Market Access Trends in the US, Europe, and Emerging Markets
Introduction

Rising drug spending and increased desire for expenditure controls are consistent themes across the US, Europe, and emerging markets. With governments and private healthcare systems under increasing pressure to fund high-cost, innovative therapies, which often launch with limited clinical trial evidence, payers are looking towards new and enhanced reimbursement processes which align drug funding with patient value. Based on these growing demands, the healthcare policy environment remains fluid, with payers introducing increasingly restrictive cost-control mechanisms in order to limit the burden on constrained healthcare budgets. For pharmaceutical manufacturers, success will require increasing flexibility on price and the ability to adapt to new access scenarios brought about by changing access dynamics and geographical differences.

Pricing pressures are present in all surveyed markets, with payers either looking to introduce new mechanisms or enhance existing ones to control healthcare spending. While the majority of European markets have existing processes to control drug prices, national healthcare authorities are continually looking to sharpen these tools in response to changing market dynamics. In contrast, with a fragmented healthcare system and lack of formal health technology assessment process, mechanisms for price control are relatively absent in the US. However, with rising drug spending and high out-of-pocket costs, public appetite for action on prescription drug prices is strong, resulting in a proliferation of new healthcare policies, growing demand for value-based pricing, and increased transparency within the pharmaceutical supply chain.

Although sales of branded medicines have typically been driven by self-funding in emerging markets, governments are under growing pressure to provide patients with access to innovative, and sometimes life-saving drugs. While subsidized access to more innovative medicines is being pursued in a number of emerging markets, it is accompanied by greater pricing controls and growing use of more sophisticated cost-control mechanisms.

Figure 1: Market access policy changes across the US, Europe, and emerging markets

<table>
<thead>
<tr>
<th></th>
<th>US</th>
<th>Europe</th>
<th>Emerging markets</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pricing</strong></td>
<td>Growing demand for pricing controls and price transparency</td>
<td>Increasingly tough line on pricing negotiations</td>
<td>Expansion of scope of drug price controls and tighter limits</td>
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<tr>
<td><strong>Health technology assessment (HTA)</strong></td>
<td>Rising prominence of ICER (value-based assessments)</td>
<td>Growing number of drugs subject to HTA procedures. Increasing clinical evidence demands</td>
<td>Nascent, but growing use of HTA as a means of controlling both prices and access</td>
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<tr>
<td><strong>Reimbursement</strong></td>
<td>Tighter payer controls, including formulary exclusions</td>
<td>More restrictive reimbursement conditions</td>
<td>Limited expansion of existing public programs</td>
</tr>
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US

The demand for value-based pricing grows as drug spending continues to soar in the US

Drug prices in the US have been the subject of significant debate over the past few years, following a surge in spending on prescription medicines, and substantial yearly price increases in some categories. President Donald Trump, who took office in January 2017, has vowed to intervene and tackle rising drug spending, highlighting increased transparency between different players in the pharmaceutical supply chain as a key action point. While several reforms have been proposed, the implications and feasibility of the changes are currently unknown. Nonetheless, growth in drug spending has significantly raised the requirement for drug manufacturers to justify the prices of their therapies, with increasing demand for value-based pricing mechanisms such as outcomes-based contracts, and cost-effectiveness assessments.

Several drug pricing policies have been proposed under the Trump administration, including international price indexing to European countries, and the elimination of safe harbors which enable pharmacy benefit managers (PBMs) to negotiate confidential discounts with manufacturers for Medicare- and Medicaid-covered therapies. These proposals could have far-reaching implications for manufacturers, plans, PBMs, pharmacies, and beneficiaries – however, it is currently difficult to predict what these consequences will be, or whether these reforms can legally be introduced.

Considering the growing public scrutiny of drug pricing policies, and the increased use of cost-effectiveness methods by payer organizations, value-based pricing is high on the agenda in the US. So far, value-based pricing efforts have primarily taken the form of outcomes-based contracts (OBCs), with insurance companies negotiating these agreements for a wide range of different therapies. However, with the exception of curative therapies, payers and policymakers seem to be unconvinced of the long-term cost savings these agreements provide. As drug prices continue to soar, the Institute for Clinical and Economic Review (ICER), a US-based organization which assess the comparative effectiveness of therapeutics, has been gaining considerable attention. While most payers are yet to formally incorporate ICER findings in their reimbursement decisions, its value assessments have begun to have an indirect impact on drug prices, and many believe the organization will have increasing influence in the future as the demand for value-based pricing grows.
Drug pricing debate

The Trump administration has proposed several reforms to tackle rising drug prices

Several drug pricing reforms have been proposed by the Trump administration over the past year, triggering intense speculation about the shape and reach of potential new price controls. In May 2018, the administration published a blueprint identifying key challenges in the American drug market and proposing a number of reforms to address these issues. Key challenges include high list prices, senior and government programs overpaying for drugs due to a lack of negotiating power, high and rising out-of-pocket (OOP) costs, and lastly, foreign governments “free-riding” off US investment in innovation1. Based on these identified issues, proposed reforms include international price indexing (IPI) to European countries and increased negotiating power for Medicare plans (see the table below for further information). While there seems to be true bipartisan support for action on lowering drug prices, which of these proposals are likely to take effect, and what the long-term impact of these changes will be, is currently unknown. Several payers interviewed by Datamonitor Healthcare are skeptical about the chances of any meaningful change being implemented under the current administration.

“I think we will have to change administrations quite frankly, I do not see anything happening in terms of healthcare until the end of the Trump administration.”
US payer

Figure 2: Key challenges identified in Trump’s 2018 Drug Pricing Blueprint

Table: Key challenges identified in Trump’s 2018 Drug Pricing Blueprint

<table>
<thead>
<tr>
<th>Challenges</th>
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<tbody>
<tr>
<td>High list prices</td>
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<td>European governments free-loading off US investment in innovation</td>
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<tr>
<td>Lack of negotiating power for government programs</td>
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<td>High out-of-pocket costs for beneficiaries</td>
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Source: Datamonitor Healthcare

