TRINITY

WHITE PAPER

Annual State of Global Market Access

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Contents

Introduction

In 2023, the life sciences industry saw key therapeutic advances in sickle cell disease, obesity/weight management, and Duchenne muscular dystrophy, among others, and the continued approvals of therapies with cutting edge mechanisms, including the first CRISPR therapy. While 2022 (refer to 2022 Trends Report) was characterized by accelerated development processes and the rapid evolution of therapeutic standards, 2023 featured increased implementation of cost-effectiveness policies and the emergence of the consequences of these pricing controls and cost-effectiveness measures, including the Inflation Reduction Act (IRA) and Germany's Financial Stabilization Act. Regulatory and payer strategies continued to evolve in 2023, and **this white paper seeks to illustrate the key consequences of new therapeutic advances and policies aiming to control costs globally and assess their impacts for pharmaceutical manufacturers.**

Key Global Market Access Trends of 2023

1 Cell and Gene Therapy Continued Expansion and Other New Drug Modalities

Multiple cell and gene therapies were approved in 2023, including the first therapy to make use of CRISPR. These therapies are potentially one-time and/or curative treatments, and the evidence required to demonstrate their value at high prices continues to evolve.

2 Evolving Evidence Expectations

Greater data availability and the ability to generate real-world evidence have affected payer evidence expectations for the evidence package used to assess both the clinical and economic value of products. Regulatory bodies like the FDA published guidance for evaluating real-world evidence (RWE) in the assessment of novel therapies although a limited track record of success has tempered the adoption of RWE.

3 Increased Market Delays and Withdrawals due to Low Reimbursement

In 2023, there was a substantial increase in market delays and withdrawals due to a lower reimbursement opportunity compared to previous years. The increase in delays and withdrawals was driven by policy changes across key markets, including in Germany, where pricing rules and shifts in the benefit assessment system now pose a substantial roadblock for manufacturers.

4 Exploration of New Regulatory Pathways Beyond the FDA and EMA

In an effort to reduce reliance on the United States Food and Drug Administration (FDA) and the European Medicines Agency (EMA) and increase local/regional control of regulatory processes, multiple countries and regions implemented changes to their market authorization processes.

5 Spread of Collaboration HTA Procedures

The trend towards collaborative Health Technology Assessment (HTA) procedures and the cross-country collaboration to enhance country-specific evaluations continued in 2023. The EU's Joint Clinical Assessment (JCA) is projected to enable high quality clinical assessments of new pharmaceuticals across participating EU countries and has spurred increased conversation around ways to stimulate collaboration across Southeast Asia and Latin America.

6 IRA Impacts on the U.S. Pricing & Market Access Landscape

The impacts of the 2022 IRA continued to unfold in 2023, including numerous lawsuits from manufacturers questioning the constitutionality of the Drug Price Negotiation Program (e.g., the product identification and negotiation process).

Payer Perspectives

A survey was conducted in November 2023 to capture payers' insights about the trends discussed in this white paper.

The sample consisted of 17 U.S. payers and 26 payers from global markets across 4 continents.

U.S. payers (n=17)
Ex-U.S. payers (n=26)

Country of Respondent	Number of Respondents (n)
Brazil	2
Canada	2
China	2
France	3
Germany	5
Italy	2
Mexico	2
Saudi Arabia	3
Spain	3
United Kingdom	3
United States	17

Insights from this survey have been included with each trend, including the mean average score within **U.S. and ex-U.S. payer groups** about their perception of impact for each category.

Expansion of Cell and Gene Therapies and Other New Drug Modalities

Cell and Gene Therapies

The cell and gene therapy space continued to grow in 2023, as of the end of 2023 there were 29 gene therapies and 65 non-genetically modified cell therapies approved globally since the flourishing field saw its first launch.[1,2] One notable entry in 2023 is CASGEVY™, indicated for sickle cell disease which was approved by MHRA in November and the FDA in December, making it the first CRISPR-based therapy to achieve this status.[3,4] Merely a decade after the publication of pivotal papers demonstrating potential use of the CRISPR mechanism in eukaryotic cells, these approvals mark the beginning of an exciting new chapter for the revolutionary gene editing mechanism, with broader application across a number of indications in the near future.[5] Also among these therapies, Sarepta's ELEVIDYS™ received FDA approval in June 2023 through the Accelerated Approval pathway and is the first gene therapy to treat Duchenne muscular dystrophy. In late December 2023, Sarepta filed an additional efficacy supplement containing results from the EMBARK study to remove current demographic restrictions (e.g., age, ambulatory status) from the ELEVIDYS label. Further, ROCTAVIAN™'s recent launch in hemophilia marks a rare entry into a relatively well managed indication with greater competition (e.g., HEMLIBRA).[6]

As these therapies continue to launch, they have provoked discussions of how to assess their value. For example, in budget impact analyses, high cost but potentially curative therapies may be downgraded based on absolute costs over the short term; in contrast, in cost-effectiveness analyses, multiple therapies have been able to clear cost-effectiveness thresholds. In the case of recently-approved CASGEVY and LYFGENIA™ in sickle cell disease (SCD),[7,8] gene therapies were found to have acceptable value even at high price points. In July 2023, the Institute for Clinical and Economic Review (ICER) released an assessment of CASGEVY or LYFGENIA to treat sickle cell disease in patients ≥ 12 years of age.[9] When evaluating the evidence to support the value of SCD therapies, clinical evidence for both CASGEVY and LYFGENIA were found to

> "I anticipate further increasing relevance of cell and gene therapies to be the most significant trend to impact my management as a payer in 2024."
>
> **U.S. National MCO Payer Medical Director**

Payer Perspectives

How impactful do you perceive the trend of cell and gene therapy expansion in 2023?

Rating:
1 = Hardly any impact
10 = A dominating force

U.S. Payer Perception of Impact:

9/10

Ex-U.S. Payer Perception of Impact:

8/10

*Compared to U.S.=9 and ex-U.S.=8.6 in 2022

have limitations due to sample size and uncertainties of duration of benefit – however, given the disease severity and the rate of treatment success, both therapies were believed to provide at least an incremental net benefit. The assessment found either therapy to be cost-effective below $2,050,000, driven by substantial perceived benefits to length and quality of life. These ICER assessments, which are used to supplementarily inform payer decision-making,[10] indicate that despite high launch prices, there is acceptance for therapies that drive high value in markets driven by cost-effectiveness. However, in markets centered on budget impact payers struggle to more significantly rationalize high price tags. Further, multi-payer health systems like the U.S. often have shorter time horizons to recognize budget impact (e.g., 3-5 years due to patients changing health plans) compared to single payer health systems that can extend horizons far longer.

