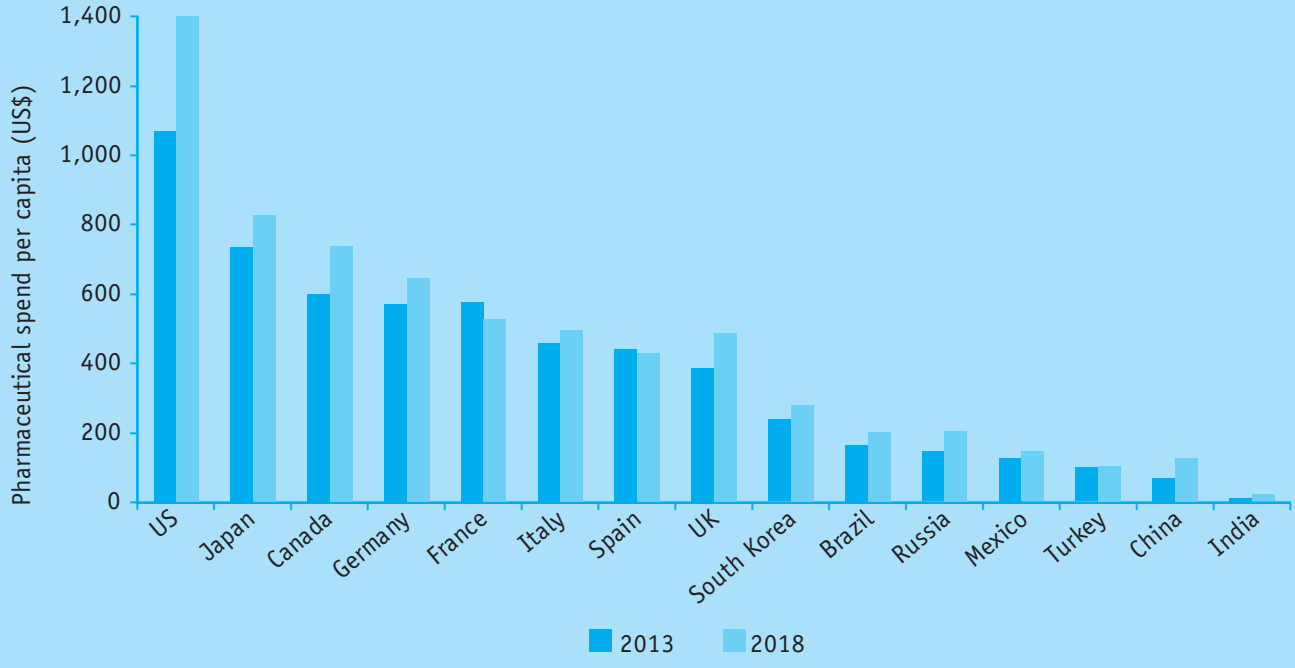
TRENDS AT A GLANCE

The IMS Institute for Healthcare Informatics has published a report revealing that global spending on pharmaceuticals is forecast to total US$1.3 trillion (€1.05 trillion) by 2018, up by 30% compared to 2013. In addition, the report reveals that pharmaceutical expenditure per capita is forecast to increase in most countries in 2018 compared to 2013 (see Figure 1). Indeed, only France and Spain are expected to see a decline in pharmaceutical spending per capita over this period, which the IMS Institute puts down to policies designed to control spending growth in these countries.

Over the next five years (to 2018), China's per capita spending on pharmaceuticals is set to increase by 70% – the highest rate of growth of all the countries included in the IMS Institute's report. Likewise, growth in pharmaceutical spending per capita in the US is also expected to remain strong, driven by fewer patent expiries than in previous years, the launch of innovative products and increasing drug prices.

