PRICENTRIC ONE
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INSIGHTS Newsletter

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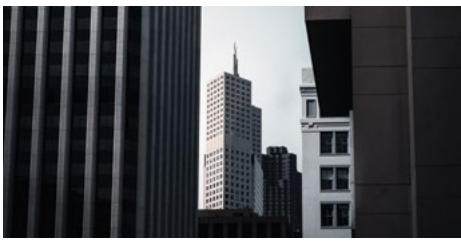
Is BeNeLuxA Equipped for a Zolgensma Assessment?

The BeNeLuxA initiative is set to take on Zolgensma (onasemnogene abeparvovec), an innovative gene therapy for children under two years old with spinal muscular atrophy (SMA), which was granted conditional approval for use in Europe in May.

Project Orbis Allows Concurrent Submissions

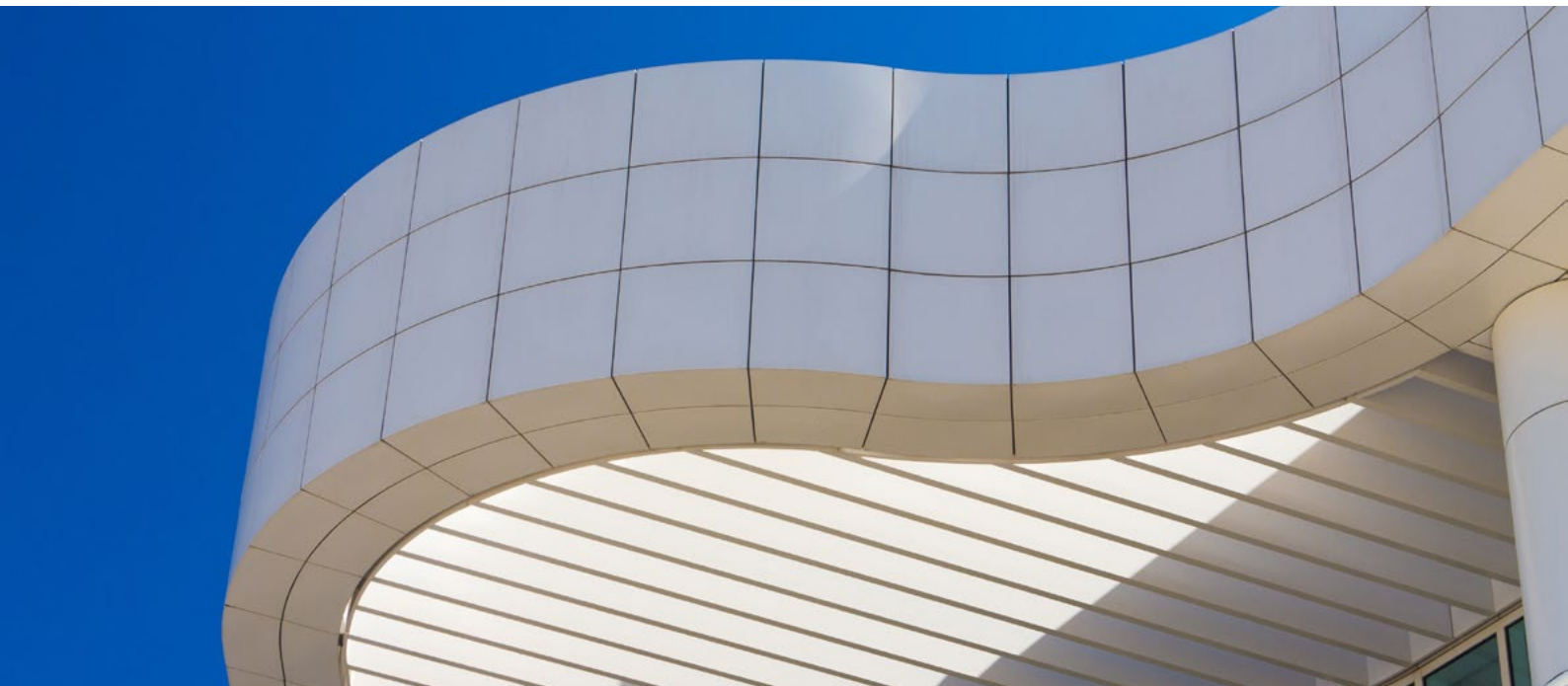
A hot topic for discussion at the Drug Industry Association (DIA) Global Annual Meeting was Project Orbis, a collaborative initiative that provides a framework for concurrent submission and review of oncology drugs among the U.S., Canada, Australia, Switzerland, and Singapore.



Uzbekistan Will Phase in IRP

The Ministry of Health of Uzbekistan has approved the implementation of an international reference pricing (IRP) system for setting the prices of domestic and foreign medicines, which will be phased in starting July 1, 2020.

Table of CONTENTS



Is BeNeLuxA Equipped for a Zolgensma Assessment?

BENELUXA TAKES ON ZOLGENSMA

The BeNeLuxA initiative is set to take on Zolgensma (onasemnogene abeparvovec), an innovative gene therapy for children under two years old with spinal muscular atrophy (SMA), which was granted conditional approval for use in Europe in May.

Belgium, Ireland, and the Netherlands will undertake a joint health technology assessment (HTA) of Zolgensma as part of the application from AveXis, a Novartis company, with Austria serving as expert reviewer. The participating national HTA bodies are committed to aligning their timelines, methodology, and content of HTA processes, and after assessment, the countries will determine if they will enter joint price negotiations. However, whether Zolgensma will be reimbursed is up to the discretion of each country's relevant agency.

CROSS-BORDER COLLABORATION

The BeNeLuxA Initiative was initially formed in 2015 to promote cross-border collaboration in horizon scanning, information sharing, policy exchange, and HTA by Belgium and The Netherlands. That same year, Luxembourg joined the Initiative, followed by Austria in 2016 and Ireland most recently, in June 2018.

Through BeNeLuxA, participating countries are aiming to increase efficiency of the assessment and pricing and reimbursement of medicines by exchanging expertise, as well as by mutual recognition of HTAs. Importantly in Zolgensma's case, the group engages in joint price negotiations for specific products, in order to try and provide faster and broader patient access.

To date, the group has completed around 15 HTAs and has been most successful with pricing and reimbursement negotiations related to another SMA treatment, Biogen's Spinraza (nusinersen), which came about in July 2018. Following negotiations, Belgium and the Netherlands successfully reached an agreement on the reimbursement of Biogen's SMA treatment.

The confidential pricing agreement gives Biogen temporary reimbursement of the SMA drug until December 2020, on the condition that in the interim the

company gathers real-world evidence (RWE) on safety, efficacy and use of Spinraza in clinical practice.

The interim entry agreement, which is the same in both Belgium and the Netherlands, demonstrated "a very clear and promising example of the benefits of working together on price negotiations and pharmaceutical policy," according to Bruno Bruins, the ex-Dutch Minister of Health, who hailed the relationship between Biogen and the Initiative as "a positive development."

Despite BeNeLuxA's success in negotiations with Biogen, Ireland's National Center for Pharmacoeconomics (NCPE) recommended against reimbursement of Spinraza because of the drug's price.

At the time, Biogen said in a statement: "Biogen provided the HSE with a significant pricing proposal, absolutely in line with the final price negotiated in countries aligned with Ireland in the Beneluxa initiative, which have each decided to reimburse Spinraza."

Eventually, Irish health regulators examined Spinraza once more after Biogen lowered its asking price and agreed to reimbursement.

Despite the initial issue with reimbursement in Ireland, the Spinraza triumph showed promise for the future of jointly assessing more expensive, innovative medicines – such as Zolgensma. Since BeNeLuxA is one of Europe's most mature cross-border collaborative initiatives, and has successfully negotiated access to Spinraza, the Initiative could serve as a test subject for the future of these types of collaborative efforts in Europe, which are not only becoming more common, but more empowered. The Nordics (Denmark, Finland, Iceland, Sweden, and Norway) recently announced their intention to enter joint negotiations with bluebird bio for Zynteglo (betibeglogene autotemcel), an evolution in their joint work from hospital medicine procurement by Denmark, Iceland, and Norway, and HTA by FiNoSe.

SPINRAZA/ZOLGENSMA PARALLELS

Zolgensma secured conditional approval from the European Medicines Agency (EMA) in May this year, joining Spinraza on the market. The latter SMA therapy was the first to gain approval from the European regulators via the accelerated assessment program, back in June 2017.

Both Spinraza and Zolgensma are first-of-their-kind SMA therapies with treatment costs that challenge the traditional payment expectations of European health systems. For reference, Spinraza costs around 600,000 euros in the first year and then around 300,000 euros each year thereafter, whereas the one-time treatment cost of Zolgensma costs nearly 2 million euros.

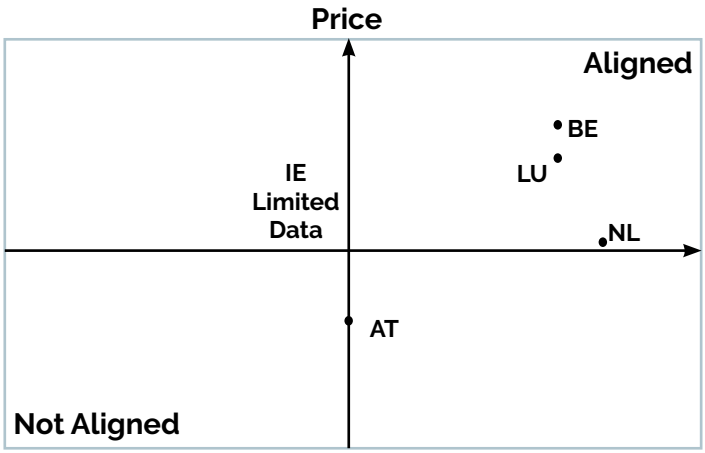
Both Spinraza and Zolgensma dramatically improve the lives of children with SMA and that of their caregivers, but they function in different ways. The latter is a gene therapy designed to replace the nonworking or missing SMN1 gene that causes the disorder, while Spinraza contains an antisense oligonucleotide that allows the body to produce more of a protein called survival motor neuron (SMN), a protein of which SMA patients do not produce enough.

The standout aspect of Zolgensma is that it is a one time, life-saving treatment to be given to patients under the age of two, consisting of a new, working copy of a human SMN gene delivered via a vector.

Novartis has previously expressed confidence that the one-time infusion gene therapy will essentially replace Spinraza as standard of-care, following positive long-term data that showed significant therapeutic benefit in patients treated before symptoms arise, and sustained durability in patients up to five years post-dosing.

ALIGNMENT ISSUES

While BeNeLuxA is by far one of the most mature cross-border collaboration efforts, there are nonetheless pricing and reimbursement decision misalignments among participating countries. An inclusive European HTA and pricing negotiation environment offers a multitude of opportunities such as saving time and money, but if the countries cannot agree on various aspects of the process, primarily due to national-level idiosyncrasies, failures can occur.



Company	Distance	Language	Population (millions)	GDP/ cap PPP (000s)
AT	Medium	N	8.9	47
BE	Short	Y	11.5	44
NL	Short	Y	17.3	50
LU	Short	Y	0.6	94
IE	Medium	N	4.8	70

Looking at drugs that have been assessed by the group in the past, common instances of HTA alignment occurred between the core three BeNeLux countries for AstraZeneca's Tagrisso (osimertinib), Pfizer's Vyndaqel (tafamidis), and Ipsen's Xermelo (telotristat ethyl).