Last year drugs such as ZYNTEGLO™ (Bluebird Bio, INC) and HEMGENIX™ (CSL Behring) entered the U.S. market at $2.8M and $3.5M price marks, respectively (refer to 2022 trends report). Since HEMGENIX's entrance, CSL Behring has been exploring outcomes-based agreements within the U.S. to mitigate concerns around its high cost, which may include the offer of a potential rebate to payers if patients return to using prophylactic factor IX during the first 3 1/2 years following infusion.[11] With increasingly high price points for new advance therapeutics that have long-term efficacy uncertainties, such outcomes-based agreements may become more likely to occur in the future.

> "The advancement in gene therapies, CAR-T, and bispecific treatments, etc. forces creative reimbursement models, such as use of third-party insurers, annuities, re-insurance, and value-based contracting. However, the approval of GLP1s for weight loss has blindsided budgets, especially for groups in total risk of care arrangements."
>
> **U.S. IDN Payer Medical Director**

In contrast to the U.S., reaching pricing agreements within the EU has been more challenging. In 2021, Blue Bird, for example, withdrew from EU markets after encountering difficulty reaching price agreements for ZYNTEGLO with regulators. Bluebird had since withdrawn from markets such as Germany's specifically.[12] These pricing disagreements around new cell and gene therapies continue in 2023 (refer to Increased Market Withdrawals due to Low Reimbursement Opportunity section). In the UK, despite receiving conditional marketing authorization in early 2023, HEMGENIX received an unfavorable assessment from NICE in their August 2023 draft guidance in part due to insufficient evidence justifying its value. In particular, NICE cited that uncertainty remains in terms of long-term clinical evidence and the assumptions used to estimate cost effectiveness for HEMGENIX.[13]

Innovative contracting has been an increasingly popular way to mitigate high price points of new cell and gene therapies. Biomarin's ROCTAVIAN in particular further found success in 2023 within Germany through establishment of a prospective cohort model agreement where price would be adjusted on an annual basis based on success in the prior year as based on real-world data collected from the German Haemophilia Registry of patients treated with ROCTAVIAN.[14] European markets have been increasingly looking to promote access to funding for gene therapies through incorporating innovative contracting implementation, including through the 2022 Swedish Dental Health & Medicines Agency (TLV) innovative contracting implementation mandate, Spain's (Valtermed) RWE registry system, France's 2023 Social Security Bill (PLFSS), establishing outcomes-based agreements for advanced therapeutic medicinal products (ATMPs) through an annuity model of staggered payments based on real-world results, and the recognition of new surrogate endpoints for ATMPs including gene therapies within Germany's 2023 statutory

health insurance (GVK) financial stabilization bill.[15, 16, 17, 18] As regulatory bodies and manufacturers continue to strike the balance between economically viable trial endpoints and the ability to demonstrate long-term impact, use of innovative contracts continues to be a key strategy to discover that balance.

> In the ATMP space assessment and reimbursement of products like ROCTAVIAN were interesting as finally an one-off payment was settled instead of complex annuity or P4P schemes. Despite first registry requirements for orphan drugs were implemented, the role of RWE to impact HTA ratings did not improve.
>
> **Ex-Germany Payer**
> **KVWL**

> We anticipate increasing attempts at innovative payments to affect our future work as payers.
>
> **Ex-China Payer**
> **Ministry of Human Resources and Social Security**

> We have seen the arrival of innovative drugs with major budgetary implications such as gene therapies. For certain indications, we have begun to think about staggered payments as a mitigant.
>
> **Ex-France Payer**
> **TC**

Related

The Innovative payments have already begun to enter China as China signs a value-based agreement for YESCARTA® (axicabtagene ciloleucel) in early January 2024. This first efficacy-based payment plan in China entitles patients who are unable to achieve complete remission on the therapy to receive refunds up to RMB 600,000 or $84,150.[19]

Strategic Implications

As the innovation delivered by novel molecular entities and drug modalities continues to grow, so too are payer expectations of evidence and affordability solutions to support the high prices that accompany new treatments.

New Drug Modalities

Drug development of a variety of modalities for diverse molecular targets continues, with an increasing focus on innovative therapies such as cell and gene therapies. In 2022, new modalities (i.e., those beyond small molecules and monoclonal antibodies) including bispecific antibodies, antibody-drug conjugates and cell or gene therapies accounted for half of biologic approvals, up from less than a third the year prior.[20] As approvals continue to roll in for these therapies, we may begin to witness growing payer acceptance towards them despite their higher price tags. Notably, the high cost of some new drug modalities may stand to benefit over traditional small-molecule products in light of the 2022 IRA (refer to IRA section). Inpatient products (e.g., many gene therapies) are exempt from drug pricing provisions laid out in the IRA, and biologic drugs are granted longer periods of patent protection over traditional products, regardless of channel.

Gene Therapies
ABECMA®
ADSTILADRIN
BREYANZI®
CARTEYVA®
CARVYKTI™
CASGEVY™
COLLATEGENE®
DELYTACT®
ELEVIDYS™
FUCASO®
GENDICINE®
HEMGENIX®
IMLYGIC®
KYMRIAH®
LIBMELDY®
LUXTURNA®
LYFGENIA™
NEOVASCULGEN®
ONCORINE®
REXIN-G®
ROCTAVIAN™
SKYSONA®
STRIMVELIS™
TECARTUS®
UPSTAZA™
VYJUVEK®
WAINUA™
YESCARTA®
ZOLGENSMA®
ZYNTEGLO™

RNA Therapies
AMONDYS 45®
AMPLIGEN®
AMVUTTRA®
ARCT-154
COMIRNATY®
CSPC PHARMACEUTICAL COVID-19 VACCINE
DAICHIRONA®
EXONDYS 51®
GENNOVA COVID-19 VACCINE
GIVLAARI®
KYNAMRO®
LEQVIO®
MODERNA COVID-19 VACCINE
NULIBRY®
ONPATTRO®
OXLUMO®
PFIZER & BIONTECH'S OMICRON BA.4/BA.5-ADAPTED BIVALENT BOOSTER
QALSODY®
SINOCELLTECH COVID-19 VACCINE
SPINRAZA®
TEGSEDI®
VILTEPSO®
VYONDYS 53®
WALVAX COVID-19 VACCINE
WAYLIVRA®

Payer Perspectives

How would you assess the difficulty of reaching a pricing and reimbursement agreement for the new products negotiated in your market this year?