Notably, an average increase in pharmaceutical expenditure of 50% is forecast for "pharmerging" markets (which encompass 21 countries including Brazil, China, India, Mexico, Russia and Turkey) over the next five years (to 2018). Nevertheless, pharmerging markets are still expected to lag some way behind more developed markets (Canada, France, Germany, Italy, Japan, South Korea, Spain, the UK and the US) in 2018 in terms of per capita expenditure on drugs PPR

Figure 1: Per Capita Pharmaceutical Expenditure in Selected Markets (2013 vs 2018)



Notes:

Expenditure used to calculate spend per capita in US$ at actual and forecasted variable exchange rates.

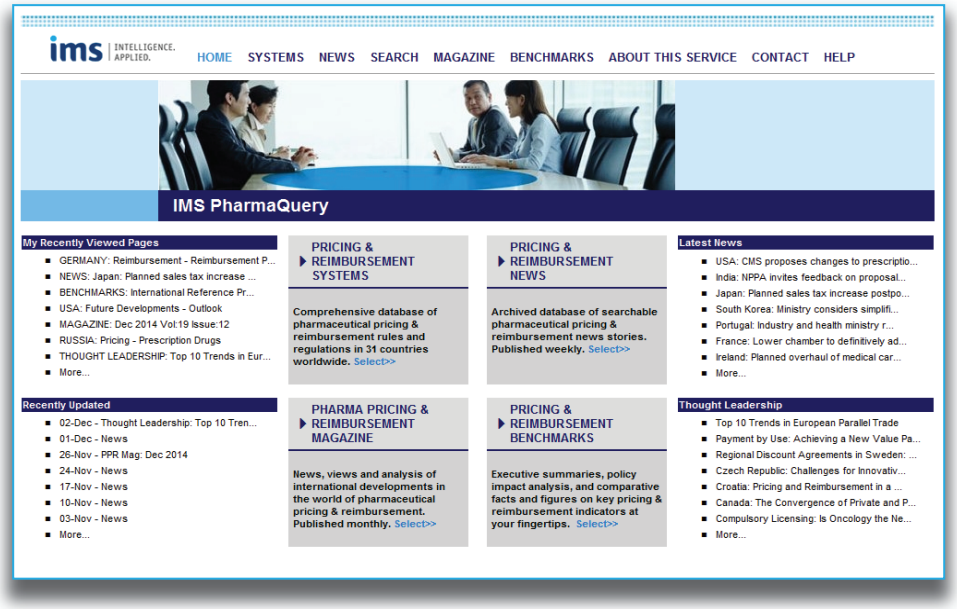
Data from Economic Intelligence Unit, 2014, IMS Market Prognosis, September 2014

Source: IMS Institute for Healthcare Informatics, "Global Outlook for Medicines Through 2018", November 2014

IMS PharmaQuery

THE ORIGINAL ONLINE DATABASE OF PRICING AND REIMBURSEMENT INFORMATION

IMS PharmaQuery is the one-stop shop for online pricing and reimbursement news and resources covering 31 major countries, designed by IMS P&R experts for P&R and market access experts.



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The website provides detailed information on the rules and regulations, theories and practices, trends and developments, in pricing and reimbursement worldwide and includes four distinct sections:

- **Pricing and Reimbursement Systems**: comprehensive database of healthcare systems in 31 key world markets, including detailed pricing and reimbursement regulations
- **Pricing and Reimbursement News**: weekly news service delivered direct to your desktop via email alert, hyperlinked to related News stories and background information in PharmaQuery Systems and archived back to over 6,000 fully searchable News stories dating from 1998
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ABOUT IMS

Operating in more than 100 countries, IMS Health is the world's leading provider of market intelligence to the pharmaceutical and healthcare industries. With more than 57 years experience, IMS Health offers leading-edge market intelligence products and services that are integral to clients' day-to-day operations, including product and portfolio management capabilities; commercial effectiveness innovations; managed care and consumer health offerings; and consulting and services solutions that improve productivity and the delivery of quality healthcare worldwide. Additional information is available at http://www.imshealth.com

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