Specifically, across the 11 drugs that have been previously assessed, the Netherlands came to positive conclusions

the most of all the countries, at 88% of the time, followed by both Luxembourg and Belgium each at 75% of the time. Austria erred on the side of agreement 50% of the time, whereas Ireland joined too recently to draw any sound conclusions. However, as seen in the case of Spinraza, at the national level, Ireland deviated before ultimately deciding to back reimbursement.

With a total population of 43 million across the Initiative, the core group of founding countries - Belgium, the Netherlands and Luxembourg - are seen to be more well aligned, with later entrants Ireland and Austria having less proven alignment or aligning their decisions less often.

The core three countries have more in common, which is conducive to them agreeing more often; on a basic level they share Dutch as a common official language and have the most similar cultures, on top of a stronger history of cooperation as a group and geographic closeness. Austria and Ireland were the most recent additions to the Initiative and Ireland has suffered from budget constraints and mismanagement, which have led it to promote more stringent reimbursement practices.

OTHER ISSUES

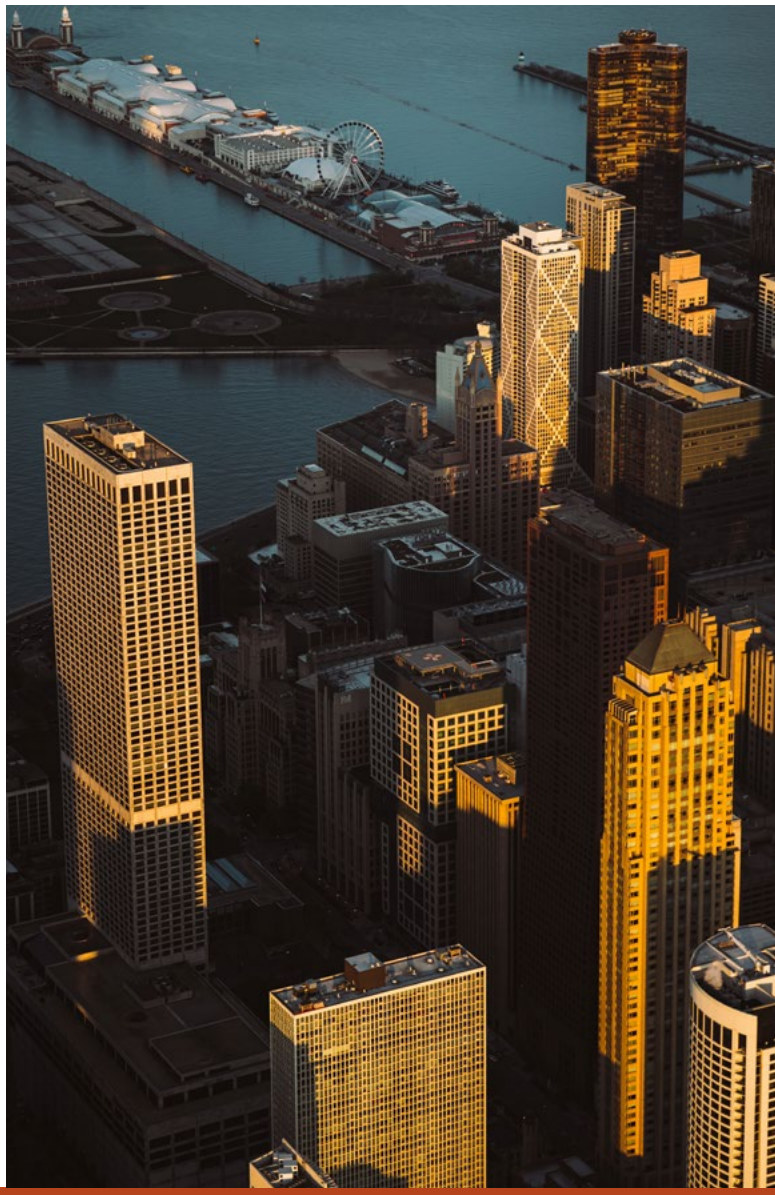
Joint decisions draw natural timeline comparisons to reimbursement and pricing differentials with non-joint decisions, as a core idea of syncing up practices is to expedite the time a drug takes to get to market.

Joint analysis can run into issues such as limited data, as well as being subject to variances in the specific product. EVERSANA data analysts found that, overall, submission through BeNeLuxA did not quicken the reimbursement timeline process for products approved in 2016 with costs > 50,000 EUR per annum; for example, in Belgium and the Netherlands there were products that secured reimbursement either more slowly or quickly than Spinraza.

However, among the BeNeLuxA countries, Austria and Ireland have trailed the Netherlands when it comes to reimbursing a medicine, and Belgium has trailed the Netherlands in time to reimbursement.

Price disagreements can also cause issues, such as when an earlier BeNeLuxA pilot for Vertex's Cystic Fibrosis (CF) medicine, Orkambi (lumacaftor/ivacaftor), failed to lead to a deal in 2016 and 2017 after the parties could not manage to reach an agreement on an acceptable price. The Netherlands' Zorginstituut had advised at the time that a discount of 82% would be needed for Orkambi to be eligible for reimbursement.

In this instance, the BeNeLuxA countries seemed dead set on concluding an appropriate price for their constituents, especially given the access deals Vertex has been entering with payers for all current and future CF medicines. The Initiative does aim to strengthen negotiating power after all. The Netherlands now reimburses Orkambi, whereas Orkambi is a non-reimbursable medicine (under Category D) in Belgium, according to data from Pricentric.



PRICEXPRESS BY EVERSANA™

PriceXpress is used to answer questions about Launch, Pricing, Loss-of-Exclusivity, Trends, and Business Development needs using secondary research methods. The team uses the data in the Pricentric tool to conduct empirical analysis of price, reimbursement, cost-of-treatment and other information to answer common pricing questions quickly.

Examples of recent customer queries

- Average timeline to reimbursement for a product class
- Price differentials across markets for weight vs. non-weight based products
- Impact of indication expansion on pricing in the EU5 for oncology
- Price of rare analogues across Asia-Pacific for purpose of estimating launch price
- Analysis of linear pricing in biosimilars by EU markets
- Average 5-year price erosion since launch of a product class across EU15

For more details, contact Max Klietmann at max.klietmann@eversana.com

LOOKING TO THE FUTURE OF JOINT HTA

The variance in success with BeNeLuxA in securing access to expensive, innovative medicines raises the question of whether the initiative represents the future of both market access and pricing and reimbursement negotiations.

Although Belgium, Ireland, and the Netherlands are aiming to align their HTA processes for Zolgensma, the negotiations for the reimbursement of the gene therapy in each market will most likely encounter some sort of strife due to the countries' idiosyncrasies, especially considering the limited data, given the novelty of Zolgensma. As seen before, the countries are not always aligned in their decision-making, but looking at the Spinraza outcome, it can be assumed there will be collaboration and agreement among the core countries (BeNeLux).

As one of Europe's most mature cross-border initiatives, BeNeLuxA and its future success with negotiating access to innovative medicines could be indicative of cross-border collaboration as future standard protocol in Europe. As mentioned previously, in a similar vein, the Nordics are teaming up to negotiate access to Zynteglo, which signals a major shift in their policy. The initiative to jointly negotiate access to medicines is the next natural evolutionary step for these markets.

Likewise, the ten-country Valletta Declaration group announced towards the end of 2019 that it would be working to set up a framework to formulate more coherent pricing policies in regional markets and build trust around collective negotiations on regional prices for bulk purchases. Since then, there has been little action. But, in the future, it will be interesting to see how this plays out due to the varying sizes of the participating markets, as well as other barriers.

"As the trend of joint HTA assessment gains increased traction, it will be critical to thoughtfully assess potential impacts at the global level," said Max Kleitmann, EVERSANA Senior Consultant. "The inherent conflict in trying to balance collective HTA assessment against individual countries' particular needs and resources presents a complex business challenge for companies for a number of reasons, including downstream IRP implications and launch sequencing considerations."

BeNeLuxA's success in joint negotiation suggests that when certain factors such as language and geography, as well as policy, are aligned, cross-border collaboration has the potential to hold the key to the future of market access.

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BY EVERSANA

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30 Countries Sign WHO COVID-19 Access Pool

Originally published: June 2, 2020 | Country: ARGENTINA, BANGLADESH, BELGIUM, BRAZIL, CHILE, EGYPT, INDONESIA, LEBANON, LUXEMBOURG, MALAYSIA, MEXICO, NETHERLANDS, NORWAY, OMAN, PAKISTAN, PANAMA, PERU, PORTUGAL, SOUTH AFRICA, SRI LANKA, URUGUA | Region: AFRICA, ASIA & SOUTH PACIFIC, EUROPE, MIDDLE EAST, NORTH AMERICA, SOUTH AMERICA | Type: Policy | Keywords: #access #affordability #c-tap #covid-19 #healthtechnologypool #iprights #vaccines #voluntaryscheme #who

PRICENTRIC BRIEF:

- Thirty countries and a variety of international partners and institutions have signed the World Health Organization's (WHO) COVID-19 Technology Access Pool (C-TAP), an initiative first proposed by Costa Rican President Carlos Alvarado to make vaccines, tests, treatments, and other health technologies used in the fight against COVID-19 accessible to all
- Aiming to expedite the discovery of vaccines, medicines, and other technologies to combat the virus, C-TAP will be voluntary, providing a "one-stop shop" for scientific data, knowledge, and intellectual property (IP) to be shared with the global community
- The initiative consists of five key elements: public disclosure of gene sequences and data; transparency around the publication of all clinical trial results; governments and other funders are encouraged to include clauses in funding agreements with pharmaceutical companies and other innovators about equitable distribution, affordability, and publication of trial data; licensing any potential treatment, diagnostic, vaccine or other health technology to the United Nation's (UN) Medicines Patent Pool; and promotion of open innovation models and technology transfer that increase local manufacturing and supply capacity, including through joining the Open Covid Pledge and the Technology Access Partnership (TAP)

THE DETAILS

GENEVA, Switzerland – Thirty countries and a variety of international partners and institutions have signed the World Health Organization's (WHO) COVID-19 Technology Access Pool (C-TAP), an initiative first proposed by Costa Rican President Carlos Alvarado to make vaccines, tests, treatments, and other health technologies used in the fight against COVID-19 accessible to all.

The following countries have backed the C-TAP: Argentina, Bangladesh, Barbados, Belgium, Belize, Bhutan, Brazil, Chile, Dominican Republic, Ecuador, Egypt, El Salvador, Honduras, Indonesia, Lebanon, Luxembourg, Malaysia, Maldives, Mexico, Mozambique, Norway, Oman, Pakistan, Palau, Panama, Peru, Portugal, Saint Vincent and Grenadines, South Africa, Sri Lanka, Sudan, The Netherlands, Timor-Leste, Uruguay, Zimbabwe

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- licensing any potential treatment, diagnostic, vaccine or other health technology to the United Nation's (UN) Medicines Patent Pool; and
- promotion of open innovation models and technology transfer that increase local manufacturing and supply capacity, including through joining the Open Covid Pledge and the Technology Access Partnership (TAP).

WHO, Costa Rica, and all co-sponsor countries likewise issued a "Solidarity Call to Action" to ask relevant stakeholders to join and support this global initiative.

President Alvarado of Costa Rica, said, "The COVID-19 Technology Access Pool will ensure the latest and best science benefits all of humanity. Vaccines, tests, diagnostics, treatments and other key tools in the coronavirus response must be made universally available as global public goods".