Rating:
1 = Not difficult at all
10 = Extremely difficult

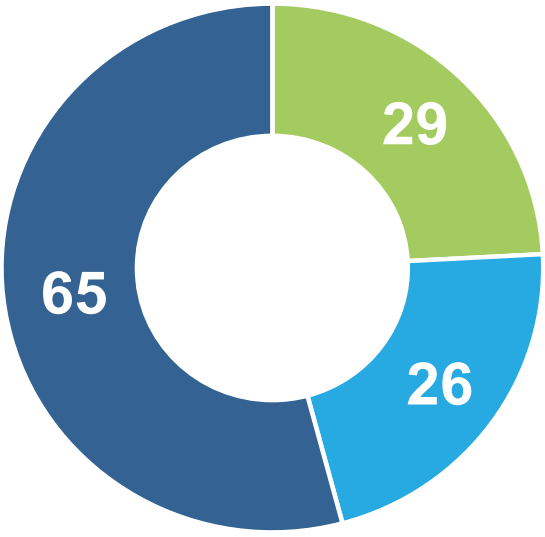
U.S. Payer Perception of Difficulty:

7/10

Ex-U.S. Payer Perception of Difficulty:

8/10

*Compared to U.S.=5 and ex-U.S.=8 in 2022



*includes genetically modified cell therapies

Owing to high unmet need and small patient populations, a number of the new modality therapies have followed the FDA's accelerated approval pathway.[21] However, there have been signs indicating more judicious use of this pathway by the FDA over the last years. 2022 was the first year to show a decrease in the number of therapies approved through the U.S. accelerated approval pathway.[22] This trend continued in 2023 with accelerated approvals remaining at lower levels than prior trajectories, despite a few key approvals such as Sarepta's ELEVIDYS through the pathway and signaling from the FDA that they intend to lean into accelerated approvals of gene therapies.[20] The delayed return to the previous trajectory is likely resulting from growing efforts of the FDA to withdraw accelerated approvals which have failed to produce post-approval studies to validate predicted effect, including through the passing of Food and Drug Omnibus Reform Act (FDORA).[23]

74% (17 of 23) of withdrawn accelerated approvals for cancer indications have been in the past 3 years.[24] Despite post-approval studies being part of the accelerated approval pathway's requirements, prior to passing of FDORA in January 2023, there was a lack of guidance around these post-approval studies, as well as the withdrawal process for those studies failing to provide such follow-up data. Other updates include establishing the need for specifying post-approval study elements prior to accelerated approval, enabling the FDA to provide concrete timelines for post-approval studies, and mandatory publishing of FDA rationale for not specifying the need for post-approval studies.[23]

> "In terms of evidence, the innumerable launches on an accelerated basis with limited Phase 2 and related data is a huge challenge, especially at the price points these agents are arriving at. Data remains scant, especially comparative effectiveness, but the access expectations have remained high."
>
> **U.S. Regional MCO Payer Medical Director**

> "More differentiation of precision-medicine approaches and increasing emergence of cell and gene therapies (with RNA therapies expected to increase) have increased challenges to assessing the benefit of these therapies including in the longer-term, while also increasing budget impact. These developments together make it harder to balance appropriate but fast patient access with affordability to national health systems or social security systems, in the regulation of market access for innovative drugs."
>
> **Ex-German Payer GBA**

Evolving Evidence Expectations

Over the last several years, evidence generation has been shaped by the availability and evolution of real-world evidence (RWE), which includes evidence generated from multiple data sources, such as electronic health records, claims, chargemaster data, registries, prospective studies or other types of observational research. The growing impact of RWE is illustrated by the increase in publications referencing RWE from 2019 to 2023. In addition to providing evidence to support patient burden of illness, clinical outcomes and healthcare resource utilization, RWE has growing acceptability in regulatory contexts worldwide. In the United States, the FDA released new guidance in 2023 on the use of real-world evidence to support regulatory decision-making for drugs and biological products and guidance on the development of clinical trials using external control arms (ECAs). Similarly, in Europe, there has been increased focus on adoption and implementation of RWE in healthcare decision-making, including best practices and priorities for adoption in developing evidence for novel digital health technologies.[25] In both of the aforementioned contexts, regulatory agencies and related institutions have highlighted the potential power of RWE, especially in rare diseases, and noted the enablement of richer data through RWE with wearable devices, smartphone applications and digitalization of health records.[26] They have placed an emphasis on standardized practices based on limitations of the data sources, including consideration of missing data, generalizability, equity, confounders and fitness for purpose. As such, in addition to strengthening regulatory application, RWE stands to benefit payers who wish to better understand disease prevalence and cost, current treatment patterns and standard of care, as well as adverse event profiles beyond clinical trials, which may often not reflect real world care.[27]

Despite the benefits of including RWE, in the United States, a systematic review of oncology drug approvals showed that among 133 original and 573 supplemental approvals, only 11 and 2 included RWE respectively.[28] These numbers illustrate that while new policies and the growing availability of real-world data sources have widened the opportunities to apply RWE analyses and thus increase RWE utilization, this expansion of RWE to new use cases still faces headwind. These findings indicate that there are still perceived risks of using RWE in regulatory contexts without an existing track record of successful approvals. A roundtable discussion of evidence generation experts in digital health discussed the possibility that regulatory risks were a driving factor in lack of inclusion of RWE in submissions for digital health applications, even with the availability and richness of RWE in this setting, and identified a need for standardized practices for addressing limitations to foster trust in the insights from RWE.[25] With the FDA guidance in place to address many of these concerns, RWE may see a larger role in pre-approval evidence generation in the U.S., and potentially other non-U.S. markets that may follow.

Payer Perspectives

How impactful do you perceive the trend of evolving evidence expectations in 2023?

Rating:
1 = Hardly any impact
10 = A dominating force

U.S. Payer Perception of Impact:

7/10

Ex-U.S. Payer Perception of Impact:

6/10

*Compared to U.S.=4 and ex-U.S.=3 in 2022

How would you assess the difficulty in assessing the clinical value of new therapies in your market this year?

Rating:
1 = Not difficult at all
10 = Extremely difficult

U.S. Payer Perception of Impact:

6/10

Ex-U.S. Payer Perception of Impact:

7/10

*Compared to U.S.=4.7 and ex-U.S.=7.1 in 2022

Increased Market Withdrawals Due to Low Reimbursement Opportunity

Countries of Relevance: Global

Compared to previous years, 2023 featured an increased number of market withdrawals and delays due to lower reimbursement opportunity, driven by both policy and intensive cost cutting in both EU and U.S. markets. In the U.S., policies set forth within the IRA prompted concerns around lifecycle pricing and the value of indication expansion, particularly given the discount requirements set forth in the maximum fair price program (see IRA section for more details). Meanwhile, the medicines levy within the UK, in which the rebate rate increases from 5.1% in 2021 to nearly 26.5% in 2023, has severely impacted branded drug availability and resulted in an estimated £50B loss in R&D investment.[29, 30, 31] According to the British Generic Manufacturers Association, the voluntary scheme for branded medicines pricing and access (VPAS) rebate rate is the key reason for the rise in shortages, which were reported for more than twice as many medications in 2023 versus 2022. Supply issues were reported for 111 products, including 55 branded medicines.[29]

The consequences of pharmaceutical companies potentially diverting investment from the UK as a direct result of the levy expansion were noted by the (now former) CEO of Bristol Myers Squibb, Giovanni Caforio, who noted that "low pricing for medicines purchased by the NHS from pharmaceutical companies (is) a major issue that (threatens) the UK's ambition to become a leader in the life sciences industry."[32] Apart from potential divestment, another impact of lower reimbursement opportunity and challenges with access may be the pursuit of launches based on cash payments rather than reimbursement through payers. In the U.S., for example, some GLP-1s for the treatment of obesity are launching directly through direct-to-consumer health and wellness companies, including Him&Her, Ro and WeightWatchers, to increase access of these medications to patients.[33, 34] Eli Lilly, for example, launched LillyDirect, to Support home delivery of its drugs including ZEPBOUND™ with direct discounts to patients.[35]

Payer Perspectives

How impactful do you perceive the trend of increased market withdrawals due to low reimbursement opportunity in 2023?