Figure 3: Pricing reforms proposed under the Trump administration

<table>
<thead>
<tr>
<th>Proposal</th>
<th>When?</th>
<th>Impact?</th>
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<tr>
<td>Removal of the safe harbor exemption for rebates negotiated between PBMs, payers, and manufacturing companies for Medicare Part D and Medicaid-managed care covered drugs</td>
<td>Proposed: 1 February 2019</td>
<td>This plan is likely a positive step forward, but payers do not expect the impact to be significant. Medicare and Medicaid beneficiaries with high drug costs will likely benefit from these reforms, however, the shift could also result in higher insurance premiums for all beneficiaries.</td>
</tr>
<tr>
<td>“International price indexing” of Medicare Part B therapies to European markets</td>
<td>Proposed: October 2018</td>
<td>The proposal for IPI has been met with widespread criticism from industry, patient groups, and health economists who suggest that the plan will not yield significant reductions in US pharmaceutical prices but could negatively impact access to therapies in Europe. Payers are skeptical as to whether this policy will be passed considering the significant criticism it is facing.</td>
</tr>
<tr>
<td>Medicare Advantage plans allowed to impose step therapy restrictions and negotiate prices with pharmaceutical manufacturers for drugs reimbursed under Part B</td>
<td>Passed: 2018</td>
<td>Significant rebates will likely only be negotiated for therapies approved in highly competitive indications, in which there is limited differentiation of products. Furthermore, the impact of these new rules will be limited by the fact that only 35% of Medicare patients are covered by Medicare Advantage plans.</td>
</tr>
<tr>
<td>Prohibition of pharmacy gag clauses which bar pharmacies from telling patients about less-expensive treatment options</td>
<td>Passed: September 2018</td>
<td>While this legislation is only expected to have a small positive impact on patient costs, it is certainly a step in the right direction for patients.</td>
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<tr>
<td>Insurance companies permitted to exclude and restrict the reimbursement of therapies in Medicare Part D protected classes</td>
<td>Proposal due to be finalized in April 2019</td>
<td>This reform could have a substantial impact on the pricing of therapies in the Medicare protected drug classes, which are often highly expensive. However, critics argue that these changes could reduce patient access to drugs treating high-risk and life-altering diseases. This proposal is expected to face significant pushback from patient groups and members of Congress.</td>
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IPI = international price indexing; PBM = pharmacy benefit manager

Sources: 2, 3, 4, 5

Backlash from stakeholders reduces the chances that international price indexing will be introduced

The Trump administration’s proposal to internationally price index Medicare Part B products against prices in Europe is one of the most extreme to date, with the reform facing extensive pushback from numerous stakeholders. This proposal has been formed off the back of statements from the Department of Health and Human Services (HHS) and the Council of Economic Advisers (CEA), which have accused European nations of “freeloading” off high US drug prices. The CEA report suggests that innovation in the EU is not impacted by pricing, and therefore payers in member states can use various restriction methods to keep prices of pharmaceuticals just above marginal cost, including cost-effectiveness methods or reference pricing policies. The report concludes that meaningful reforms could address the free-riding that takes unfair advantages of American innovation, whether through enhanced trade policy, or by tying public reimbursement in the US to prices paid by foreign governments.

Figure 4: Proposed method for introducing international price indexing

<table>
<thead>
<tr>
<th>The proposed IPI model would incorporate two main elements</th>
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<tbody>
<tr>
<td>• Replace the current buy and bill system for Medicare Part B drugs, under which manufacturers are reimbursed based on a drug’s ASP + 6%, with a modified version of CMS’s previous competitive acquisition program.</td>
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<tr>
<td>• Hospitals would enrol with private sector IPI vendors, which would acquire and provide Part B therapies for administration, and bill Medicare Part B for the drug itself. Hospitals would then bill Medicare part B only for the drug’s administrations and a fixed “drug add-on payment”.</td>
</tr>
</tbody>
</table>

ASP = average selling price; CMS = Centers for Medicare & Medicaid Services; IPI = international price index

“There is really very little said about actual value. It basically says oh, we are just going to accept the evaluations that are created by other entities, whether they have a different set of values, whether it is a bigger or smaller problem in their country, and it does not really reflect what we are doing here in the States.”

US payer

The proposal for international price indexing has been met with significant criticism

The proposal for IPI has been met with significant criticism from the pharmaceutical and biotech industries (including the lobbying bodies; the Pharmaceutical Research and Manufacturers of America and the Biotechnology Innovation Organization), hospitals, patient groups, and health economists. Based on these criticisms, and the significant legal changes required for this reform to take place, interviewed payers are skeptical as to whether the bill will be passed. Major points of criticism include:

• **Reduced access to drugs in the US**
  Pharmaceutical lobbyists and patient groups argue that this reform will jeopardize access to medicines for US citizens and discourage innovation in healthcare. Patients in the US obtain the fastest and widest access to therapies in any developed country, and if passed, these policy changes would likely reduce patient access in line with European counterparts.

• **Higher list prices in Europe, but higher rebates also**
  While this regulation could result in pharmaceutical companies setting higher list prices in Europe, critics suggest the overall net price impact is expected to be nominal as governments and health technology assessment (HTA) agencies would reactively negotiate higher confidential discounts. Furthermore, the worst-case scenario would be that manufacturing companies abandon the European markets altogether, in order to avoid reference pricing to lower-income countries.

• **Overly simplistic attempt at introducing value-based pricing through the “back door”**
  Critics suggest that this proposal is an attempt to bring value-based pricing in through the back door in the US. They highlight that value-based pricing of pharmaceuticals should be a highly nuanced, multi-stakeholder process, reflecting the willingness-to-pay and budget constraints of the country in question. Linking US prices to countries with completely different healthcare systems, budget priorities, and expenditure limits goes against the concept of value-based pricing and would likely have a negative effect on research and development, with limited overall impact on global pharmaceutical expenditure.

“The mechanism does not account for drugs that are not in the index, if you have a new drug and you introduce it into the United States first, then you cannot index it because there is nothing to index against. [...] so, companies will introduce in the US first at very high prices and do that for a year until they get into Europe.”

US payer

Prohibiting rebate negotiations for Medicare Part D drugs may have a positive impact on beneficiaries with high OOP costs

HHS has announced a proposal that would eliminate the drug rebate process between PBMs, payers, and manufacturing companies for Medicare Part D and Medicaid-managed care covered drugs, aiming to increase transparency in the supply chain, and encouraging discounts to go directly to patients. Under the new plans, PBMs would get a flat fee from manufacturing companies for including drugs on their plans. HHS believes that by removing the need for manufacturing companies to offer increasing rebates to PBMs in exchange for formulary inclusion and preferable tier positioning, there will be less incentive to hike list prices up year-on-year. This rule would also create a new so-called “safe harbor” for drug discounts to be passed onto patients at the pharmacy counter, reducing overall OOP costs. Manufacturing companies and pharmaceutical lobbying groups have expressed significant support for these proposals.

While it is far from certain whether the safe harbor exemption can be easily lifted in 2019, and whether this proposal would actually result in lower drug prices, there seems to be bipartisan support for increased transparency within the rebate system. It is likely that those Medicare and Medicaid beneficiaries with high drug costs, who have not yet met their deductibles, or have co-insurance based on a percentage of a drug’s list price, will benefit from these reforms. However, the shift could also result in higher insurance premiums for all beneficiaries as plans stop applying manufacturer rebates to reduce these payment obligations.

Overall, it is expected that certain beneficiaries will see net cost reductions, but the increased costs and savings will not be evenly distributed.

Value-based reimbursement

With growing public scrutiny over high drug prices, the demand is increasing for manufacturing companies to justify the costs of their therapeutics based on the patient benefit they provide. Unlike in many European markets, the US healthcare system does not have a formal HTA or reimbursement body which assesses the clinical effectiveness and economic value. Formulary decisions are dictated by numerous different stakeholders, including PBMs, individual health plans, and government-funded agencies (eg Medicaid and Medicare), all of which employ different methods to regulate patient access to therapeutics. Payers in the US report very minimal ability to negotiate prices for high-impact drugs, especially in oncology and other indications where there are limited alternative treatment options. Payers’ inability to negotiate prices based on a drug’s perceived clinical and cost-effectiveness levels, along with the fragmented healthcare system, has heavily contributed to soaring drug prices in the US. Payers and decision-makers express increasing desire for new methods of value-based pricing, however, there is currently minimal consensus over the appropriate next steps.