WHO Director-General Dr. Tedros Adhanom Ghebreyesus, said, "Global solidarity and collaboration are essential to overcoming COVID-19. Based on strong science and open collaboration, this information-sharing platform will help provide equitable access to life-saving technologies around the world."

Industry Against IP Pool Clauses, Despite Support for Equitable Distribution

However, major pharmaceutical companies have called the initiative "nonsense," citing nationalism as a main inhibitor to equal access due to the potential for bidding wars and global shortages, reported The Guardian.

Companies support efforts to ensure equitable distribution of vaccines and treatments for COVID-19 but expressed concern over the pooling of IP rights. If pooled, vaccines and treatments would be up for grabs by generic drugmakers.

US Senator Grassley: Prescription Drug Pricing Act "Needed Now More Than Ever"

Originally published: Jun 3, 2020 | Region: NORTH AMERICA | Type: Regulation | Keywords: #chuckgrassley #covid19 #drugprices #prescriptiondrugpricingact #pricecontrols #vaccines

PRICENTRIC BRIEF:

- The National Institute of Health (NIH) is working with a private-sector biotech company on a potential COVID-19 vaccine and has even commenced human trials, but according to Senate Finance Committee Chairperson Chuck Grassley (R-Iowa), "The soaring prices of prescription drugs are making life-saving treatments and cures simply unaffordable for many Americans"
- "The pandemic made clear two things: Americans urgently want a cure and when life-saving cures and therapies come to market, Americans must be able to afford them when their providers prescribe them," said Grassley
- Grassley intends to push for a vote for part of his drug plan that would limit price hikes for drugs—if this measure is not passed, Grassley fears drugmakers will be able to charge "whatever they want to" for COVID-19 vaccines

THE DETAILS

WASHINGTON, D.C., The United States – The National Institute of Health (NIH) is working with a private-sector biotech company on a potential COVID-19 vaccine and has even commenced human trials, but according to Senate Finance Committee Chairperson Chuck Grassley (R-Iowa), "The soaring prices of prescription drugs are making life-saving treatments and cures simply unaffordable for many Americans."

The senator claims that the "bi-partisan" Prescription Drug Pricing Act is "needed now more than ever" to combat rising drug prices by ensuring Americans can afford their prescription drugs.

"The pandemic made clear two things: Americans urgently want a cure and when life-saving cures and therapies come to market, Americans must be able to afford them when their providers prescribe them," said Grassley.

Amid the pandemic, Grassley intends to push for a vote for part of his drug plan that would limit price hikes for drugs because Grassley fears drugmakers will be able to charge "whatever they want to" for COVID-19 vaccines.

It's important to note that the U.S. government has invested heavily into the development of a vaccine for the coronavirus, most notably in the one from AstraZeneca and the University of Oxford, and anticipates a return for its investment which could impact the price charged to the U.S. upon availability.

President Donald Trump previously showed support for Grassley's drug pricing bill. During his State of the Union address, Trump said, "I have been speaking to Senator Chuck Grassley of Iowa and others in the Congress in order to get something on drug pricing done and done properly. I am calling for bipartisan legislation that achieves the goal of dramatically lowering prescription drug prices."

PDPA at a Glance

Grassley's proposed bill is an amendment to titles XI, XVIII, and XIX of the Social Security Act to reduce prescription drug prices covered under Medicare and Medicaid programs, improve transparency related to drug prices and sales, and cut down on patients' out-of-pocket costs. Grassley said last month that the bill would introduce a "year-over-year" price cap "in line with the rate of inflation."

Grassley noted, "We would put a big cap on the amount of money that one consumer would have to spend out-of-pocket… It would take some of the secrecy out of the pricing of drugs."

Canada Publishes Budget Impact Analysis Guidelines Under New PMPRB Amendments

PRICENTRIC BRIEF:

- The Government of Canada has published "Budget Impact Analysis Guidelines" for conducting pharmaceutical budget impact analyses for submission to public drug plans in Canada, as part of the new amendments to the Patented Medicine Prices Review Board (PMPRB)
- Budget impact analyses (BIAs) will focus on the financial impact of a drug; therefore, these guidelines are specifically designed to assist those who develop, submit, and evaluate BIAs in determining the financial impact and affordability of listing a new drug for reimbursement by the Canadian Agency for Drugs and Technologies in Health (CADTH), as well as participating local or national drug plans
- The analytic framework under the BIA recommendations will consider perspective, time horizon, population, drug costs, and discounting and inflations, among other factors, while input and data source recommendations will consider estimations of the current market size, relevant comparators, and forecasting of the market under reference and new drug scenarios, plus additional information

Originally published: Jun 5, 2020

Country: CANADA-ONTARIO | Region: NORTH AMERICA | Type: Policy | Keywords: #budgetimpactanalysis #cadth #guidelines #newdrug #pmprb #referencepricing #reimbursement

THE DETAILS

OTTAWA, Canada – The Government of Canada has published "Budget Impact Analysis Guidelines" for conducting pharmaceutical budget impact analyses for submission to public drug plans in Canada, as part of the new amendments to the Patented Medicine Prices Review Board (PMPRB).

Due to the COVID-19 pandemic, the new amendments are now set to take effect on January 1, 2020, six months later than anticipated.

Budget impact analyses (BIAs) will focus on the financial impact of a drug. As such, these guidelines are specifically designed to assist those who develop, submit, and evaluate BIAs in determining the financial impact and affordability of listing a new drug for reimbursement by the Canadian Agency for Drugs and Technologies in Health (CADTH), as well as participating local or national drug plans.

These new guidelines supersede guidelines published by the PMPRB back in May 2007, because previous guidelines no longer reflect best business practices – as such, an update was necessary to ensure developments in Canadian BIA methods align with international guidelines.

The analytic framework under the BIA recommendations will consider perspective, time horizon, population, scenarios to be compared, drug costs, discounting and inflations, model design, characterizing uncertainty, and validation.

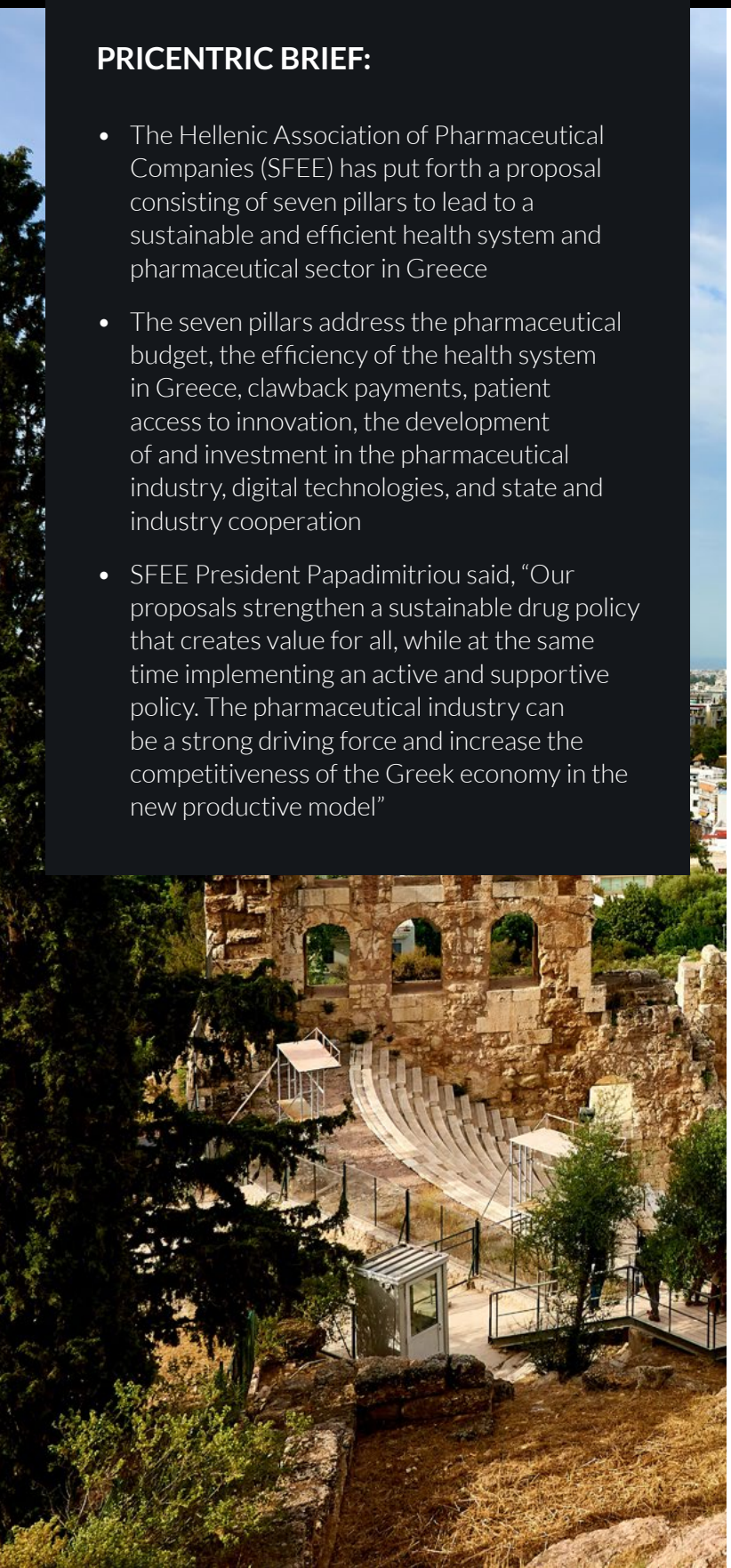
Similarly, input and data source recommendations will consider estimations of the current market size, relevant comparators, forecasting of the market under reference and new drug scenarios, estimating drug costs, and interactive budget impact model.

Greece Pharma Association Puts Forth 7 Pillars to Boost Sector

Country: GREECE | Region: EUROPE | Type: Policy | Keywords: #healthsystem #sfee | Originally published: June 11, 2020

PRICENTRIC BRIEF:

- The Hellenic Association of Pharmaceutical Companies (SFEE) has put forth a proposal consisting of seven pillars to lead to a sustainable and efficient health system and pharmaceutical sector in Greece
- The seven pillars address the pharmaceutical budget, the efficiency of the health system in Greece, clawback payments, patient access to innovation, the development of and investment in the pharmaceutical industry, digital technologies, and state and industry cooperation
- SFEE President Papadimitriou said, "Our proposals strengthen a sustainable drug policy that creates value for all, while at the same time implementing an active and supportive policy. The pharmaceutical industry can be a strong driving force and increase the competitiveness of the Greek economy in the new productive model"



THE DETAILS

ATHENS, Greece – The Hellenic Association of Pharmaceutical Companies (SFEE) has put forth a proposal consisting of seven pillars to lead to a sustainable and efficient health system and pharmaceutical sector in Greece.

The framework, which was presented by SFFE President Olympios Papadimitrou and General Manager Michalis Heimonas, has been submitted to the government and Greek Prime Minister.

The seven pillars address the pharmaceutical budget, the efficiency of the health system in Greece, clawback payments, patient access to innovation, the development of and investment in the pharmaceutical industry, digital technologies, and state and industry cooperation.

SFEE believes that the budget for pharmaceuticals in Greece doesn't correlate with reality – in that, additional funds are needed to account for the entry of new drugs, while over-prescribing needs to be addressed and cost controls must be implemented to pave the way for new drugs. Medicines are experiencing loss of patent exclusivity, which will allow for savings to be generated, too.