Rating:
1 = Hardly any impact
10 = A dominating force

U.S. Payer Perception of Impact:

5/10

Ex-U.S. Payer Perception of Impact:

6/10

The rapidly increasing demand for weight loss medications emerged as a key, unexpected budget impact in 2023, with 41% of payers surveyed highlighting MOUNJARO™, WEGOVY® and other GLP-1 products as the most significant anticipated budget impact over the next 5-10 years. Many U.S. payers noted the use of obesity riders, which is when coverage is on an opt-in basis with an associated premium, as a method of managing the budget impact of these therapies.

> The rare disease space and the ultra high-cost agents are prominent, but what is really new in 2023 is the weight loss drug dynamic and incorporating it into benefit plans.
>
> **U.S. National MCO Payer Medical Director**

> Looking ahead to 2024, one trend that I anticipate changing my work as a payer is the increasing utilization of incretin mimetics for weight loss.
>
> **U.S. Regional MCO Payer Clinical Pharmacist**

> BMI management so far has been considered a lifestyle issue. The GBA is exploring use of broader programs to manage obesity. Yet, the outcome of the analysis remains unknown so far, and budgetary considerations are likely to play a substantial role in the decision forthcoming.
>
> **Ex-German Payer GKV**

Payer Perspectives

With anticipated widespread usage of weight loss therapies such as WEGOVY, ZEPBOUND, MOUNJARO and OZEMPIC®, how impactful do you perceive the weight management space on budget impact?

Rating:
1 = Hardly any impact
10 = High impact

U.S. Payer Perception of Impact:

8/10

Ex-U.S. Payer Perception of Impact:

6/10

In Germany, two particularly impactful pricing changes resulted from Germany's Financial Stabilization Act (GKV-FinStG; passed in early 2023). The law specifies a 20% discount applied to combination products unless they are able to achieve the highest two categories of additional benefit and an increase in the mandatory manufacturer rebate from 7% to 12%.[36, 37, 38] The 20% discount has the potential to impact a much broader list of combination therapies than originally anticipated, with Germany publishing a list of 56 possible combination therapies (see combinations section for more details).[39]

> "There is increased focus on pricing, with evidence requirements becoming stricter for the orphan drug space. In the past a high price can be achieved with a non-quantifiable benefit rating or no added benefit but this is no longer possible now."
>
> **Ex-German Payer**
> **GKV**

In March 2023, Bristol Myers Squibb decided not to launch OPDUALAG™, a combination therapy consisting of nivolumab and the novel antibody relatlimab, despite European approval in September 2022, citing the recent GKV-FinSTG reforms.[40] Bristol Myers Squibb was not the only company to withdraw from the German market in 2023. In August, Boehringer Ingelheim discontinued the sale of SPEVIGO®, a treatment for flares in generalized pustular psoriasis (GPP), upon receiving a no additional benefit decision.[41] SPEVIGO had received its conditional marketing authorization from the EMA just six months prior. Similarly, in September, Novartis removed TABRECTA®, a therapy for non-small cell lung cancer, after being unable to reach an agreement with GKV-Spitzenverband for a rebated price.[42] Meanwhile, Gilead elected to bypass the German market altogether with the HIV therapy SUNLENCA®, noting "the great clinical benefit that the product offers patients will not be reflected in a corresponding assessment in the AMNOG process."[43]

A survey conducted on the impact of the Statutory Health Insurance Finance Stabilization Act (SHIFSA) of 2022 further found that 21 companies have decided to delay or avoid launching new drugs/indications in Germany as a consequence of the measures contained within the Statutory Health Insurance Finance Stabilisation Act (SHIFSA).[44] SHIFSA enacted amendments to the drug pricing and reimbursement laws with the Act on the Financial Stabilization of the Statutory Health Insurance System including the modification of AMNOG rebate negotiations (refer to The German Financial Stabilization of Statutory Health Insurance System Act blog for more detail). Although withdrawals and delays increased following

Further Reading

The German Financial Stabilization of Statutory Health Insurance System Act

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the passage of the SHIFSA, the impact is also observable in a decrease in market launches versus prior years. In an assessment of the SHIFSA's impact, the Verband Forschender Arzneimittelhersteller (VFA) concluded that in the first half of 2023, the availability rate for drugs approved in 2022 was 10% below the average for those approved in Germany in the years leading up to 2022 (88.1%).[45] Further, by mid-August 2023, only 20 new drugs were launched in Germany, which was 14.5% fewer than the previous five years through the same time period.[45]

To further increase patient access, affordability and availability of new therapies, the EU recommended the "Pharmapackage" policy on April 26, 2023 – though this is currently still being debated and has not been voted into policy to date. The new package policy would decrease the 8-year loss of exclusivity (LoE) for new therapies to 6 years unless the manufacturer launches in all EU markets within 2 years of EMA approval.

Overall given the potentially lower reimbursement opportunity in markets such as Germany, the U.S., and the UK, companies may benefit from diversifying their to-market strategies by also considering growth in other markets, potentially including those within the Middle East and Asia. These trends may also further result in a change in strategy within Europe itself from targeting a few larger markets to focusing on initial entrance into multiple traditionally less-prioritized countries. A few companies have already begun instituting this change, such as Bayer who cites recent policies in Germany and the UK as cause for the shift in their focus away from these "innovation unfriendly" countries towards the United States and China.[46]

Strategic Implications

Having a clear understanding of potential pricing and reimbursement hurdles early on and developing a robust mitigation strategy to ensure the right evidence is available at time of approval is critical for successful market entry across global markets.