Payers utilise OBCs in the US, but are yet to be convinced of their value

The main way pharmaceutical companies have engaged in value-based reimbursement in the US has been through product-specific OBCs penned


“These [OBCs] do not save money, it is really a pretence, if the drug does not work they stop taking it, if the drug works well they take it longer, the patient does better and the company does better because they get more money, and if they think the drugs are overpriced, rather than create this crazy value-based pricing exercise to reduce the cost a little bit, just reduce the cost upfront and save everybody all the work.”

US payer
with individual health plans. In outcomes-based models, innovator companies are paid for their therapies based on mutually agreed-upon timed measures and achievements of clinical performance or outcomes in the real world. If those goals are not met, the companies are not reimbursed, or are only partially reimbursed. Such deals have mainly been employed in competitive drug classes, demonstrating a divergence from the European trend of utilizing risk-sharing deals mainly in oncology. However, many payers lack the belief in the value of OBCs, viewing such deals as little more than positive public relations exercises from Pharma. In order to be convinced to utilize OBCs more widely, payers want to see evidence that OBCs create value savings that outweigh their administrative costs or savings that could be generated through simple rebate deals.

“One exception seems to be curative therapies
While payers express concern surrounding the long-term value obtained from OBCs in general, one exception seems to be curative therapies. Many US payers agree that risk-sharing/pay-for-performance deals are going to become the norm for gene therapies in the future and should work well given the high upfront costs, uncertainties around efficacy, and relatively small patient populations. The main benefit of the performance-based approach for payers is that the risk is put onto the developers, which is highly relevant for cell and gene therapies which often only have limited safety and efficacy data available at the time of launch. If the therapy does not work, the payer does not pay. This type of program is easier to integrate into existing payer systems where patients stay enrolled for a long time, such as with the US government programs Medicare or Medicaid. Another feature that could help with implementation is the use of patient data registries for products that need to comply with post-marketing surveillance, making it easier to track performance outcomes. For these reasons, pay-for-performance models are ideal for therapies that have some well-defined measures of benefit in clinical trials, or have outlined ways to predict clinical benefit that can be easily measured.

“I think gene therapy, if it does not work why should you pay for it? With things like that I can see it... If it is a binary, quick answer with a very expensive drug – maybe.”

US medical director
Rising influence of ICER

As the demand for value-based pricing increases, ICER, a US-based organization which assess the comparative effectiveness of therapeutics, has been gaining considerable traction. Funded primarily by non-profit foundations, ICER acts as an independent body which assesses the value that a drug or medical test brings to patients and the healthcare system, calculating a value-based price benchmark range that aims to facilitate discussions between payers and manufacturers. In alignment with national HTA bodies in the UK and Canada, ICER utilizes the incremental cost-effectiveness ratio, which is a standardized cost-effectiveness ratio that expresses dollars per quality-adjusted life years (QALYs) gained, to determine the value-based price of an intervention based on its demonstrated patient benefit. However, whereas NICE in the UK and CADTH in Canada have set thresholds upon which reimbursement decisions are based, ICER has no such remit, and instead acts as an advisory body providing maximum cost-effective prices for therapies relative to several different thresholds.

The majority of payers are yet to formally incorporate ICER reviews within their reimbursement processes

While payers would like to leverage findings from ICER reports in order to manage spending on therapeutics, they highlight certain issues which prevent widespread adoption. These include lack of assessments for all drugs, delays in publishing, methodological/transparency problems, and the fact that the agency is independent and non-regulated. Based on these factors, few payer organizations formally utilize ICER reviews in their reimbursement processes. Nonetheless, ICER seems to have at least an indirect impact on pricing as companies increasingly seek to avoid the negative publicity they tend to get if their product is judged to be overpriced by ICER. For example, Sanofi/Regeneron collaborated with ICER prior to the launch of the atopic dermatitis drug Dupixent (dupilumab), in order to develop a cost-effective pricing strategy for the novel biologic11. The manufacturing companies also agreed to cut the price of the cholesterol-lowering therapy Praluent (alirocumab), to a level ICER deemed cost-effective, in exchange for the removal of payer reimbursement restrictions12. While ICER reports that other drugmakers have expressed interest in working with the group in a similar way, the Praluent and Dupixent reviews so far are the only specific examples.

“At the end of the day, most of that [ICER analysis] is almost a wasted exercise because we cannot change the price once it is announced, we cannot change what we are going to have to pay for the product based on whatever contracts we have in place.”

US payer

CVS Caremark has referenced ICER thresholds in its self-insured plans
In September 2018, CVS Caremark announced that it would be instituting a $100,000 per QALY threshold, based on publicly available ICER reviews, above which it would deny patient access. Specifically, the PBM has stated that it will allow insurance companies to exclude therapies launched at a price greater than $100,000 per QALY from their plans, but it will make exceptions for therapies considered to be “breakthrough”\(^\text{13}\). Critics of this decision highlight the arbitrary nature of the $100,000 per QALY threshold, and further argue that the process incentivizes manufacturing companies to launch drugs at the maximum cost-effective price – a practice which is not aligned to the concept of value-based pricing\(^\text{14}\). Nonetheless, considering the size of the PBM, as well as its recent merger with Aetna, this move will likely have a considerable impact on patient access to therapeutics, especially for high-cost treatments with cheaper or generic alternatives.

ICER collaborates with NICE and CADTH on assessment of curative therapies
ICER has recently announced that it will be working in collaboration with NICE and CADTH, the UK and Canadian HTA bodies, respectively, to develop and test different methods that are specifically tailored for evaluating different types of expensive but potentially curative treatments and determining a value-based price\(^\text{15}\). The project aims to build consensus across HTA groups in anticipation of a rising tide of gene therapies and other potential cures. While there are currently no value frameworks that specifically address cell and gene therapies, this collaboration could enhance ICER’s presence and credibility in the space, paving the way for future involvement in the value-based pricing and reimbursement of curative treatments in the US.

Europe
Rising costs necessitate a change in market access dynamics

Europe’s payers face a thorny problem. As regulators strive to expedite the approval of innovative medicines, they are being asked to fund a steady stream of new drugs targeting serious, intractable, and often life-threatening diseases. Most carry hefty price tags, but a growing proportion are backed by limited clinical data, making it difficult to gauge their true, long-term therapeutic value. Demand for access to these products is strong, but healthcare finances across the region are under intense pressure. While authorities in the EU’s five biggest markets have continued to grant reimbursement for most new drugs, they have also pursued the implementation of measures designed to limit the impact of coverage decisions on healthcare budgets.

Pressure on healthcare budgets has also seen haggling over issues such as cost and cost-effectiveness emerge as an increasingly frequent cause of delays in the completion of P&R procedures. And restrictive conditions attached to the reimbursement of costly new drugs have affected patient access to such products, acting as a drag on their European revenues.

Drug price negotiations with payers are increasingly tough. Recent developments in both the UK and France have narrowed negotiation-free pricing avenues, while German payers are calling for the abolition of free pricing periods.