Similarly, SFEE is seeking reformations to the clawback system, as the mechanism merely transfers risk to pharmaceutical companies rather than offer a safety net. Mandatory discounts and refunds can act as an investment incentive, SFEE proposed, and all parties can contribute; for example, through risk-sharing agreements and more pointed calculations of overspend based on actual prices and not retail prices.

Removing obstacles and implementing "effective, dynamic, and continuous" health technology assessment (HTA) will increase equal and timely access to new medicines, boosting Greece from its position as one of the last markets in Europe to see the launch of newer products.

Greece should be invested in the pharmaceutical industry because patients benefit when there's financial interest in the sector. SFEE wants to see increased high value and return on investment.

The use of digital technologies and integrating systems (prescriptions, tests, etc.) will not only modernize Greece's healthcare system, but allow for the collection of more accurate and reliable data.

The seventh pillar, which appears as a general declaration on the need for enhanced collaboration, posits that the Government and industry can work in tandem to improve the system and meet social responsibility and solidarity needs.

Papadimitriou commented, "In our country, the timely implementation by the State of protection measures against COVID-19 highlighted the country, internationally, at the top of the ranking of successful management models and offered valuable time in the health system to be able to cope with the health crisis with absolute success.

"After a long financial crisis with disputed accounting measures between the victims and the Public Health system, Greece is given the opportunity to review and modernize the perception of the systemic structure of the healthcare system. This success must now be capitalized on.

"Our proposals strengthen a sustainable drug policy that creates value for all, while at the same time implementing an active and supportive policy. The pharmaceutical industry can be a strong driving force and increase the competitiveness of the Greek economy in the new productive model," Papadimitriou concluded.

Spain Must "Go Further, Bet on R&D, Innovation, Knowledge," Says Farmaindustria President Sellés

Originally published: Jun 15, 2020 | Country: SPAIN | Region: EUROPE | Type: Policy |
Keywords: #access #affordability #clinicaltrials #covid19 #farmaindustria #industry #investment #r&d #sns

PRICENTRIC BRIEF:

- In its pharmaceutical industry proposals for economic and social reform, the National Trade Association of the Spanish-Based Pharmaceutical Industry (Farmaindustria) is requesting more investment in research and production in Spain
- Sellés explained that investment in R&D and innovation and public-private collaboration are crucial to be "faster in finding pharmacological and more efficient solutions" to problems with the health system
- A medium-long-term pharmaceutical strategy is therefore needed; Spain and its industry have "to go further and bet on R&D, innovation, and knowledge," said Farmaindustria President Sellés, which includes a more homogenous policy of access to treatments among Spain's autonomous communities and increased funding for the national health system (SNS)

THE DETAILS

MADRID, Spain – In its pharmaceutical industry proposals for economic and social reform, the National Trade Association of the Spanish-Based Pharmaceutical Industry (Farmaindustria) is requesting more investment in research and production in Spain.

Farmaindustria highlighted how crucial the industry was in combatting the coronavirus outbreak and can continue to play a relevant, even necessary role in strengthening the economy of Spain as it moves forward from the health crisis.

Martin Selles, President of Farmaindustria, presented the industry group's proposal to members of Spain's Health Working Group of the Commission for Social and Economic Reconstruction as a way to help revive the Spanish economy and enhance the National Health Service (SNS).

Selles explained that investment in R&D and innovation and public-private collaboration are crucial to becoming "faster in finding pharmacological and more efficient solutions" to problems with the health system in Spain.

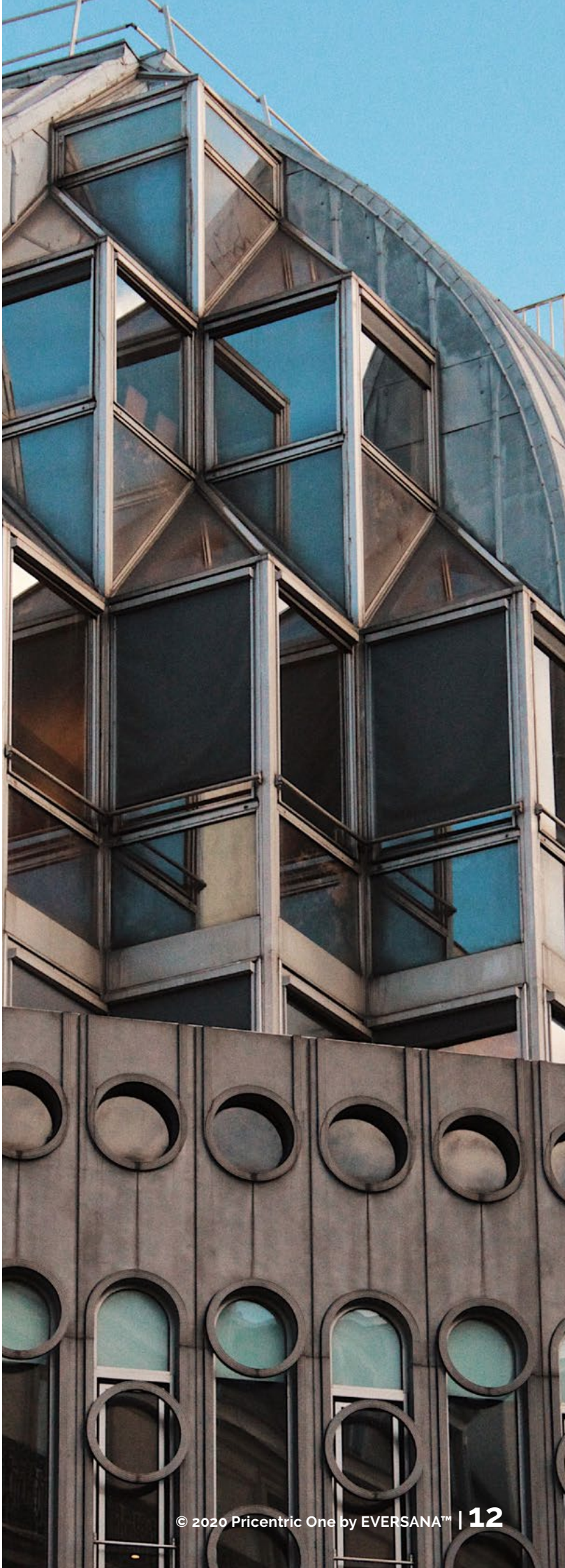
During the COVID-19 pandemic, the industry has so far managed to provide 25 million Spaniards who need medicine each day with what they need and kept the 82 drug production plans functioning at full capacity. Similarly, Spain's industry worked to ensure medicines from abroad were shipped to Spain in a timely manner.

Spain has become "an international benchmark in clinical research," Sellés added, making it the European country with the most clinical trials and the fourth country worldwide for clinical trials.

The industry is striving to rapidly develop vaccines going forward, with the aim of making them affordable and equitable in access; not just in Spain, but in all countries.

To accomplish these goals, the production of active ingredients should be returned to Spain and Europe, as the continent relies heavily on production in Europe for these products. Spain will need to invest more than just 1.24% of GDP in R&D—the European Union average is 2.2%.

A medium-long-term pharmaceutical strategy is therefore needed; Spain and its industry have "to go further and bet on R&D, innovation, and knowledge," said Selles, which includes a more homogenous policy of access to treatments among Spain's autonomous communities and increased funding for the SNS.



Sweden's Medicines Costs Rose SEK 1 Billion in 2019

Country: SWEDEN | Region: EUROPE | Type: Price Changes | Keywords: #consumption #drugprices #tlv #volume | **Jun 16, 2020**

PRICENTRIC BRIEF:

- Last year, the costs for medicines in Sweden rose by about SEK 1 billion, according to the Dental and Pharmaceutical Benefits Agency (TLV)
- The rise in costs is not driven by new medicines, which account for half of the rise in costs in 2019, but by the increased use of medicines that have been on the market for some time and are experiencing greater volumes of use
- Side agreements have controlled the costs of new medicines, particularly those with high costs and levels of uncertainty, and TLV hopes Sweden can curb costs for medicines experiencing increased volumes of consumption and higher prices through tripartite collaborations between the regions, TLV, and pharmaceutical companies

THE DETAILS

STOCKHOLM, Sweden – Last year, the costs for medicines in Sweden rose by about SEK 1 billion, according to the Dental and Pharmaceutical Benefits Agency (TLV).

A recent report from TLV measured the cost trend for medicines in outpatient care, specifically those sold among the drug benefits and infectious drugs that are financed in Sweden.

Total costs amounted to SEK 33.3 billion excluding refunds and SEK 30.4 billion including refunds. Between the years In 2018 and 2019, costs increased by SEK 1.1 billion, including reimbursement and 1.2 billion excluding reimbursement. These numbers include both benefit costs and deductibles paid by patients.

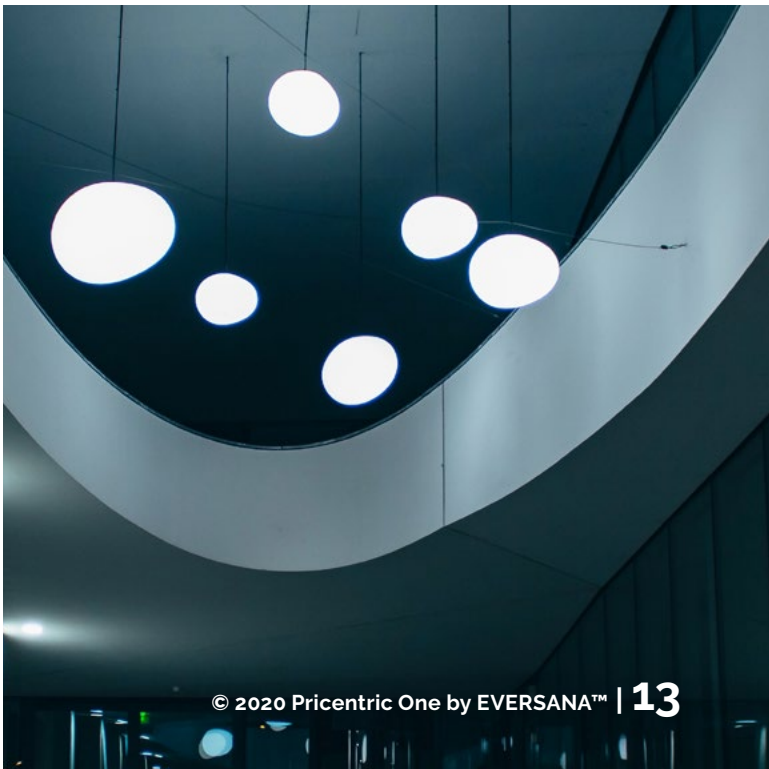
The rise in costs is not driven by new medicines, which account for half of the rise in costs in 2019, but by the increased use of medicines that have been on the market for some time and are experiencing greater volumes of use (meaning, increased volumes and also higher prices).

Side agreements have controlled the costs of new medicines, particularly those with high costs and levels of uncertainty. In 2019, side agreements led to Sweden's regions receiving nearly SEK 3 billion from pharmaceutical companies in payback.

On the other hand, the increase in use of oncology, atrial fibrillation, and type 2 diabetes medicines is driving up the costs of medicines in Sweden. While in some cases – for example, with hepatitis C medicines – costs have gone down due to decreased volumes of consumption, overall the more widespread use of drugs is leading to more spending on medicines.