Exploration of New Regulatory Pathways Beyond the FDA and EMA

Countries of Relevance: Global

In 2023, ex-U.S. and ex-EU countries expressed a desire to increase sovereignty in their regulatory decision making and to move away from reliance on foreign regulatory authorities, such as the EMA and FDA. In one study of LATAM regulatory agencies and their reliance on external authorization bodies, 13 out of 27 regulatory agencies (representing Argentina, Colombia, Costa Rica, Dominican Republic, Ecuador, El Salvador, Guatemala, Mexico, Panama, Paraguay, Peru and Uruguay) were found to directly recognize or abbreviate the marketing authorization process based on prior approval by an agency from either the U.S. or EU jurisdictions.[47] Regulators in Mexico, Colombia and Cuba affirmed plans to create a new Latin America and Caribbean Medicines Agency.[48] This decision was driven by a desire to increase access to innovative medicines through a more centralized authorization process across Latin American markets. These integration efforts are also reflected within HTA processes across Latin America, where although countries remain at different stages of developing HTA expertise and integration, there is overall increasing focus on the development of joint HTA agencies in Latin America.[49] Similarly within the Middle East and North Africa region, a drive towards localization of pharmaceutical manufacturing has been accompanied by policy incentives such as quicker approval and registration, easier licensing, and better pricing both for generics and branded products locally produced.[50]

As some countries may be moving away from foreign regulatory agencies, others have instead opted to work more collaboratively with foreign regulatory agencies. Several countries have formed partnerships with the U.S. to facilitate patient access to innovative cancer therapies and these efforts have proven effective on a global scale (see Collaborative HTA section for further cross-country collaborations). Beginning in 2019, the FDA Oncology Center of Excellence (OCE) launched Project Orbis in partnership with international counterparts, including Canada's HC, Brazil's Anvisa, Israel's MoH, Singapore's HAS, Switzerland Swissmedic and UK's MHRA. Project Orbis created a framework establishing concurrent submission and review of oncology products.

Payer Perspectives

How impactful do you perceive the trend of movement towards regulatory and assessment processes and collaboration beyond the FDA and EMA in 2023?

Rating:
1 = Hardly any impact
10 = A dominating force

UK Payer Perception of Impact:

7/10

LATAM Payer Perception of Impact:

7/10

APAC Payer Perception of Impact:

6/10

MENA Payer Perception of Impact:

8/10

Understanding the role and requirements of HTA collaborations will be critical in future global launch strategies.

Since Orbis' inception, regulatory health authorities (RHAs), project Orbis partners (POPs), and manufacturers have achieved faster marketing authorization for new products and have reduced duplicative Information Requests (IRs). For instance, five evaluations conducted via Project Orbis were approved by the TGA (AUS) with a median time of 68 days, compared to a median time of 330 days for new active substances under the TGA Standard Pathway.[51, 52, 53]

Despite successes with Project Orbis, the workload, resource requirements and logistical coordination required have been a challenge for partnering countries and have dissuaded other countries from participating. Nevertheless, POPs and the FDA expect to continue their partnerships in the future with modifications, including improving collaboration and expanding to other regulatory applications (e.g., diagnostic devices, cell and gene therapy products).[51, 52, 53]

The development of new collaborative regulatory pathways may lead to the need for increased engagement and go-to-market opportunities in regions outside of the U.S. and EU.

IRA Changing the P&MA Landscape

Countries of Relevance: United States

The Inflation Reduction Act (IRA) of 2022 was a key market event last year, which included long-awaited changes to drug price regulation in the U.S. in addition to other key policy changes. The landmark federal law aimed to curb inflation and contained several rules relevant to innovative medicines. Initial impacts realized in 2022 included speculation on which products would be subject to negotiations by the Centers for Medicare & Medicaid Services (CMS) and establish a maximum fair price (MFP).[54] 2023 has moved speculation into fruition as CMS selected the initial ten therapies to undergo negotiations, introduced legal action by multiple manufacturers, all while the "march in rights" case has demonstrated alternative avenues for cost reductions in the American biopharmaceutical market.

Throughout 2023 the IRA has been surrounded by controversy, as numerous lawsuits regarding the constitutionality of its Drug Price Negotiation Program were filed in the past year by manufacturers including Novartis, AstraZeneca, Boehringer Ingelheim and Bristol Meyers Squibb.[55] Some manufacturers, however, have since withdrawn from the lawsuit. Astellas, for example, withdrew their IRA lawsuit once their product, XTANDI®, did not make inclusion among the ten therapies on CMS' price negotiation list. Without a product targeted for negotiation, Astellas lacked standing to claim they would be negatively impacted by the new policy.[56] While the other companies who have lobbied against the program have at least one product on CMS' price negotiation list, manufacturers clearly aim to mitigate impacts the policy may have on revenue. Other outcomes from manufacturers' lawsuits remain to be seen, but in the interim the pharmaceutical industry has begun adjusting to the new policy.

Payer Perspectives

How impactful do you perceive the Inflation Reduction Act to be in 2023?

Rating:
1 = Hardly any impact
10 = High impact

U.S. Payer Perception of Impact:

8/10

Apart from the IRA policies resulting in additional governmental pressures on pharmaceutical pricing, another government response includes the threatened use of a "march-in rights" based on the Bayh-Dole Act of 1980, which would enable the government to grant third party licenses for products developed using federal funds if the original patent holder does not make them available to the public on "reasonable terms."[101] This compulsory licensing proposal intends to lower pricing through introduced competition and was included in a draft proposal released by the Biden Administration in early December.

> With the IRA reducing members' max out of pocket (from 80% to 30%), yet not providing additional funding to cover catastrophic costs, there are very significant cost pressures on health plans and expenditures that we did not anticipate 4-5 years ago. Looking ahead to 2024, we are implementing changes to accommodate the impact of the IRA.
>
> **U.S. National MCO Payer Pharmacy Director**

Unsurprisingly, the ten medications CMS chose for its first round of negotiations focus on some of the most common and expensive disease areas for Medicare patients such as diabetes and heart disease.[57, 58] Additionally, the blockbuster arthritis/psoriasis agents STELARA® and ENBREL® were chosen for negotiation, yet surprisingly IMBRUVICA® represents the only common oncology treatment on the list.[57] Further, IMBRUVICA is generally prescribed to treat blood cancer rather than one of the more common oncology indications like breast, lung or prostate.[59] The precise algorithm CMS employed to determine which therapies would kick off negotiations remains unclear, nevertheless, beyond analyzing which therapies are likely to be chosen for negotiation with CMS, manufacturers have begun analyzing the direct impacts of being selected.