Although the main cost-containment targets may be medicines that are linked to large patient populations, orphan drugs have begun facing stiffer access challenges in some markets. The scale of the challenge posed by orphan drugs has increased since the beginning of this decade, reflecting moves by regulators to fast-track authorization for rare disease treatments and a progressive rise in the proportion of new drugs that boast orphan status.

**HTA reach in Europe grows as criteria become increasingly restrictive**

The cost-containment imperative has driven reform of established national HTA procedures in a number of EU member states since the beginning of this decade. In some, this has had a significant impact on market access – especially for innovative, high-cost specialty medicines. Across Europe, the number of drugs subject to health technology assessment is growing, and will continue to rise in the wake of recent policy developments (see the following table).

Furthermore, as HTA bodies apply increasingly restrictive approaches to the application of existing assessment mechanisms, these in turn will have implications for decisions on the funding, price, and uptake of new drugs. With further change being implemented or debated in several countries, the HTA landscape in Europe will remain fluid, forcing manufacturers to tweak existing development and commercialization strategies on a country-by-country basis.
Figure 5: Direction of HTA travel in the 5EU

<table>
<thead>
<tr>
<th>Country</th>
<th>Reach</th>
<th>Mechanics</th>
<th>Outcomes</th>
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<tbody>
<tr>
<td>France</td>
<td>No major change</td>
<td>Increasingly restrictive: SMR rating of ‘important’ or ‘major’ and ASMR score of I–III now required for hospital drugs to access the ‘list en sus’ if their comparator does not feature on the schedule</td>
<td>Increasingly restrictive: High ASMR scores (I–III) have become increasingly elusive</td>
</tr>
<tr>
<td>Germany</td>
<td>Increasing: Hospital drugs and some pre-AMNOG active ingredients are now subject to G-BA benefit assessments</td>
<td>No major change</td>
<td>Increasingly restrictive: Payers are pursuing a more aggressive approach in negotiations with manufacturers for drugs with low added benefit ratings. Greater flexibility is allowed in pricing negotiations for some medicines with no added benefit following reforms in 2017, though application is expected to be in select special cases only.</td>
</tr>
<tr>
<td>Italy</td>
<td>No major change</td>
<td>Changing: New algorithm being used by AIFA to determine the level of innovation offered by new drugs</td>
<td>Changing: Seven of the first 11 products assessed using the new algorithm were declared ‘non-innovative’</td>
</tr>
<tr>
<td>Spain</td>
<td>Increasing: The number of drugs subject to Therapeutic Positioning Reports has risen progressively over the past five years, while more pharmaceutical products are being assessed at regional and local level</td>
<td>No major change</td>
<td>Increasingly restrictive: Cost and cost-effectiveness are a feature of regional and local assessments, which can inform both reimbursement and clinical practice</td>
</tr>
<tr>
<td>UK</td>
<td>Increasing: NICE now assessing all cancer drugs and ultra-orphan products</td>
<td>Increasingly restrictive: Standard NICE ICER threshold now applied to oncology products that are candidates for inclusion in the Cancer Drugs Fund. Sliding, QALY-based ICER threshold being applied to ultra-orphans to determine NHS commissioning</td>
<td>Increasingly restrictive: Broader application of ICER thresholds will see NICE reject standard NHS funding for more drugs unless manufacturers give significant ground on price</td>
</tr>
</tbody>
</table>

SEU = five major EU markets (France, Germany, Italy, Spain, and the UK); AIFA = Italian Medicines Agency; AMNOG = Pharmaceutical Market Reorganization Act (Arzneimittelmarktneuordnungsgesetz); ASMR = additional medical benefit; G-BA = Federal Joint Committee (Gemeinsamer Bundesausschuss); HTA = health technology assessment; ICER = incremental cost-effectiveness ratio; NICE = National Institute for Health and Care Excellence; QALY = quality-adjusted life year; SMR = actual medical benefit
New AIFA innovation algorithm will determine funding as well as HTA outcomes

In 2017, Italy’s National Medicines Agency (AIFA; Agenzia Italiana del Farmaco) began working with a new algorithm that is applied by its Technical Scientific Committee, the CTS, to determine the degree of innovation offered by new drugs. The outcome of CTS assessments will have direct and significant implications for individual products, with those deemed “innovative” gaining immediate access to regional formularies (at least on paper), and to a share of €1bn ($1.16bn) in annual federal government funding designed to encourage the uptake of innovative medicines. Innovative drugs will also not be exposed to potential repayments that are often a feature of managed access agreements negotiated by regulators.

The new approach gauges the therapeutic need and added therapeutic value offered by a drug, and the quality of scientific evidence available to support the evaluation of those two criteria. Therapeutic need and added therapeutic value are ranked from “maximum” to “absent,” while the quality of scientific evidence on which those rankings are based may be categorized variously as high, moderate, low, or very low. Based on the outcome of CTS assessments, a drug will be designated as either innovative, conditionally innovative, or not innovative.

Early evidence confirms that added therapeutic value will be the key to securing innovative status under the new AIFA algorithm – even where, for rare disease treatments, the quality of scientific evidence in support of a drug is not deemed to be particularly high. By early May 2018, AIFA had published full details of 11 assessments completed using the new algorithm. The agency had conferred innovative status on three of those products, granted conditionally innovative status to another, and concluded that the drug in question was not innovative in the remaining seven cases16.

RESULTS OF THE IMPLEMENTATION OF THE NEW INNOVATION ALGORITHM SO FAR

All three of the drugs granted innovative status were deemed to offer an “important” degree of added therapeutic value, despite the fact that the quality of evidence in support of that rating was deemed “moderate” for AbbVie’s Mavyret (glecaprevir + pibrentasvir), and “low” for Biogen’s Spinraza (nusinersen) and Dompé’s Oxervate (cenegermin). No other drug was deemed to offer more than “moderate” added therapeutic value. Eli Lilly’s rheumatoid arthritis treatment, Olumiant (baricitinib), which was the only product deemed to be supported by high-quality scientific evidence, was gauged not to be innovative on the basis of moderate therapeutic need and low added therapeutic value16.

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New drug prices are under growing pressure
Unlike in the US, introductory prices for new drugs seeking reimbursement are subject to explicit negotiation in France, Italy, and Spain. Manufacturers are free to set their own launch prices in the UK, though they will hit access hurdles if they do satisfy NICE’s cost-effectiveness criteria, while in Germany companies may sell drugs containing new active substances at higher list prices for 12 months, after which prices negotiated by manufacturers and statutory health insurance funds apply.

Where new drug prices are subject to negotiation, regulators and payers are pursuing an increasingly tough line, while opportunities for manufacturers to set their own prices – where these exist – are being squeezed in a bid to limit rates of increase in reimbursement spending. Both of these trends are acting as constraints on market access. Haggling over price is delaying the completion of P&R procedures, while the launch of some new drugs has been put on hold by manufacturers where they believe negotiated prices are unsatisfactory. At the same time, regulators in countries such as the UK and France have implemented new rules designed to close down unregulated launch price avenues or render them less attractive.