TLV hopes Sweden can curb costs through tripartite collaborations between the regions, TLV, and pharmaceutical companies.

The agency noted that the Swedish krona is weak at the moment and pharmaceutical companies might have to increase prices to compensate.



Uzbekistan Will Phase in IRP System July 1, 10 Countries Comprise Reference Basket

Originally published: June 17, 2020 | Region: ASIA & SOUTH PACIFIC | Type: Reference Pricing (IRP) | Keywords: #healthministry #inn #maximumprices #medicineprices #prescribingguidelines #regulation

Pricentric Brief

- The Ministry of Health of Uzbekistan has approved the implementation of an international reference pricing (IRP) system for setting the prices of domestic and foreign medicines, which will be phased in starting July 1, 2020
- The applicant holder of a registration certificate or their authorized representative is responsible for submitting through Uzbekistan's online system the selling price in the country of origin, the 10 reference countries, and Uzbekistan of a medicine of the same manufacturer with the same active ingredient, including the dosage form, number of units in the package, dosage, concentration, volume, and packaging
- Uzbekistan's reference basket will include the following 10 countries with high, above average, or below average per capita income: Hungary, Russia, Ukraine, Poland, Tajikistan, Slovenia, Kazakhstan, Bulgaria, Belarus, and Kyrgyzstan

The Details

TASHKENT, Uzbekistan – The Ministry of Health of Uzbekistan has approved the implementation of an international reference pricing (IRP) system for setting the prices of domestic and foreign medicines, which will be phased in starting July 1, 2020.

The applicant holder of a registration certificate or their authorized representative is responsible for submitting through Uzbekistan's online system the selling price in the country of origin, the 10 reference countries, and Uzbekistan of a medicine of the same manufacturer with the same active ingredient, including the dosage form, number of units in the package, dosage, concentration, volume, and packaging.

Uzbekistan's reference basket will include the following 10 countries with high, above average, or below average per capita income: Hungary, Russia, Ukraine, Poland, Tajikistan, Slovenia, Kazakhstan, Bulgaria, Belarus, and Kyrgyzstan.

The online system will collect data on registered maximum prices for the trade name of the medicine and maximum wholesale and retail prices, with consideration of maximum allowed commercial prices.

As a general rule, the maximum retail price of medicines cannot be higher than 15% of the reference price for wholesale distributors and 20% for retail organizations such as pharmacies.

The Agency for the Development of the Pharmaceutical Industry (the Agency) under the Ministry of Health will be responsible for monitoring and analyzing the efficacy of the system.

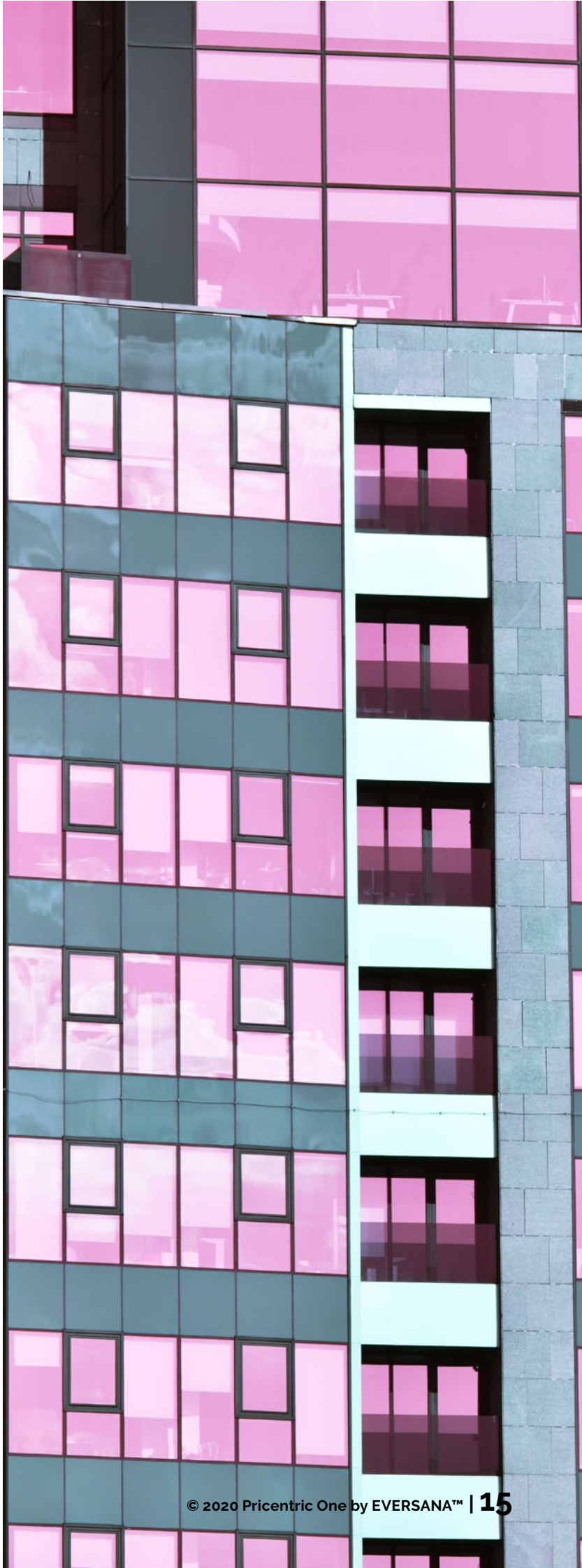
Additionally, the Agency will manage the registration of maximum prices for each trade name of a medicinal product taking into account the dosage form, number of units in a package, dosage, concentration, volume and packaging, which cannot be delivered to Uzbekistan (for imported medicines) and released by a domestic producer (for domestic medicines).

When Uzbekistan first announced it would be implementing an IRP system, it was specified that only generic medicines would be affected, not original medicines of domestic or foreign production. With this most recent update, which drugs will be affected has not been specified.

Along with the implementation of the IRP system, Uzbekistan is mandating prescription by international non-proprietary name (INN) to increase the use of generic medicines.

Sardor Kariev, Director of the Agency for the Development of the Pharmaceutical Industry, said, "There are branded medicines and their cheap counterparts. Molecularly, this is one and the same drug, but marketing costs are included in the price of the former, including monetary rewards, expensive gifts to doctors or their departure to a conference abroad. Introducing INN is the most civilized method of combating corrupt schemes. It is practiced all over the world."

The mandate is part of the Uzbekistan's push to boost its domestic manufacturing capabilities, as domestic drugmakers can only cover about 27% of the needs of the population. Uzbekistan seeks to increase the share of domestically-produced pharmaceuticals in the domestic market up to 50% in value terms.



Clawback Expected to Reach Nearly 2 Billion Euros in Greece, Says SFEE's President

Region: EUROPE | Type: Policy | Keywords: #clawback #covid19 #eopyy #funding #healthministry #r&d #rebates #regulation #sfee

Originally published: Jun 18, 2020

PRICENTRIC BRIEF:

- In an interview with iEidiseis, President of the Hellenic Association of Pharmaceutical Companies (SFEE) Olympios Papadimitriou revealed that clawback payments from pharmaceutical companies to Greece's National Organization for the Provision of Health Services (EOPYY) are increasing dramatically
- This year, clawback is expected to reach 1 billion euros, and considering mandatory rebates, this number will easily reach 1.8 billion, according to Papadimitriou, and the problem is not being addressed by Greece's Ministry of Health
- "The ongoing underfunding of public pharmaceutical spending combined with the complete indifference of the Ministry of Health to implement substantial measures to control demand leads to unrealistic over-taxation of pharmaceutical companies that is really testing their resilience," said Papadimitriou

THE DETAILS

ATHENS, Greece – In an interview with iEidiseis, President of the Hellenic Association of Pharmaceutical Companies (SFEE) Olympios Papadimitriou revealed that clawback payments from pharmaceutical companies to Greece's National Organization for the Provision of Health Services (EOPYY) are increasing dramatically.

There has been a 45% increase in pharmaceutical expenditure in Q1 2020 compared to Q1 2019. Already in the first quarter, EOPYY expenditure has reached 234 million euros, and hospital spending remains currently unknown. Clawback is expected to reach 1 billion euros, and considering mandatory rebates, this number will easily reach 1.8 billion.

According to SFEE President Papadimitriou, the problem is not being addressed by Greece's Ministry of Health.

"The ongoing underfunding of public pharmaceutical spending combined with the complete indifference of the Ministry of Health to implement substantial measures to control demand leads to unrealistic over-taxation of pharmaceutical companies that is really testing their resilience," said Papadimitriou.

Rebates essentially shift the responsibility for excess spending to the industry, Papadimitriou added. Despite multiple European Commission surveillance reports finding the way Greece is using clawback payments is incorrect, hazardous, and unsustainable for the healthcare system, the Ministry of Health acts "as if they are just observers."

SFEE's 7 Pillars and COVID-19 Response

SFEE aims to address this issue in its 7 pillars for a sustainable and efficient health system and pharmaceutical sector in Greece, which the industry group presented last week. The seven pillars cover the pharmaceutical budget, the efficiency of the health system in Greece, clawback payments, patient access to innovation, the development of and investment in the pharmaceutical industry, digital technologies, and state and industry cooperation.

The exigency for change is also being fueled by the COVID-19 pandemic. Papadimitriou also recommended three areas of improvement to help combat the virus and lessen its impact on the health system.

To keep the health system afloat during these times, Papadimitriou proposed the redefinition of public pharmaceutical expenditure based on the epidemiological data of our country and the real needs of the population; the creation of an additional separate account (€ 200 million) to cover vaccines; and the removal of barriers to access to innovative treatments, new drugs and vaccines (and for COVID-19), including the unlimited clawback mechanism.

"In Greece, too, the government, as in other countries, needs to redefine funding for public health, research and development, and vaccination. And resources must be allocated based on the real needs of our country - it is not possible for ever-increasing needs to be met for the last at least 4 years with the same resources. Something will be ruined by this approach and the damage will be irreversible," concluded Papadimitriou.

CMS New Rule Allows for Value-Based Pricing Arrangements

Originally published: Jun 19, 2020 | Country: UNITED STATES | Region: NORTH AMERICA | Type: Policy | Keywords: #bestprice #cms #curativetherapies #innovativepaymentschemes #valuebasedpayments

PRICENTRIC BRIEF:

- The Centers for Medicare & Medicaid Services (CMS) has proposed a new rule that would allow for Medicaid to enter into innovative payment schemes for promising, curative therapies while ensuring sustainability
- These new payment arrangements will focus on the value provided to a patient and increase accountability for outcomes, rather than quantities or volumes—plus, collecting more evidence could help providers use new medications and treatments in a more targeted manner
- While in general drugmakers must provide CMS their "best price," in a notice of proposed rulemaking (NPRM), CMS suggests that drugmakers should report multiple "best prices" for a curative therapy in a Medicare Drug Rebate Program (MDRP) if it is tied to a value-based payment arrangement

THE DETAILS

WASHINGTON, D.C., The United States – The Centers for Medicare & Medicaid Services (CMS) has proposed a new rule that would allow for Medicaid to enter into innovative payment schemes for promising, curative therapies, while ensuring sustainability.

CMS Administrator Seema Verma commented, "CMS's rules for ensuring that Medicaid receives the lowest price available for prescription drugs have not been updated in thirty years and are blocking the opportunity for markets to create innovative payment models.