Now that initial impacts have been analyzed by key stakeholders, discussion of indirect impacts has begun including decreased manufacturer incentives to pursue drug development in certain therapeutic areas as well as disincentivizing additional evidence generation. In addition to the MFP negotiation process, the IRA includes an inflation rebate provision forcing manufacturers to pay a rebate to CMS if their price (Average Sales Price (ASP) for Part B drugs but Average Manufacturer Price (AMP) for Part D drugs) increases faster than inflation. Critics point to a flaw in this methodology which assumes that the value of a drug is static, when in reality it fluctuates over time as additional efficacy and safety data is generated by the manufacturer after launch. While critics concede price increases in the past have not fully accounted for value fluctuations of a therapy, the new policy also makes manufacturers less flexible when determining the launch price of new therapies because their ability to negotiate up the price as additional evidence is generated is diminished.[60]

Further Reading

The Implementation Game: The Inflation Reduction Act Medicare Drug Price Negotiation Program Guidance

Read Now >

Strategic Implications

Based on ongoing lawsuits with biopharma manufacturers, IRA rules may evolve, especially as relevant new programs, such as the Medicare Drug Price Negotiation program, move forward with the first set of manufacturers.

Additionally, manufacturers have begun limiting development of pipeline products in therapeutic areas that will be subject to negotiation with CMS (i.e., most drugs launched in the U.S.). Eli Lilly CEO David Ricks notes that the company has deprioritized multiple drugs as a result of the new drug negotiation program and further mentions that the 9 years of protection for small molecules before they are subject to negotiations compared to the 13 years of protection received by biologics reduces interest in developing potentially beneficial small molecule drugs.[61] Extending beyond product development, the long-term price limits introduced by the IRA via the Medicare Drug Price Negotiation program may affect global launch strategy paradigm by decreasing a price-based incentive to launch in the U.S. ahead of other nations due to limited years of free pricing for future blockbuster therapies. Despite these policies, the U.S. will likely still remain a critical area of focus in global launch strategies.

Looking to the future, patent litigation strategies may evolve based on price negotiation regulations in the IRA because single-source therapies are at risk of being selected for price negotiation with CMS. Given risk of selection for price negotiation with CMS, patent holders may have financial incentives to facilitate entry of competitors' generic or biosimilar entry. As a result, triumphing in patent infringement lawsuits against a competitor may be less valuable than it has been in the past and further cooperation between patent holders and competitors may prove to be more financially beneficial.[62] Biologics typically have a 12-year exclusivity period and the new IRA regulation mandates that biologics are eligible for price negotiation after 11 years on the market with negotiated fair prices impacting the market after 13 years on the market. As such, high selling biologics may become eligible for price negotiations before biosimilar competitors are able to launch.

Since the launch of a biosimilar protects manufacturers from price negotiations, manufacturers may be less incentivized to stave off biosimilar launch. Importantly, the likelihood of this strategy's implementation will depend heavily on the percentage discounts announced for the first round of negotiated products anticipated for the spring of 2024. If discounts trend toward the lower end (e.g., 25%) the financial incentive to support a generic may be too weak, but if heavy discounts (e.g., 50%) are instituted the strategy becomes more likely. While additional levers and economics in settling patent infringement lawsuits remain at play (e.g., antitrust and consumer protection laws, limits on biosimilar sales in a given time period), as manufacturers assess the impacts of CMS negotiations, biosimilar launches may emerge as the lesser of two evils[63] (see section on biosimilars for more).

Strategic Implications

The creation of long-term price limits for mature therapies prior to loss of exclusivity via the Medicare Drug Price Negotiation program adds an additional consideration for global launch strategies within the U.S.

Patent litigation strategies may become more cooperative between patent holders and competition.

Spread of Collaborative HTAs

Countries of Relevance: Ex-U.S.

Health technology assessments (HTAs) remain the key regulatory process to inform the funding of new medicines in Europe, and a positive HTA evaluation is essential for successful access and reimbursement. Europe is pushing for increased HTA collaboration across countries to promote transparency/objectivity and streamline drug review. A new pan-European HTA regulation established in January 2022 will require member states to give "due consideration" to joint clinical assessment (JCA) reports within their national HTA assessments starting in 2025. Currently, the framework for JCA is projected to be finalized in 2024 with a potential launch in 2025; JCA will initially focus on new cancer drugs and advanced therapeutic medicinal products (ATMPs).[64] In 2028, orphan drugs will be incorporated, followed by all other drugs by 2030.[64] Although JCA will not come into effect until January 2025, discussions of the implementation and implications of JCA were a hot topic in a variety of stakeholder forums given publication of the first JCA report by EUnetHTA 21 in June of 2023[65]

> "At least for a transition phase, introducing EU-HTA and linking it to national decision making may mean an increase of bureaucratic requirements and value concepts as compared to the current, primarily national market access perspective."
>
> **Ex-German Payer GKV**

Overall, despite high confidence in the parameters and evaluation criteria within the JCA, payers still expect their countries to conduct their own supplemental clinical assessments. However, rather than create redundancies in work, most payers foresee the JCA inputs feeding into/enhancing their country-specific evaluations. Payers broadly expect some initial adoption as they develop increased understanding of the JCA's clinical assessment of new products versus their own assessment mechanisms and methodologies (e.g., countries may initially repeat full assessments to understand the differences that exist). While acknowledging early challenges, German payers notably have expressed optimism for the relatively seamless integration of the JCA (likely due to the match in both local clinical priorities plus high confidence in JCA parameters).

Payer Perspectives

How impactful do you perceive the trend of collaborative HTAs in 2023?

Rating:
1 = Hardly any impact
10 = A dominating force

Ex-U.S. Payer Perception of Impact:

6/10

Further Reading

Implications of the Implementation of the Joint Committee Assessment on Launch Planning for Medical Technologies in Europe

Read Now >

> We are waiting for the impact of the JCAs, which we foresee as leading to the initiation of relative effectiveness evaluations with the identification of a PICO at the European level.
>
> **Ex-Italy Payer**
> **Hospital HTA Executive**

Once fully implemented, a successful, standardized European HTA process through the JCA could enable high quality, rapid clinical assessment of new pharmaceuticals and an easier regulatory process for manufacturers looking to launch new products in Europe. However, payers and manufacturers have expressed some skepticism around the number of standardized research questions, formerly categorized under PICOs (Population Intervention, Comparator, Outcomes), that must be addressed in dossier submissions for new products. EUnetHTA 21 has outlined an approach to consolidate the EU PICOs based on those from member states, with the goal being to use the lowest number of PICOs possible that still represent all member states' PICOs.[66] However, even with this approach, test product cases demonstrate that double digit numbers of PICOs will likely be required for new products. The new process will be further tested and refined prior to implementation in January 2025.

Although payers acknowledge that collaborative clinical assessments have the potential to increase efficiency through a streamlined process and increase the consistency of decision-making across geographies, they also note key challenges to be navigating differences in standard of care and methodological approaches across countries and the coordination of data integration.