Low HTA scores weaken the hand of manufacturers during price negotiations
The outcome of health technology assessments has a direct bearing on prices in several 5EU countries. As such, increasingly conservative benefit scores being chalked up by HTA agencies have strengthened the hand of payers and regulators involved in the negotiation of new drug reimbursement prices.

The trend has been most noticeable in France, where there has been a sharp decline in the added medical benefit (ASMR) scores being awarded to new drugs. This has direct and significant implications on the price likely to be achieved by the majority of new drugs reaching the French market, since only those granted ASMR ratings of I–III benefit automatically from a “European price guarantee,” under which the price authorized in France will not drop below the lowest price prevailing in the four other 5EU markets in the five years following initial approval for reimbursement.

While they did not enjoy any such price guarantee, drugs deemed to offer a minor added benefit (ASMR IV) could traditionally expect a modest price premium over the existing standard of care. That is no longer the case, however, with the ministry of health having called on the Economic Committee for Health Products (CEPS; Comité Économique des Produits de Santé) to ensure that new drugs with ASMR IV ratings do not trigger a net increase in health system costs17. As a result, some medicines with ASMR IV ratings and generic comparators have faced protracted price negotiations. One notable example is Novartis’s heart failure drug Entresto (sacubitril + valsartan). The drug was approved by the EMA in 2015 and despite a National Health Authority (HAS; Haute Autorité de Santé) assessment conducted in 2016, it still has no price listing.


“Entresto tried to get a premium price because the comparator is enalapril, and they said well you should have enalapril plus something, but something small, and of course it is not doable, and for this reason Entresto has not yet an official price.”

Former French national payer
Free pricing periods are the focus of growing criticism in Germany

German payers are increasingly unhappy with rules that oblige them to fund the provision of costly drugs at the manufacturer’s chosen price for 12 months following launch – especially where the Federal Joint Committee (G-BA; Gemeinsamer Bundesausschuss) has been unable to quantify the degree of additional benefit offered by such products. This is a particular issue for orphan drugs, in respect of which the G-BA is frequently unable to quantify additional benefit levels, but the free pricing rule also means German payers were heavily exposed to the initial cost of reimbursing new-generation hepatitis C treatments.

Where payer spending on the reimbursement of orphan drugs exceeds €50m ($58m), full benefit assessments are undertaken. These have delivered mixed results, with some high-profile products such as Imnovid/Pomalyst (pomalidomide; Celgene) and Imbruvica (ibrutinib; AbbVie/Johnson & Johnson) deemed to offer no additional benefit over existing therapy in some subsections of the patient populations they target. The outcome of such assessments has strengthened calls for a more restrictive approach to the reimbursement and pricing of rare disease treatment in Germany, including a reduction in – or even the outright abolition of – free pricing periods for orphan drugs.

Measures designed to prevent a repeat of the situation faced by payers following the launch of new-generation hepatitis C treatments were contained in early drafts of the Pharmaceutical Market Reorganization Act (AMNOG; Arzneimittelmarktneuordnungsgesetz) reform package adopted in 2017. Where a new drug generated payer spending of more than €250m ($290m) before the 12-month free pricing period had elapsed, this would have seen prices negotiated by manufacturers and health insurance funds applied retrospectively, from the point at which that threshold was exceeded. The provision was removed from the final version of the 2017 reform package, which was ratified in May 2017 as the Act to Strengthen Pharmaceutical Supply in the Statutory Health Insurance System (AM-VSG). However, the calls for introduction of retrospective rebate are likely to be repeated, with a lower threshold affecting a larger number of medicines on the cards.

“The next loophole that gets closed is the orphan drug loophole. I am not sure whether it is in two years or four years, but that will happen”

German payer

“I think 250 million is not realistic if this regulation comes back, and it will come back, for sure.”

German regional payer

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Disparate approaches to orphan HTA are splintering access to rare disease treatments

Conducting meaningful assessments on rare disease treatments has always been difficult, given the often limited nature of clinical data to support such reviews, and the frequent absence of traditional, explicit clinical endpoints traditionally used by HTA agencies to inform their assessments. Coupled with the fact that national approaches to orphan drug HTA vary widely, this has driven a significant degree of divergence where the outcome of national assessments is concerned, which has had a growing impact on market access for rare disease treatments in Europe. The fate of Vertex Pharmaceuticals’ cystic fibrosis drug, Orkambi (lumacaftor + ivacaftor), highlights the impact that national approaches to HTA can have on the availability of rare disease treatments (see the box).

With spending on orphan drugs increasing rapidly, and with revolutionary new treatments for rare diseases nearing the market, this is an area where further change is likely to be witnessed. HTA has already begun to pose a stiffer challenge for many orphan drugs in the UK, where NICE has been handed broader responsibilities in the sector, and where new cost-effectiveness thresholds have been introduced for some rare disease treatments. Calls for the imposition of tighter scrutiny on orphan drugs are also growing in Germany, where existing rules mean rare disease treatments are not required to undergo full health technology assessments.

ORKAMBI CASE STUDY

Granted EU marketing authorization in November 2015, Orkambi began generating sales in Germany – where the G-BA concluded that it offered “considerable additional benefit” to cystic fibrosis patients with specific gene mutations targeted by the product – at an early stage in 2016. More than two years later, Vertex was still struggling to obtain NHS coverage for Orkambi in the UK, where NICE had concluded in March 2016 that the product was not a cost-effective treatment option. The rejection was followed by a protracted negotiation between NHS England and Vertex, which culminated in the company’s rejection of a portfolio coverage deal put forward by NHS England in July 2018. The deal would have allowed for immediate and expanded access to Kalydeco (ivacaftor) and Orkambi, as well as immediate access to Symdeko (tezacaftor + ivacaftor) from the date it is licensed, for which Vertex would have been reimbursed £500m over five years. In its rejection of the offer, Vertex highlighted that this would have worked out at only £14,000 per patient per year, which would have been equivalent to a 90% discount to the German price. The deadlock in negotiations continues despite the case having been referred to Parliament.

Funding issues are driving use of new cost-containment tools

European payers have gritted their teeth and stumped up funds to bankroll coverage for a growing number of pricey rare disease treatments. They have done so secure in the knowledge that, while per-patient treatment costs for these drugs may be extremely high, small patient cohorts mean their overall impact on pharmaceutical budgets is manageable. Payers were caught out by the arrival of new direct-acting antiviral (DAA) drugs for the treatment of hepatitis C virus (HCV) infection in the early part of this decade, however, and struggled to cope with the implications of funding products that carried not just a sizable price tag, but also indications for use in a much larger patient population. In an effort to allow access to those most in need of treatment without breaking the bank, European payers have resorted to a range of tools, including managed entry agreements, patient prioritization criteria, and dedicated funds.

While the arrival of further competing products handing payers greater leverage in pricing negotiations and reducing patient numbers has all but eliminated the challenge, the funding crisis created by the launch of DAAs has led to the creation of new financial tools designed to moderate the budget impact of innovative medicines. These novel tools, such as budget ceiling agreements, have now been agreed for immunotherapies in France, while payers in Italy are also foregoing the more complex risk-sharing deals in favor of price-volume agreements. Regulatory changes could pave the way for more widespread use of price-volume agreements in Germany, while in the UK the introduction of the £20m budget impact test could be construed as a way of UK payers trying to avoid another hepatitis C-like crisis.