"By modernizing our rules, we are creating opportunities for drug manufacturers to have skin in the game through payment arrangement that challenge them to put their money where their mouth is."

For CMS, these new payment arrangements will focus on the value provided to a patient and increase accountability for outcomes, rather than quantities or volumes.

In addition, the widespread adoption of these value-based payment schemes will lead to the collection of more evidence, which could help providers use new medications and treatments in a more targeted manner. Thus, increasing the link between reimbursement and efficacy should encourage payers to facilitate patients access to new therapies by easing traditional utilization management practices.

"By offering more flexibility for payers and manufacturers to enter into value-based agreements while still ensuring that Medicaid always gets the best deal, CMS is continuing our efforts to foster innovation, increase access to the latest technologies, and ensure that the Medicaid program is sustainable and can continue to serve our most vulnerable populations," CMS added in a press release.

While in general drugmakers must provide CMS their "best price," in a notice of proposed rulemaking (NPRM), CMS suggests that drugmakers should report multiple "best prices" for a curative therapy in a Medicare Drug Rebate Program (MDRP) if it is tied to a value-based payment arrangement.

On top of this, CMS has proposed to permit revisions to AMP and best price reporting beyond the current thirty-six month time limit to allow for revisions to pricing metrics as a result of VBP arrangements.

ICER's 2020 Unsupported Price Increase Analysis Will Focus on 13 Drugs

Originally published: Jun 22, 2020 | Country: UNITED STATES | Region: NORTH AMERICA | Type: Cost Effectiveness | Keywords: #clinicalevidence #icer #prescriptiondrugs #pricechanges

PRICENTRIC BRIEF:

- The Institute for Clinical and Economic Review (ICER) published its protocol for its upcoming "Unsupported Price Increase" (UPI) report in which the institute will examine significant price increases for prescription drugs and determine if new evidence is needed to support the increases
- ICER's report will focus on up to 13 prescription drugs that experienced the most significant price increase in the U.S. over a one-year period and the Institute will base its decision on which net price increases had the most significant budget impact on the U.S. health system
- In its 2019 UPI report, ICER assessed AbbVie's Humira (adalimumab), Pfizer's Lyrica (pregabalin), Gilead's Truvada (tenofovir disoproxil fumarate and emtricitabine), Genentech/Roche's Rituxan (rituximab), Amgen's Neulasta (pegfilgrastim), Eli Lilly's Cialis (tadalafil), and Tecfidera (dimethyl fumarate), Gilead's Genvoya (elvitegravir, cobicistat, emtricitabine, and tenofovir alafenamide), and Celgene's Revlimid (lenalidomide)

THE DETAILS

BOSTON, Massachusetts, The United States – The Institute for Clinical and Economic Review (ICER) published its protocol for its upcoming "Unsupported Price Increase" (UPI) report in which the institute will examine significant price increases for prescription drugs and determine if new evidence is needed to support the increases.

ICER's report will focus on up to 13 prescription drugs that experienced the most significant price increase in the U.S. over a one-year period. The Institute will base its decision on which net price increases had the most significant budget impact on the U.S. health system.

Initially, ICER is obtaining a list of the 100 drugs with the largest net sales in the U.S. The manufacturers of the top 15 drugs will be contacted by ICER, who will inform them that their product will potentially be up for review.

From this list, ICER will select 10 drugs for review based on pricing data and ICER will consider three additional drugs pending public feedback. When it comes to the additional three drugs, ICER is considering products with extremely high price increases that impact the budget on a national level or those used by millions of Americans with price increases that fell just below two times the medical CPI, among other factors.

ICER will review any updated clinical evidence to assess whether it supports a price increase for the drugs in question.

In its 2019 UPI report, ICER assessed AbbVie's blockbuster Humira (adalimumab), Pfizer's Lyrica (pregabalin), Gilead's Truvada (tenofovir disoproxil fumarate and emtricitabine), Genentech/Roche's Rituxan (rituximab), Amgen's Neulasta (pegfilgrastim), Eli Lilly's Cialis (tadalafil), and Tecfidera (dimethyl fumarate), which were noted as drugs with price increases unsupported by new clinical evidence, as well as Gilead's Genvoya (elvitegravir, cobicistat, emtricitabine, and tenofovir alafenamide) and Celgene's Revlimid (lenalidomide), which were deemed as drugs with price increases with new clinical evidence.

Public input on the three additional drugs will be accepted by ICER until July 17, 2020.

EFPIA Sends Letter Urging for Mutual Recognition Agreement Between EU and UK

PRICENTRIC BRIEF:

- The European Federation of Pharmaceutical Industries and Associations (EFPIA) has written a letter highlighting the need to prioritize health and patients' access to medicines in the EU-UK negotiations
- The letter comes following the outcome of a High-Level meeting of June 15, 2020, in which the board discussed creating the most conducive conditions for concluding and ratifying a deal before the end of 2020
- EFPIA is "extremely concerned about the lack of progress with only 6 months until the end of the Transition Period, which could lead to a failure to reach a negotiated outcome on the future EU-UK relationship"

Originally published: June 22, 2020

Country: BELGIUM, UNITED KINGDOM | Region: EUROPE | Type: Policy | Keywords: #brexit #collaboration #deal #efpia #negotiation #trade

THE DETAILS

BRUSSELS, Belgium - The European Federation of Pharmaceutical Industries and Associations (EFPIA) has written a letter to the Honorable Presidents and Commissioner, Honorable Chief negotiator, highlighting the need to prioritize health and patients' access to medicines in the EU-UK negotiations.

The letter comes following the outcome of a High-Level meeting of June 15, 2020, in which the board discussed creating the most conducive conditions for concluding and ratifying a deal before the end of 2020.

However, the organization is "extremely concerned about the lack of progress with only 6 months until the end of the Transition Period, which could lead to a failure to reach a negotiated outcome on the future EU-UK relationship."

EFPIA says that for the life science sector, irrespective of readiness, such a result will, in the short-term, introduce disruptions to medicine supply chains causing delays in access to medicines for both EU and UK patients and, in the long term, reduce the competitiveness of the EU and UK life science hubs vis-à-vis the US, Japan, and China.

The letter continues, "In addition to Brexit, Covid-19 has underlined the importance of global medicine supply chains, and the industry has undertaken a sustained global effort to ensure continued access to medicines for patients throughout the crisis.

"The crisis has highlighted the need for closer international health collaboration and dialogue, and the need for governments to work together with industry to ensure a resilient health sector and medicine supply chains."

As such, EFPIA "would like to respectfully call on you to prioritize health and patients' access to medicines in the EU-UK negotiations and shield them from larger political considerations."

The organization ultimately states that it is "crucial to ensure as much cooperation as possible with regard to regulatory processes and the import and export of medicines and medical supplies across UK/EU borders, in order to minimize delays in products reaching patients."

Project Orbis Allows Concurrent Submissions Among International Regulators, but Timing is Key

Originally published: June 18, 2020 | Country: AUSTRALIA, CANADA-ONTARIO, SINGAPORE, SWITZERLAND, UNITED STATES | Region: ASIA & SOUTH PACIFIC, EUROPE, NORTH AMERICA | Type: Regulation | Keywords: #acceleratedapproval #drugapprovals #earlyaccess #fda #healthcanada #hsa #oncology #projectorbis #submissions #swissmedic

PRICENTRIC BRIEF:

- A hot topic for discussion at the Drug Industry Association (DIA) Global Annual Meeting was Project Orbis, a collaborative initiative that provides a framework for concurrent submission and review of oncology drugs among the U.S., Canada, Australia, Switzerland, and Singapore
- Initially, Project Orbis involved only the U.S., Canada, and Australia, but shortly after its September 2019 launch, the Project was expanded to include the two other participating countries from the Australia-Canada-Singapore-Switzerland (ACSS) Consortium, Singapore and Switzerland
- While the Project's review team has no formal process, the timing of submissions is important for determining participation in Project Orbis, and pharmaceutical companies are more than welcome to inquire about participating in the Project to "allow patients with cancer to receive earlier access to products in other countries where there may be significant delays in regulatory submissions," the Project's goal

THE DETAILS

WASHINGTON, D.C., The United States – At the Drug Industry Association (DIA) Global Annual Meeting, which was held virtually this year due to the COVID-19 pandemic, representatives from the European Medicines Agency (EMA), the U.S. Food and Drug Administration (FDA), and Health Canada detailed issues related to accelerated approvals in each of their respective jurisdictions.

A hot topic for discussion was Project Orbis, a collaborative initiative through the FDA Oncology Center of Excellence that provides a framework for concurrent submission and review of oncology drugs among the U.S., Canada, Australia, Switzerland, and Singapore.

Initially, Project Orbis involved only the U.S., Canada, and Australia, but shortly after its September 2019 launch, the Project was expanded to include the two other participating countries from the Australia-Canada-Singapore-Switzerland (ACSS) Consortium, Singapore and Switzerland.

Project Orbis allows for the simultaneous submission of applications for oncology products to the regulators of these five countries: The U.S. FDA, Health Canada, Australia's Therapeutic Goods Administration (TGA), Singapore's Health Sciences Authority (HSA), and Switzerland's Swissmedic.

Under Project Orbis, the FDA granted accelerated approval to Eisai's Lenvima (lenvatinib) in combination with Merck's (known as MSD outside the U.S. and Canada) Keytruda (pembrolizumab) for the treatment of patients with advanced endometrial carcinoma with certain specifications.

Since then, the FDA has approved a handful a drugs through this initiative, including, but not limited to, Roche's Tecentriq (atezolizumab) plus Avastin (bevacizumab) for hepatocellular carcinoma (HCC), Bristol-Myers Squibb's (BMS) Opdivo (nivolumab) plus Yervoy (ipilimumab) for non-small cell lung cancer (NSCLC), and, as of this week, Jazz's Zepzelca (lurbinectedin) for NSCLC.

The FDA, Health Canada, and TGA have simultaneously reviewed medicines together before, as in the case of AstraZeneca's (AZ) Calquence (acalabrutinib) for chronic lymphocytic leukemia (CLL). In addition, approvals have been granted in a relatively timely manner: Swissmedic approved Seattle's Tukysa (tucatinib) for HER2+ breast cancer less than a month after the FDA, following concurrent submission through Project Orbis.

But at the DIA global meeting, Patricia Keegan, Associate Director for Medical Policy at the FDA's Oncology Center for Excellence explained that the Project's review team has "formalized process" when it comes to identifying products that would be suitable for concurrent submission among the five participating countries.

However, the timing of submissions is important, and has been a point of concern for the regulatory agencies, because pharmaceutical companies oftentimes submit initial applications to multiple agencies, including EMA, which so far isn't a part of Project Orbis. The Project's review committee will reach out about the timing of submissions for oncology products, but according to Keegan, sponsors are more than welcome to inquire about participating in the Project.

Nevertheless, Project Orbis has allowed new indications or products to be approved much more rapidly, as the Director of Health Canada's Center for Evaluation of Radiopharmaceuticals and Biotherapeutics pointed out at the global meeting.

Which is a major goal of the Project, according to the FDA: "Collaboration among international regulators may allow patients with cancer to receive earlier access to products in other countries where there may be significant delays in regulatory submissions."