> The benefits to joint clinical assessments include efficient management of information and its distribution; it prevents redundancy in work. However, clinical assessment also subsequently entails an incorporation into the health system, posing a problem given national and regional decisions cannot be shared. Before making any decisions [to join the JCA], countries will consider their economic resources and particular organizations.
>
> **Ex-Spain Payer**
> **Advisor**

APAC

Multiple countries in Asia are in the early stages of establishing HTA assessments. To aid in the establishment of a more cohesive HTA system, The Association of South-East Asian Nations (ASEAN) launched the ASEAN HTA Harmonization Project[67] to harmonize the HTA process and standards among the ASEAN Member States (AMS). The Harmonization project is intended to assist countries in addressing gaps in their HTA systems through joint assessments and regional databases for knowledge management and information exchange activities.[68, 69] Given some countries in ASEAN do not currently have a dedicated HTA body but are already performing HTA-related assessments, inter-regional collaboration is expected to be beneficial although challenges may remain at the local and inter-regional level (e.g., coordination, funding).[67, 69]

LATAM (Latin America)

While the JCA was a frequent topic of discussion, there were other collaborative efforts in development. In Latin America and the Caribbeans, 2023 marked the early stages of a new partnership similar to the European Medicines Agency (EMA). Mexico, Colombia and Cuba announced plans to create a new Latin American and Caribbean Medicines Agency, with the aim of improving access to innovative medicines through the development of aligned regulatory processes.[48] Since the initial announcement, other well-established regulatory agencies, such as Brazil's Anvisa and Argentina's Anmat,[48] have bought into the partnership, further solidifying the concept of a LATAM Medicines Agency.[70] Ultimately, a harmonized LATAM Medicines Agency would reduce regulatory burden on manufacturers while making it easier to bring products to market.

Notably, LATAM countries have previously engaged in partnership with NICE dating back to 2019. NICE has delivered tailored support to LATAM nations to fill gaps in knowledge on health technology assessments (e.g., via workshops in Brazil, Colombia, Mexico and Panama).[71] Given the EU's well-established HTA bodies and NICE's involvement in South America, there is likely to be pressure to model the LATAM Medicines Agency's administrative structures after the EMA. Given the long road to achieve a JCA, such an occurrence can be expected if LATAM follows the European model.[48, 71]

Further Reading

Beyond the Price Tag: Understanding Colombia's New Pricing Policy

Read Now >

Strategic Implications

Incentivized HTA collaboration across partnering nations for a more streamlined evaluation process can address gaps/limitations in countries with less equipped HTA bodies and ultimately assist manufacturers in getting their products on the market more quickly.

Additional Highlights of 2023

Growth in Branded Combination Therapies

The number of combination therapies coming to market continued to increase in 2023.[72] Manufacturers highly value the benefits of Targeted Combination Therapies (TCTs), especially in oncology*, given the potential for synergistic effects versus a single, standalone therapy.[73] In combination, products are sometimes further administered in lower concentrations, ultimately reducing, or delaying the development of drug resistance compared to monotherapy.[74] However, reimbursement considerations have limited the overall access of patients to combination therapies, resulting in new policies such as those from the Competition and Markets Authority (CMA) in the UK that have incentivized manufacturers to work closely with reimbursement bodies.

**Currently, TCTs are used in a number of tumor types, including immunotherapy and tyrosine kinase inhibitors in melanoma (BRAF/MEK) and NSCLC (EGFR and ALK-TKIs).*

> "The use of multiple drugs to treat one condition (i.e., combination therapy) is becoming more and more common, and is especially prevalent in the oncology space."
>
> **U.S. Regional MCO Payer Pharmacy Director**

The Pricing & Reimbursement process (P&R) of pharmaceutical products has historically been tailored for monotherapies. For combinations, one of the therapies is usually registered first and is considered the "backbone" while the remaining products are "add-on therapies."[75] While this may not be an issue when combinations are made by a common manufacturer, budgetary negotiation and legal challenges arise when this is not the case.[75, 76] When combinations include medications from different manufacturers, the add-on therapy may be incapable of generating a price proportional to its incremental benefit; therefore, it is unlikely to reach a price that accurately reflects a therapy's value.[75, 76, 77] As for the backbone therapy, if it is expected to be under patent protection for many years, then its manufacturer is unlikely to be incentivized to moderate its pricing.[75, 76] The adaptive nature of the P&R in addition to legal challenges between manufacturers regarding competition law complicate price negotiations (i.e., laws forbid manufacturers from participating in joint price negotiations) while inadvertently restricting patient access to TCTs.[75, 76, 77] Mechanisms expected to

be enforced in upcoming years involving partnership with stakeholder groups (e.g., academia, clinical and patient communities, HTA bodies, Minitsty of Health) have therefore been proposed to enable companies to lawfully negotiate prices with each other for the benefit of patient outcomes.[78, 79] This promotion of joint development of combination therapies has been further reinforced by a press release in early November 2023 by UK's Competition and Markets Authority (CMA) clarifying that "certain types of engagements between competing drug firms working on 'combination therapies' will not be prioritized for investigation."[80] Encouragement of collaboration across manufacturers is thus expected to increase the development of combination therapies.

> "There is significantly more pressure on reducing pharmacy spend in 2023 compared to other years. We are especially experiencing challenges with the budget impact of high-cost oncology combination regimens."
>
> **U.S. National MCO Payer Pharmacy Director**

Policies & the Future of Combination Therapies

To address the issues that arise when assessing the value of combination therapies in the P&R, future policies may enable manufacturers to work closely with HTA bodies to ensure compatibility of methodology and processes; this would be done while adhering to cost-effectiveness thresholds to validate combinations' economic value. Takeda Pharmaceuticals, in partnership with NICE and NHS England, designed a framework to improve patient access to combinations. The framework revealed that the entities will refrain from changing/introducing steps to accommodate combinations. Instead, regulations with respect to competition laws may be relaxed to enable exchange of pricing and/or other sensitive information between competing manufacturers.[76, 81] Further, in a recent announcement in the UK from the Competition and Markets Authority (CMA) pharmaceutical companies may now not receive enforcement action when implementing a specific 'negotiation framework' to make more combination therapies available on the National Health Service (NHS) if certain market conditions are met.[82]

Trinity Life Sciences asked payers to rank the list in the figure to the right of therapeutic areas in terms of their priority to their respective organizations as well as budget impact and organizational focus over the past year. Results remained consistent with that of 2022, indicating a similar prioritization globally in terms of therapeutic area. Across both U.S. and ex-U.S. markets, payers cited oncology as the top therapeutic area in 2023. Other top ranking therapeutic areas of the year included cardiology, autoimmune, neurology and rheumatology.