“There is a target from the minister of the budget not to go beyond €700m for all the PD-1s, like we have done for hepatitis C, so it is very similar.”

Former French national payer

“We will try to implement mechanisms which are giving us more flexibility on pricing, so price-volume contracts, maybe hidden rebates on a national level if a certain volume threshold is hit.”

German regional payer
Budget impact test could delay UK market access for one in five new drugs

Under normal circumstances, the NHS is required to make new drugs available not more than 90 days after the publication of a positive NICE technology appraisal. But under new rules adopted in April 2017, one in every five new drugs could now face much lengthier market access delays and greater squeezes on price.

The new rules introduced a budget impact test, which will apply to any drug deemed cost-effective by NICE but forecast to increase net NHS spending by more than £20m ($26.6m) in any of the first three years in which it is funded. Products expected to generate spending in excess of that threshold will be subject to separate negotiations between manufacturers and NHS England (NHSE) before routine commissioning commences. Where these fail to elicit an agreement under which a product would generate net annual spending of less than £20m ($26.6m), NHSE may request “a variation to the statutory funding requirement”23. In effect, this is likely to involve the phased introduction of funding for a drug, limiting its availability for up to three years in a bid to mitigate the impact on NHS finances.

By NICE’s own admission, the new budget impact threshold is likely to trigger additional negotiations on around one in five new drugs, but the watchdog has said it hopes commercial agreements between companies and NHSE will minimize or, in some cases, avoid completely the need to delay access to a new drug24. What is clear though is that the route to securing market access in the NHS has only got tougher, as well as longer, with new haggling expected not only around the suitability of the cost-effectiveness models but also reliability of projections of patient numbers, treatment duration, as well as overall impact on the patient pathway.

So far, only one drug affected by the budget impact test has emerged through the price negotiation following failure to pass the £20m budget impact test; Merck & Co’s Keytruda (pembrolizumab) for first-line PD-L1-positive non-small cell lung cancer. Any details of the outcome other than its inclusion in routine commissioning are lacking, but it is likely Merck & Co had to agree to a substantial price concession.

“I think the lessons that I would give would be do not forget the ‘I’ in the middle of that budget impact test, ‘I’ stands for impact, so it is not how much your drug is going to cost, it is the extra cost of your drug’s effect on the pathway, and to be brutally realistic about what that is.”

NHS England payer

New rules jeopardize funding for some hospital drugs in France
Since 2004, costly inpatient drugs have been funded through an initiative designed to enable their use in hospitals reimbursed via diagnosis-related group (DRG) payments. Products that qualify for funding through this route are contained on a schedule known as the “liste en sus”, which allows for use of the drugs that would not otherwise be covered by the DRG tariff. Spending on the initiative has risen sharply since the beginning of this decade, and in 2016 – in a move designed to generate annual savings of €205m ($237.6m) – regulators amended conditions governing the inclusion of drugs on the list25.

Under the new rules, drugs with comparators that do not already feature on the liste en sus may only be included if they have obtained an SMR rating of either “important” or “major” and an ASMR rating of I–III. Cancer drugs delivered in the hospital setting were particularly hard hit, with Amgen’s multiple myeloma drug Kyprolis (carfilzomib) achieving a listing only in July 2018, over 2.5 years after it received the European marketing authorization. The listing success occurred following submission of more mature data demonstrating an overall survival benefit and an upgrade in ASMR from IV to III.

Conditions attached to funding for products already on the list were also tightened, triggering the removal of several high-profile brands with treatment costs significantly higher than the average in their specified indications (see the box below)25.

“If you get an ASMR IV you would be reimbursed on paper but you would have no access because the recommendations would not be followed on top of the DRG.”
Former French national payer

FIRST CASUALTIES OF THE LISTE EN SUS REMOVALS
Pfizer’s leukemia drug Zavedos (idarubicin) and United Therapeutics’ pulmonary arterial hypertension treatment Remodulin (treprostinil) were removed completely from the liste en sus in the first half of 2016, along with four other products. Later in that year, hospital funding for several cancer drugs was withdrawn – this time partially, on a per-indication basis. The move dealt a particular blow to Roche and Janssen. Roche saw liste en sus funding for three indicated uses of Avastin (bevacizumab) terminated, while subsidies for Herceptin (trastuzumab) were trimmed. Like Avastin and Herceptin, Janssen’s Velcade (bortezomib) and Caelyx (pegylated doxorubicin) remained on the liste en sus, but with funding restricted to fewer indications25.

Emerging Markets
Payers tighten their belts as economic growth slows

In the past decade, governments in many of the leading emerging markets have implemented reforms aimed at improving access to healthcare for their populations. Typically, as far as drug coverage is concerned, public healthcare programs focus on the provision of free or heavily subsidized generics, reflecting the limited nature of budgets available to underpin public sector reimbursement. As a result, patients are still heavily exposed to pharmaceutical costs in most emerging markets, and measures to cut out-of-pocket spending on medicines are often an integral feature of reforms designed to improve access to healthcare. While these include expansion of subsidized access to more innovative medicines, drug prices have also been a frequent target of cost-containment initiatives across several emerging markets.

The rollout of drug coverage initiatives in many emerging markets was announced or embarked upon during periods of strong economic growth. Even then, costs associated with these schemes were daunting. Now, with many emerging economies slowing – and some struggling to recover from recent periods of recession – that challenge has been magnified. Funding issues have already delayed the rollout of planned reimbursement initiatives in some countries, and pose a threat to the long-term viability of schemes rolled out recently in others. As a result, efforts to limit costs associated with expanded access to medicines are being stepped up.

Prescribing controls and the imposition of strictly defined patient populations may both help to limit reimbursement costs. The price of medicines funded by governments or social health insurance programs can also help to maximize the impact of finite budgetary resources however, and where access to new drugs is being broadened, pressure on prices is increasing.

Figure 6: Key forces shaping access in emerging markets

- Growing patient demand for access to healthcare and innovative treatments
- Expansion of public healthcare programs over the past decade
- Inclusion of innovative medicines in some subsidized medicines programs
- Economic slowdown limits expansion of subsidized drug programs
- Growth in public reimbursement programs puts pressure on medicines’ prices and drives greater prescribing controls
- Inadequate funding limits prescribing of innovative brands included on reimbursed drug lists
Pressure on new drug pricing is increasing

New drug prices in many emerging markets have traditionally been free from explicit regulatory control. That remains the case in some countries, but the prevailing trend is towards a more interventionist approach – especially where governments are footing the bill for the reimbursement of innovative medicines. This has seen existing public sector purchasing mechanisms overhauled in a bid to lever down procurement prices, while the imposition of ceilings on the price of new drugs, often set via reference to those in other countries, is increasingly widespread. More recently, policymakers in some emerging markets have begun to adopt some of the strategies employed by governments and payers in developed healthcare systems, including pharmacoeconomic analysis, health technology assessments (HTAs), and the use of managed entry agreements (MEAs).