HTA Decisions: Germany

- IQWIG has published a health benefit assessment report on **Novartis' Kisqali (ribociclib)** for breast cancer in combination with an aromatase inhibitor. In postmenopausal patients with HR-positive, HER2-negative locally advanced or metastatic breast cancer there is no evidence of an added benefit of ribociclib in combination with an aromatase inhibitor as initial endocrine therapy compared to the appropriate comparator therapy, so an added benefit is thus not proven. The procedure for deriving an overall statement on the additional benefit is a suggestion by IQWIG. G-BA decides on the additional benefit.
- IQWIG has published a health benefit assessment report on **Novartis' Kisqali (ribociclib)** for breast cancer, combination with fulvestrant. In postmenopausal patients with HR-positive, HER2-negative, locally advanced, or metastatic breast cancer that was previously treated with an endocrine received therapy, no evidence was found, of an added benefit of ribociclib in combination with fulvestrant compared to the comparator fulvestrant, so an additional benefit is therefore not proven. G-BA decides on the additional benefit.
- IQWIG has published a health benefit assessment report on **Janssen's Erleada (apalutamid)** for prostate cancer. In summary, for patients with mHSPC, there is good general condition evidence of an unquantifiable added benefit of apalutamide over the conventional ADT in combination with docetaxel and prednisone or prednisolone.
- G-BA has published the benefit assessment report on **Vertex's Kalydeco (ivacaftor)** used to treat infants from 6 months old, Infants and children with bodyweight between 5 kg and less than 25 kg with cystic fibrosis. The committee noted the probability of the additional benefit of Ivacaftor by children and adolescents from 6 to 11 years or 12 to 18 years children aged 6 to <12 months with cystic fibrosis with the following gating mutations is adopted in this age group. The uncertainty caused by transferring the added benefit to a younger population can be a clue to determine a non-quantifiable additional benefit.
- IQWIG has published a health benefit assessment report on **Astellas' Dificlir (fidaxomicin)** for clostridioides difficile infection in children and adolescents. In summary, for patients from birth to <18 years severe and/or recurrent course of a CDI disease, there is a possibility for considerable added benefit of fidaxomicin over the purposeful comparative therapy vancomycin.
- IQWIG has published a health benefit assessment report on **Bayer's Adempas (riociguat)** for pulmonary arterial hypertension. The committee noted that available evidence did not give an additional benefit over comparators. Hence, the committee decided to give an unfavorable decision against Adempas. The G-BA decides on the additional benefit.
- IQWIG has published a health benefit assessment report on **Bayer's Adempas (riociguat)** for chronic thromboembolic pulmonary hypertension. The committee noted that available evidence did not give an additional benefit over comparators. Hence, the committee decided to give an unfavourable decision against Adempas. G-BA decides on the additional benefit.
- IQWIG has published a health benefit assessment report on **Novartis' Beovu (brolucizumab)** for neovascular age-related macular degeneration. There are no data available to assess the added benefit of brolucizumab in adult patients with neovascular (moist) age-related macular degeneration compared to the appropriate comparator therapy. An added benefit of Beovu is therefore not documented.
- IQWIG has published a health benefit assessment report on **UCB/Amgen's Evenity (romosozumab)** for osteoporosis. In summary, in postmenopausal women with overt and osteoporosis significantly increased fracture risk, there is an indication of a considerable added benefit of romosozumab versus the ACT alendronic acid.

HTA Decisions: United Kingdom

- NICE has published a technology appraisal guidance on **Teva's Ajovy (fremanezumab)** for preventing migraine. The committee noted that Ajovy is recommended as an option for the treatment if the migraine is chronic, that is, 15 or more headache days a month for more than 3 months with at least 8 of those having features of migraine and the company provides it according to the commercial arrangement.
- NICE has published a technology appraisal guidance on **Genentech's Kadcyla (trastuzumab emtansine)** for human epidermal growth factor receptor 2 (HER2) positive early breast cancer in adults who have the residual invasive disease in the breast or lymph nodes after neoadjuvant taxane-based and HER2+ targeted therapy. NICE has noted that clinical trial evidence shows that in people with the residual invasive disease after neoadjuvant therapy and surgery, trastuzumab emtansine increases the time people remain free of disease compared with trastuzumab alone and the cost-effectiveness estimates are within what NICE considers an acceptable use of NHS resources. Therefore, trastuzumab emtansine is recommended.
- NICE has published a technology appraisal guidance on **Janssen's Stelara (ustekinumab)** for treating moderately to severely active ulcerative colitis in adults when conventional therapy or a biological agent cannot be tolerated, or the disease has responded inadequately or lost response to treatment. The committee noted that ustekinumab is recommended if the tumor necrosis factor-alpha inhibitor has failed (that is the disease has responded inadequately or has lost response to treatment) or a tumor necrosis factor-alpha inhibitor cannot be tolerated or is not suitable.

HTA Decisions: France

- HAS published a technology assessment report on **Regeneron's Dupixent (dupilumab)** for the treatment of moderate to severe atopic dermatitis in adolescents aged 12 years and over who require systemic treatment. The medical service provided by the specialty Dupixent, solution for injection in a pre-filled pen is important in the treatment and at the dosages in the Marketing Authorization. This specialty does not improve the medical service provided (ASMR V) compared to the presentations of Dupixent.
- HAS published a technology assessment report on **Novartis' Kisqali (ribociclib)** for treatment of locally advanced or metastatic breast cancer RH + / HER2- in combination with fulvestrant as an initial treatment based on hormone therapy, or in women previously treated with hormone therapy. In women in pre- or peri-menopause, hormone therapy should be combined with an LH-RH agonist. The Commission considers that the addition of Kisqali to fulvestrant does not improve the medical service provided (ASMR V) compared to fulvestrant alone in the first or second line of hormone therapy for advanced breast cancer HR + / HER2- in the absence of symptomatic visceral impairment threatening the short-term vital prognosis in postmenopausal women.
- HAS published a technology assessment report on **Novartis' Afinitor (everolimus)** for treatment of advanced breast cancer RH + / HER2- in combination with exemestane, in postmenopausal women without symptomatic visceral involvement upon recurrence or progression of the disease and previously treated with a non-steroidal inhibitor of l aromatase. The Commission considers that Afinitor in combination with exemestane does not bring any improvement in the medical service rendered (ASMR V) compared to the comparators studied (exemestane or capecitabine) in postmenopausal women with advanced breast cancer RH + / HER2-, as soon as the disease recurs or progresses, previously treated with a non-steroidal aromatase inhibitor and in the absence of symptomatic visceral involvement.

HTA Decisions: France

- HAS published a technology assessment report on **Ibuprofen arrow** for the short term local symptomatic treatment of superficial tendonitis, after medical advice, in adults and adolescents over 15 years of age. The medical service provided by Ibuprofen arrow 5%, the gel, is moderate in the short-term local symptomatic treatment of superficial tendonitis, after medical advice. This specialty does not provide any improvement in the medical service rendered (ASMR V) compared to other specialties based on ibuprofen gel 5%.

- HAS published a technology assessment report on **Boehringer Ingelheim's Giotrif (afatinib)** for the treatment of locally advanced or metastatic non-small cell lung cancer with one or more activating mutation (s) of EGFR (epidermal growth factor receptor). The Commission takes note of these modifications which are not likely to modify its previous conclusions (opinion from 04/09/2019). It underlines the importance of monitoring patients treated with Giotrif (afatinib), in particular, about the risk of gastrointestinal perforation, and the need to take into account the risk factors that may represent contraindications in its prescription (concomitant use of corticosteroids).

- HAS published a technology assessment report on **Genentech's Kadcyla (trastuzumab emtansine)** for the adjuvant treatment of adult patients with HER2 positive early breast cancer who have invasive residual disease, in the breast and/or lymph nodes, after neoadjuvant treatment with taxane and anti-HER2 treatment. The medical service rendered by Kadcyla by IV route is important in the new indication for Marketing Authorization, namely "as monotherapy, in the adjuvant treatment of adult patients with HER2 positive early breast cancer who present a disease invasive residual, in the breast and/or lymph nodes, after neoadjuvant treatment based on taxane and anti-HER2 treatment". The Commission considers that Kadcyla brings an improvement in the medical service rendered moderate (ASMR III) compared to trastuzumab in the context of adjuvant treatment in adult patients with HER2 positive early breast cancer who have invasive residual disease in the breast and/or lymph nodes after neoadjuvant treatment with taxane and anti-HER2 treatment.

- HAS published a technology assessment report on **Ferring's Pabal (carbetocin)** for the prevention of postpartum hemorrhage due to uterine atony after vaginal delivery. The medical service provided by PABAL is important in the prevention of postpartum hemorrhage due to uterine atony after vaginal delivery. The Transparency Committee considers that PABAL does not bring any improvement in the medical service rendered (ASMR V) in the preventive strategy for postpartum hemorrhages due to atonic uterus.

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Drug Approvals: United States

- **BRILINTA (TICAGRELOR)** was approved by the FDA to reduce the risk of a first heart attack or stroke in high-risk patients with coronary artery disease (CAD), the most common type of heart disease.
COMPANY: ASTRAZENECA

- **RECARBRIO (IMIPENEM, CILASTATIN AND RELEBACTAM)** was approved by the FDA for the treatment of patients 18 years of age and older with hospital-acquired bacterial pneumonia and ventilator-associated bacterial pneumonia (HABP/VABP).
COMPANY: MERCK

- **OPDIVO (NIVOLUMAB)** was approved by the FDA for patients with unresectable advanced, recurrent or metastatic esophageal squamous cell carcinoma (ESCC) after prior fluoropyrimidine- and platinum-based chemotherapy.
COMPANY: BRISTOL-MYERS SQUIBB

- **NYVEPRIA (PEGFILGRASTIM-APGF)** was approved by the FDA to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia.
COMPANY: PFIZER

- **SEMGLEE (INSULIN GLARGINE)** was approved by the FDA to improve glycemic control in adults and pediatric patients with type 1 diabetes mellitus and in adults with type 2 diabetes mellitus.
COMPANY: MYLAN

- **UPLIZNA (INEBILIZUMAB)** was approved by the FDA for the treatment of neuromyelitis optica spectrum disorder (NMOSD) in adult patients who are anti-aquaporin-4 (AQP4) antibody positive.
COMPANY: VIELA BIO

- **TIVICAY PD (DOLUTEGRAVIR)** was approved by the FDA in combination with other antiretroviral agents for the treatment of HIV-1 infection in adults (treatment-naïve or -experienced) and in pediatric patients (treatment-naïve or -experienced but INSTI- naïve) aged at least 4 weeks and weighing at least 3 kg; in combination with rilpivirine as a complete regimen for the treatment of HIV-1 infection in adults to replace the current antiretroviral regimen in those who are virologically suppressed (HIV-1 RNA less than 50 copies per mL) on a stable antiretroviral regimen for at least 6 months with no history of treatment failure or known substitutions associated with resistance to either antiretroviral agent.
COMPANY: VIIV HEALTHCARE

- **GARDASIL 9** was approved by the FDA for the prevention of oropharyngeal and other head and neck cancers caused by HPV Types 16, 18, 31, 33, 45, 52, and 58.
COMPANY: MERCK

- **ZEPZELCA (LURBINECTEDIN)** was approved by the FDA d for the treatment of adult patients with metastatic small cell lung cancer (SCLC) with disease progression on or after platinum-based chemotherapy.
COMPANY: PHARMA MAR USA

- **LYUMJEV (INSULIN LISPRO-AABC)** was approved by the FDA to improve glycemic control in adults with diabetes mellitus.
COMPANY: ELI LILLY