Some of these approaches are potentially beneficial for originators, since they encourage more widespread reimbursement of costly new drugs. Expertise required to conduct HTAs is limited in many emerging markets however, and there is a danger that the approach will be used in some countries as a tool with which to lever down prices rather than to gauge the true value of innovative drugs to patients and healthcare systems. The negotiation of meaningful MEAs will also be problematic in countries where accurate monitoring of real-world data is either difficult or impossible, and agreements will be dominated in the near term by relatively straightforward, finance-based deals which cap prices or overall reimbursement liabilities.

Figure 7: Policies shaping pricing dynamics in emerging markets

| External reference pricing (ERP) | • Widely employed but the size and nature of reference-country baskets employed varies.  
• Price is often set at the lowest price prevailing in any reference country. |
|----------------------------------|---------------------------------------------------------------------------------------------------------------------------------------|
| Managed entry agreements (MEAs) | • An emerging tool in countries where governments are attempting to provide subsidized access to more new drugs.  
• Most are simple financial agreements as the systems and procedures required to collect outcomes data are often either rudimentary or completely lacking. |
| Health technology assessment (HTA) | • Some countries are turning to use of HTA and pharmacoeconomics to inform their coverage decisions, but most are in early stages.  
• Wider HTA use could impose stronger pressure on some new drug prices, and threaten existing drug reimbursement. |
| Public sector procurement       | • Government-linked procurement agencies are an established feature of several emerging Asian and South American markets.  
• Pressure on prices is ramped up through consolidated procurement for the supply of public hospitals. |
Public formulary access can be a lengthy, complex process

Most emerging-market countries are still predominantly self-pay pharmaceutical markets, and gaining access to public sector formularies poses a difficult, often complex challenge for originators. The scarcity of funds available to underpin subsidized medicines provision militates heavily against the widespread listing of costly patented drugs, and while listing procedures may involve the consideration of other factors on paper, cost is often the main determinant of formulary inclusion in practice.

National formularies are typically restrictive, with many based largely on the WHO’s model lists of essential medicines, and are subject to delayed updates. Comprehensive access to public sector formularies may also be complicated by the multi-layered nature of responsibility for medicines provision, and hospital compliance with national or regional listings varies, with drug inclusion subject to delays or lack of appropriate funding.

Notwithstanding the challenges involved in gaining access to public sector reimbursement, the number of innovative, patented medicines contained on major public formularies has increased appreciably in some emerging markets over the past five years, in China in particular. That trend looks set to continue – partly because governments are under growing pressure to improve access to innovative products, but also because measures designed to limit or manage the budgetary impact of new drug reimbursement listings have been put in place, reassuring regulators that coverage of specific products will not impose unsustainable pressure on reimbursement budgets.

Coverage is often partial, however, posing affordability issues for many patients. Access may also be reserved for the inpatient setting, with out-of-pocket purchases still key for drugs used outside of hospitals. And while catastrophic drug funds provide controlled access to some high-cost products, typically, these provide access to treatments for a strictly defined range of conditions and patient populations.

Patients in some countries have turned to the courts, arguing that the refusal of governments or payers to reimburse a particular product breaches their constitutional right to health. This poses additional challenges for payers attempting to prioritize the use of scarce healthcare funding resources. As a result, policymakers have begun to push back. In Brazil, the Supreme Court has raised the bar for lawsuits seeking access to medicines.

CHINA: PRICE NEGOTIATIONS HAVE PAVED THE WAY FOR A SLEW OF NRDL LISTINGS

In February 2017, the National Reimbursement Drug List (NRDL), which shapes provincial and local medicines coverage, was updated for the first time since 2009. Shortly after the February 2017 NRDL update, regulators published a list of 44 more high-cost drugs selected for national price negotiations. Agreements were reached for 36 of the 44 products involved and, in July 2017, the government announced the addition of those drugs – including more than 20 multinational brands – to List B of the NRDL. More than half of the 36 products were oncology or immune-modulating drugs, and the list included around a dozen multinational cancer brands. The July 2017 NRDL listings were granted in return for price cuts averaging 44%, though some prices were up to 70% below those prevailing prior to the national negotiation process. 2018 saw 15 more oncology multinational brands added to the NRDL.

27. FT (2017) China slashes prices of patented western drugs by up to 70%. Available from: https://www.ft.com/content/ef1566be-6c7b-11e7-bfeb-33fe0c5b7eeaa [Accessed 31 October 2018].
Private formularies are key early targets for innovators

The restrictive nature of public sector reimbursement means private formularies have traditionally been the main initial target for originators in emerging markets. Reimbursement by private payers is often limited, however, and while private providers generally take a liberal approach to new drug listings, patient finances act as a significant constraint on demand for costly medicines.

The private insurance market in many emerging economies is limited in terms of sophistication as well as size. Private cover often involves the provision of a lump-sum payment for the treatment of serious health conditions, and payers do not operate explicit drug formularies. Where private payers do operate their own formularies, these are used predominantly as a cost-containment tool, rather than as a means through which to attract affiliates. As a result, private payer formularies are often almost identical, and are seldom expanded voluntarily.

Instead, inclusion on high-end private hospital formularies is the main early goal of originators seeking market access for new drugs. This often presents few barriers, since patients seeking treatment in these establishments have high expectations where standards of provision are concerned, while drug sales generate income for private hospitals. However, private hospital formularies tend to vary dramatically within individual markets, reflecting differences in the patient populations targeted by individual facilities.

Market access outlook across major emerging markets offers a mixed picture

Out-of-pocket spend and private formularies will remain the key access routes for high-cost innovative drugs in emerging markets, despite efforts to expand public sector reimbursement in many countries. While access to subsidized medicine programs is still challenging in most emerging markets, there are definite signs that innovative new drugs will be reimbursed more widely in several countries as a result of MEAs – provided both regulators and manufacturers are willing to give some ground. China is substantially ahead of most other emerging economies where improving public market access is concerned, and has witnessed several rapid changes over the past couple of years.
### Figure 8: Access outlook in subsidized medicine provision across key emerging markets

<table>
<thead>
<tr>
<th>Country</th>
<th>New drug pricing</th>
<th>New drug reimbursement</th>
<th>Formulary access</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brazil</td>
<td>Few new drugs are able to achieve premium pricing. International referencing will limit launch prices. Permitted annual price hikes for patented drugs will lag inflation.</td>
<td>CONITEC will continue to pursue a highly restrictive approach to new drug reimbursement listing. Access to costly new drugs through the courts will become more challenging.</td>
<td>MEAs could pave the way for an increase in the proportion of new drugs granted access to the RENAME. Pressure on private payer finances will rule out more expansive approaches to private formulary listing.</td>
</tr>
<tr>
<td>Russia</td>
<td>International referencing will limit the maximum ex-manufacturer price of drugs included on the EDL. Obtaining approval for currency-based adjustments to EDL prices is challenging.</td>
<td>Few innovative new drugs will be reimbursed under existing federal and state schemes. The rollout of a national outpatient drug reimbursement scheme has been delayed.</td>
<td>Additions to the ONLS and VZN formularies were announced in the run-up to the 2018 presidential election. Coverage of three additional conditions will be provided by the VZN from 2019.</td>
</tr>
<tr>
<td>India</td>
<td>Caps on the price of more prominent multinational brands will be triggered by future expansion of the NLEM. Pressure on the government to regulate patented drug prices will continue to grow.</td>
<td>Where subsidized pharmaceutical provision exists, it will be confined almost exclusively to low-cost, multi-source drugs.</td>
<td>The NLEM remains a formulary on which originators would rather their products did not appear, since inclusion triggers the imposition of price caps.</td>
</tr>
<tr>
<td>China</td>
<td>National prices have been negotiated for a slew of innovative originator products since the beginning of 2017.</td>
<td>National price negotiations are paving the way for the inclusion of patented multinational brands on List B of the NRDL. The new State Medical Insurance Administration will identify more candidates for inclusion on the national list.</td>
<td>Provincial reimbursement formularies have been updated rapidly in the wake of recent NRDL revisions. Poorer provinces will struggle to fund the reimbursement of some NRDL drugs, and will remain less extensive than those in more prosperous areas of the country.</td>
</tr>
<tr>
<td>Mexico</td>
<td>Public sector prices for patented drugs are set via negotiation with the CCNPMIS.</td>
<td>Pressure on public payer budgets has driven a highly restrictive approach to the reimbursement of expensive new drugs.</td>
<td>Catalogue II of the IMSS formulary, which lists costly, innovative medicines reimbursed by the institute, contains only 24 molecules. MEAs could pave the way for the inclusion of more new drugs on major public formularies.</td>
</tr>
<tr>
<td>Indonesia</td>
<td>Substantial discounts or bonusing commitments will be required to secure access to the national formulary and e-catalogue, which inform public sector prescribing and procurement.</td>
<td>Delays in inclusion of new drugs on the national formulary will continue. Requests for inclusion on the reimbursement schedule will not be accepted directly from manufacturers.</td>
<td>The FORNAS, which determines access to medicines under the new NHI scheme, was updated at the beginning of 2018, triggering the first-time inclusion of several patented brands.</td>
</tr>
<tr>
<td>Turkey</td>
<td>Restrictive rules – and ad hoc adjustments to the way they are applied – will continue to limit prices achieved by new drugs seeking reimbursement through traditional channels.</td>
<td>A new procedure allows for the negotiation of MEAs, exempting affected products from normal pricing and reimbursement rules. Access to off-label use of patented drugs is becoming more restrictive.</td>
<td>MEAs will encourage the inclusion of more innovative products on the SGK’s positive list. Imported patent-expired brands will face the risk of exclusion from the positive list.</td>
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**Outlook**

- Positive
- Neutral
- Negative

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CCNPMSI = Comisión Coordinadora para la Negociación de Precios de Medicamentos e Insumos para la Salud; CONITEC = Comissão Nacional de Incorporação de Tecnologias no Sistema Único de Saúde; EDL = Essential Drugs List; FORNAS = Formulário Nacional; MEAs = managed entry agreements; IMSS = Instituto Mexicano del Seguro Social; NLEM = National List of Essential Medicines; NRDL = National Reimbursement Drug List; ONLS = outpatient coverage scheme for vulnerable patients; RENAME = Relação Nacional de Medicamento Essenciais; SGK = Sosyal Güvenlik Kurumu; VZN = orphan drug coverage scheme.
Brazil: CONITEC remains the key gatekeeper for public reimbursement

Gaining access to public sector reimbursement for new drugs remains difficult in Brazil, reflecting the restrictive approach pursued by the country’s HTA agency, the National Committee for Health Technology Incorporation (CONITEC; Comissão Nacional de Incorporação de Tecnologias no Sistema Único de Saúde). While pressure on policymakers to fund access to more innovative medicines is intense, CONITEC still counseled against coverage for around half of all the drugs it reviewed during the first 10 months of 2018. That figure would have been significantly higher, but for a deal struck by regulators and manufacturers towards the end of 2017 which cleared the path for reimbursement of several new-generation hepatitis C treatments. Lucky recipients of CONITEC’s positive recommendations in 2018 also included Pfizer’s familial amyloid polyneuropathy drug Vyndaqel (tafamidis), and Stelara (ustekinumab; Johnson & Johnson/Mitsubishi Tanabe), Cosentyx (secukinumab; Novartis), and Humira (adalimumab; AbbVie/Eisai) for the second-line treatment of psoriasis. The number of applications rejected by CONITEC remained lengthy, however, and included requests for new indications of existing products as well as innovative medicines.

Russia: still no sign of a national reimbursement scheme

Plans for the phased introduction of a national outpatient drug reimbursement scheme were announced during the first half of this decade. These envisaged that the initiative would be piloted in several regions during 2015 and 2016, and that it would be rolled out nationally between 2017 and 2020. The financial crisis which hit the country in 2014 and 2015 put paid to those plans, however, and rollout of the scheme has yet to begin. In the meantime, it has been estimated that fewer than 20 million of Russia’s 140 million-plus citizens possess comprehensive outpatient drug coverage. Of these, most access subsidized medicines through regional programs rather than federally funded initiatives. Despite the 2018 expansion of the VZN (Seven Nosologies Program) to cover medicines to treat hemolytic uremic syndrome, juvenile arthritis, and mucopolysaccharidosis, the addition of new drugs or conditions to this list is unlikely given the current economic situation.

India: shifting from a static to a dynamic essential drugs list

In 2018, the Indian government announced the establishment of a new committee that will oversee the next update of the National List of Essential Medicines (NLEM). Significantly, it has been appointed for an initial term of three years, during which time it will meet every six months to discuss potential revisions to the list. This indicates a shift away from the publication of periodic lists that are set in stone for several years, to a more dynamic approach under which more timely updates will be implemented.

With no discernible improvement in public funding for innovative medicines, the main implication for originators will be the potential impact of this change on the price of branded specialties, a growing number of which could be subject to price caps and regulated price adjustments. Campaigners seeking affordable access to innovative medicines have called for the inclusion of all patented drugs on the NLEM. With alternative approaches to the regulation of patented drug prices also being discussed, that appears unlikely, but the number of costly original brands included on the NLEM is expected to increase progressively through the remainder of this decade.

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**Mexico: originators pursue new MEA models**

To date, offering substantial discounts has been the only way to gain access to major public payer reimbursement lists. Manufacturers are keen to begin striking more sophisticated risk-sharing deals with payers however, including outcomes-based agreements that could ease pressure on purchasing prices.

In December 2017, the national association representing research-based manufacturers (AMIIF; Asociación Mexicana de Industrias de Investigación Farmacéutica) signed an agreement with the state government of Querétaro, under which market access models for innovative specialty medicines will be developed. Manufacturers say the Social Security Institute (IMSS; Instituto Mexicano del Seguro Social) has also responded positively to the proposed development of outcomes-based deals35.

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**This analysis is based on Datamonitor Healthcare’s Market Access reports.**

**For full coverage please follow the links below:**

- Datamonitor Healthcare’s Market Access Trends in Europe
- Datamonitor Healthcare’s Access Trends in Emerging Markets
- Datamonitor Healthcare’s Value-Based Reimbursement in the US
- Datamonitor Healthcare’s Drug Pricing in the US

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