Drug Approvals: United States

- **MYLOTARG (GEMTUZUMAB OZOGAMICIN)** was approved by the FDA for newly-diagnosed CD33-positive acute myeloid leukemia (AML) to include pediatric patients 1 month and older.
COMPANY: WYETH

- **KEYTRUDA (PEMBROLIZUMAB)** was approved by the FDA for the treatment of adult and pediatric patients with unresectable or metastatic tumor mutational burden-high (TMB-H) [≥10 mutations/megabase (mut/Mb)] solid tumors, as determined by an FDA-approved test, that have progressed following prior treatment and who have no satisfactory alternative treatment options.
COMPANY: MERCK

- **TAZVERIK (TAZEMETOSTAT)** was approved by the FDA for adult patients with relapsed or refractory (R/R) follicular lymphoma (FL) whose tumors are positive for an EZH2 mutation as detected by an FDA-approved test and who have received at least 2 prior systemic therapies, and for adult patients with R/R FL who have no satisfactory alternative treatment options.
COMPANY: EPIZYME

- **CRYSVITA (BUROSUMAB)** was approved by the FDA for the treatment of fibroblast growth factor 23 (FGF23)-related hypophosphatemia in tumor-induced osteomalacia (TIO) associated with phosphaturic mesenchymal tumors that cannot be curatively resected or localized in adults and pediatric patients 2 years of age and older.
COMPANY: ULTRAGENYX

- **GIMOTI (METOCLOPRAMIDE)** was approved by the FDA for the relief of symptoms in adults with acute and recurrent diabetic gastroparesis.
COMPANY: EVOKE

- **XPOVIO (SELINEXOR)** was approved by the FDA for adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL), not otherwise specified, including DLBCL arising from follicular lymphoma, after at least 2 lines of systemic therapy.
COMPANY: KARYOPHARM

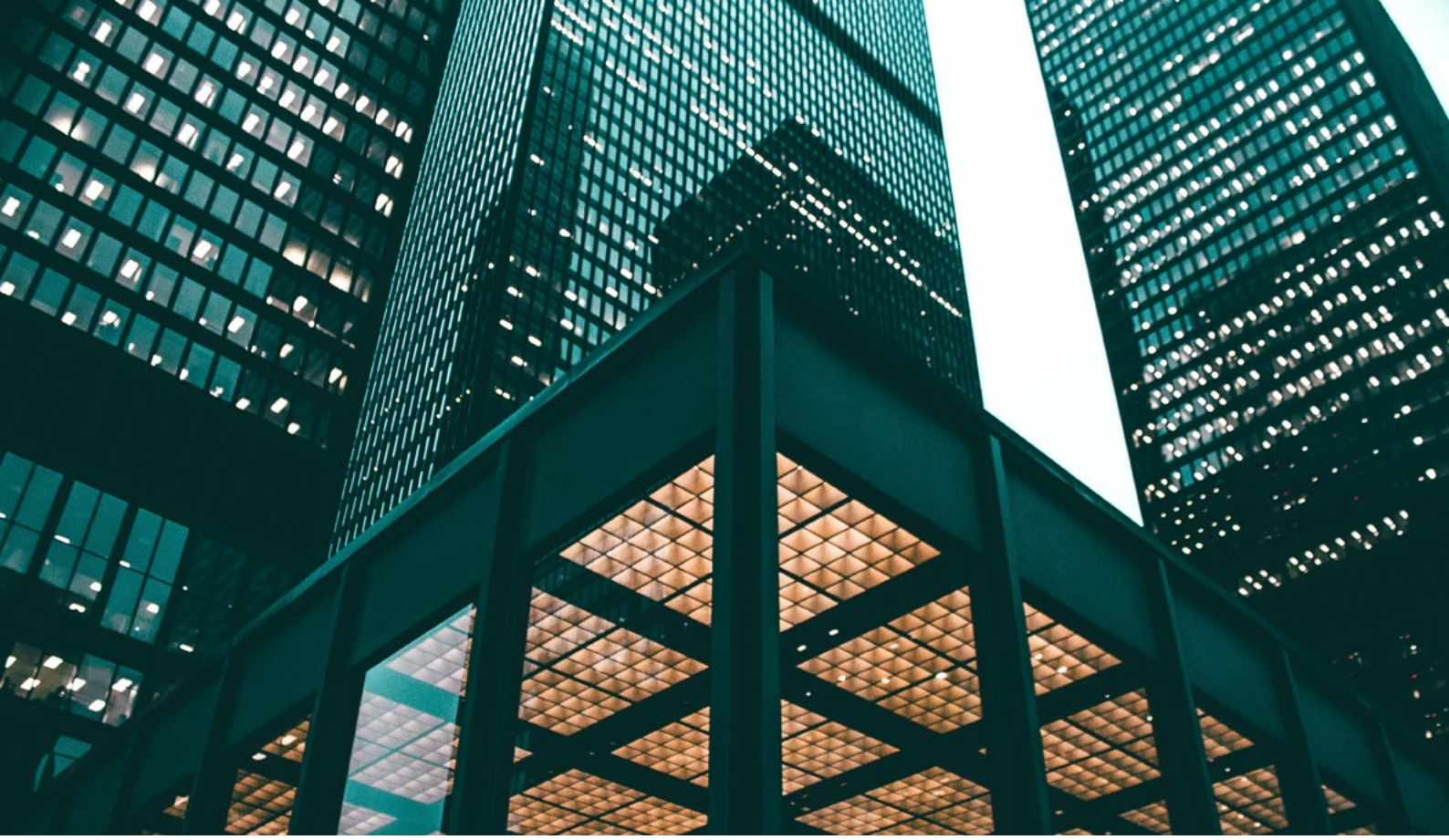
Drug Approvals: EMA

- **SARCLISA (ISATUXIMAB)** was approved by the EMA in combination with pomalidomide and dexamethasone (pom-dex) for the treatment of adult patients with relapsed and refractory multiple myeloma (MM) who have received at least two prior therapies including lenalidomide and a proteasome inhibitor and have demonstrated disease progression on the last therapy.
COMPANY: SANOFI

Drug Approvals: China

- **BRUKINSA (ZANUBRUTINIB)** was approved by the NMPA in two indications – the treatment of adult patients with chronic lymphocytic leukemia (CLL) /small lymphocytic lymphoma (SLL) who have received at least one prior therapy, and the treatment of adult patients with mantle cell lymphoma (MCL) who have received at least one prior therapy.
  COMPANY: BEIGENE

- **KEYTRUDA (PEMBROLIZUMAB)** was approved by the NMPA as monotherapy for the treatment of patients with locally advanced or metastatic esophageal squamous cell carcinoma (ESCC) whose tumors express PD-L1 (Combined Positive Score [CPS] ≥10) as determined by a fully validated test, following failure of one prior line of systemic therapy.
  COMPANY: MERCK



Drug Launches: Europe & US

Country	Generic Name	Product Group	Company	Indication	Approval Date	Launch Date
GERMANY	INFLUENZA, INACT, SPLIT VIR OR SUR ANTI	AFLURIA TETRA	SEQIRUS	INFLUENZA	22/02/2018	15/06/2020
GERMANY	MOGAMULIZUMAB	POTELIGEO	KYOWA KIRIN	MYCOSIS FUNGOIDES	22/11/2018	15/06/2020
GERMANY	TALAZOPARIB	TALZENNA	PFIZER	BREAST CANCER (BRCA MUTATION)	20/06/2019	01/06/2020
ITALY	GLUCAGON	BAQSIMI	ELI LILLY	REDUCT OF INTRAC PRES & HYPOG COMA	16/12/2019	13/06/2020
ITALY	OSILODROSTAT	ISTURISA	RECORDATI	CUSHING'S SYNDROME	09/01/2020	13/06/2020
UNITED STATES	APOMORPHINE	KYNMOBI	SUNOVION	PARKINSON'S DISEASE	21/05/2020	09/06/2020
UNITED STATES	ELAG & ESTRA & NORETH	ORIAHNN	ABBVIE	UTERINE FIBROIDS	29/05/2020	02/06/2020
UNITED STATES	LACTIC ACID & CITRIC ACID & POTA BITART	PHEXXI	EVOFEM BIO	PREGNANCY PROTECTION	22/05/2020	03/06/2020
UNITED STATES	MINOCYCLINE	ZILXI	FOAMIX	ROSACEA	28/05/2020	08/06/2020

Price Changes: Europe & US

Country	Generic Name	Product Group	Company	Therapeutic Area	Avg. Price Change all SKU	First Pricing Date
GERMANY	FREMANEZUMAB	AJOVY	TEVA	NEUROLOGY	-5.88%	15/05/2019
SPAIN	IBUPROFEN	NUROFEN	RECKITT BENCKISER	RHEUMATOLOGY	-4.71%	01/06/2017
FRANCE	IVACAFTOR	KALYDECO	VERTEX	RESPIRATORY	-6.00%	27/12/2013
GERMANY	LINAGLIPTIN & EMPAGLIFLOZIN	GLYXAMBI	BOEHRINGER	DIABETOLOGY	-28.48%	01/06/2019
GERMANY	NINTEDANIB	OFEV	BOEHRINGER	ONCOLOGY	+7.72%	15/03/2015
UNITED STATES	PAROXETINE	PAXIL	APOTEX	NEUROLOGY	+9.00%	11/01/1993
GERMANY	PEMBROLIZUMAB	KEYTRUDA	MSD	ONCOLOGY	-1.55%	15/08/2015
GERMANY	PENTOXIFYLLINE	TRENTAL	SANOFI	CVS	+11.53%	15/07/2004
GERMANY	ZOLPIDEM	STILNOX	SANOFI	NEUROLOGY	+10.20%	15/07/2004

Germany: Post-AMNOG Price Changes for Originator Drugs

Company	Product Group	Generic Name	Description	MNF (EUR)	OLD MNF	Change	%Change
BIOMARIN	BRINEURA	CERLIPONASE ALFA	BRINEURA INFUSION 2 VIAL 5 ML 150 MG	19230.77	19807.69	-576.92	-2.91%
MENARINI	ELEBRATO ELL	VILA & UME BRO & FLU FUR	ELEBRATO EL PWDR 1 INHAL 30 DOSES 169 MCG	54.03	54.14	-0.11	-0.20%
MENARINI	ELEBRATO ELL	VILA & UME BRO & FLU FUR	ELEBRATO EL PWDR 3 INHAL 30 DOSES 169 MCG	162.10	162.43	-0.33	-0.20%
MSD	KEYTRUDA	PEMBROLIZUMAB	KEYTRUDA INFUSION 1 VIAL 4 ML 100 MG	2431.00	2469.25	-38.25	-1.55%
BOEHRINGER ING	OFEV	NINTEDANIB	OFEV CAPSULES 1 PACK 60 CAPS 100 MG	2124.80	1972.60	+152.20	+7.72%
BOEHRINGER ING	OFEV	NINTEDANIB	OFEV CAPSULES 1 PACK 60 CAPS 150 MG	2616.16	2428.77	+187.39	+7.72%
GLAXOSMITHKLINE	TRELEGY ELLIPTA	VILA & UME BRO & FLU FUR	TRELEGY EL PWDR 1 INHAL 30 DOSES 169 MCG	54.03	54.14	-0.11	-0.20%
GLAXOSMITHKLINE	TRELEGY ELLIPTA	VILA & UME BRO & FLU FUR	TRELEGY EL PWDR 3 INHAL 30 DOSES 169 MCG	162.10	162.43	-0.33	-0.20%

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