Ranking of Therapeutic Areas by Priority to Payers

U.S. Payer Ranking

Most Budget Impact/Key Organizational Focus Area

- » Oncology
- » Autoimmune
- » Rheumatology
- » Endocrinology
- » Dermatology
- » Respiratory
- » Cardiovascular
- » Neurological
- » Gastroenterology
- » Ophthalmology
- » Urology

Least Budget Impact/Non-Priority Organizational Focus Area

Ex-US Payer Ranking

- » Oncology
- » Autoimmune
- » Cardiovascular
- » Neurological
- » Endocrinology
- » Rheumatology
- » Respiratory
- » Gastroenterology
- » Dermatology
- » Ophthalmology
- » Respiratory
- » Urology

Continued Increase in Biosimilar Uptake

Given the increasing number of patents expiring for biological products, biosimilars have continued to emerge across global markets. In 2023, the impact of biosimilar-friendly government policies became more apparent. For example, the 2022 IRA dictates that, for the first five years after enactment, biosimilars will be reimbursed to physicians at a rate of ASP +8% as opposed to the previous rate of ASP +6%.[83] Unsurprisingly, with this policy incentive and increased patent expiries, as of early February 2023, biosimilar-related (Intellectual Property Rights (IPRs) reached a total of 144, encompassing 70 patents and 14 reference products.[84] Biosimilars for AbbVie's blockbuster rheumatoid arthritis treatment HUMIRA (adalimumab) entered the market in 2023. Amgen's AMJEVITA™ (adalimumab-atto) launched in January 2023 and was the first of many HUMIRA® (adalimumab) biosimilars to launch. Celltrion's YUFLYMA® (adalimumab-aaty), which launched in July 2023, was the ninth adalimumab biosimilar to come onto the market. Similarly, six biosimilars are available for NEULASTA® (pegfilgrastim) and five biosimilars are available for HERCEPTIN® (trastuzumab). With increased competition in therapeutic areas with biosimilar availability, these highly competitive markets will require monitoring to understand the future impact on branded biologics and their emerging biosimilars. However, despite these increases in biosimilars, biosimilars currently compete with just 14% of biologics.[85]

> "Containment of health expenditure (i.e., setting a stable % of GDP) means that it is necessary to promote the use of biosimilars and leverage regional and hospital directives to promote or prioritize these more cost-effective options."
>
> **Ex-Spain Payer Advisor**

Additionally, despite increased incentives, biosimilar launches (even for blockbuster biologics) may still face challenges in relation to contracts with the original branded manufacturer. This may explain for the slight decrease in FDA biosimilar approvals witnessed in 2023 compared to the steady increase in 2020-2022.[86] For example, patents for Johnson & Johnson's STELARA®, the company's top-selling product since 2019, began to expire this year, opening the door to biosimilar launches in the U.S. market.[87] Among the anticipated biosimilars was Amgen's WEZLANA™, but despite approval from the FDA, WEZLANA will not be launched any sooner than January 1, 2025.[88] The delay results from a confidential settlement between

FDA Biosimilar Approvals 2023 vs. 2022[86]

FEBRUARY 2022
Biosimilar name: RELEUKO®
Reference product: NEUPOGEN

APRIL 2022
Biosimilar name: ALYMSYS®
Reference product: AVASTIN®

MAY 2022
Biosimilar name: FYLNETRA®
Reference product: NEULASTA®

AUGUST 2022
Biosimilar name: CIMERLI®
Reference product: LUCENTIS®

SEPTEMBER 2022
Biosimilar name: STIMUFEND®
Reference product: NEULASTA®

SEPTEMBER 2022
Biosimilar name: VEGZELMA®
Reference product: AVASTIN®

DECEMBER 2022
Biosimilar name: IDACIO®
Reference product: HUMIRA®

MAY 2023
Biosimilar name: YUFLYMA®
Reference product: HUMIRA®

AUGUST 2023
Biosimilar name: TYRUKO®
Reference product: TYSABRI®

SEPTEMBER 2023
Biosimilar name: TOFIDENCE™
Reference product: ACTEMRA®

OCTOBER 2023
Biosimilar name: WEZLANA™
Reference product: STELARA®

DECEMBER 2023
Biosimilar name: AVZIVI®
Reference product: AVASTIN®

Amgen and Johnson & Johnson,[89] highlighting that regulatory approval alone may not be sufficient to drive rapid biosimilar access following patent expiry. Eventual revisiting of patent law structure may be required to ensure rapid access to biosimilar drugs.

As healthcare systems continue to champion biosimilar approval and uptake to maximize cost-effectiveness and minimize budget impact, there is a need to consider incentives to biosimilar development. The FDA and other regulatory bodies have continued to seek methods to streamline the approval process for biosimilars. As the process becomes increasingly streamlined, incentives may increase among competing manufacturers to quickly develop biosimilars.[90] The size of the biosimilar market is expected to continue to grow at a compound annual growth rate of around 13%, emphasizing the substantial impact that biosimilars will continue to have.[91]

> "Our organization is facing a reclassification of covered entity type for 340b with loss of eligibility for medications where orphan drug exclusion (ODE) applies. We are assessing all biosimilars as we believe the biosimilars are less likely to have an ODE and therefore would still be eligible for 340B replenishment."
>
> **U.S. Regional MCO Payer**
> **Hospital Pharmacy Director**

Increased Drug Shortages

By end of 2023, 410 drugs had faced ongoing shortages within the U.S., the highest number in nearly a decade.[92, 93]Over 80% of ongoing shortages are of existing generics, more than 15 of these drugs being generic formulations of cancer drugs, including fludarabine (commonly used as part of CAR-T therapy as well as a part of conditioning regimen for allogenic hematopoietic stem cell transplant and cisplatin), carboplatin and methotrexate (common chemotherapy drugs.)[94, 95] Resulting from a combination of supply chain gaps including decreased supply due to product discontinuations, manufacturing delays and demand spikes, these shortages have had a negative impact in terms of care disruption for patients and increased labor costs to mitigate such disruptions. With the IRA introducing a program mandating a 25-60% discount for top-selling drugs that have been without generic or biosimilar competition, general price erosion consequences may further exacerbate such shortages.

In acknowledgement of these ongoing shortages, a press release by the White House highlighted that the FDA had been working to address emerging issues through working with manufacturers to identify opportunities for increasing manufacturing capacity as well as importing therapies from countries such as China.[96, 97] Beyond the clinical consequences of these shortages, however, these shortages may further have unintended impacts on payer management decisions. The effects of these shortages will be critical to understand as they continue into 2024.

Looking Ahead

Increased Exploration of Artificial Intelligence and its Applications

The application of artificial intelligence (AI) has been steadily growing in 2023, with the AI market anticipated to continue growing at a rate of CAGR of 38.1% between 2022 to 2030.[98] In a global survey on AI conducted by McKinsey & Company in April 2023, 16% of respondents within the pharmaceutical industry noted current use of AI at work.[99] However, slow implementation of AI has been a result both of lack of knowledge around the technology and concerns over data privacy and other related implications of AI use. Generative AI has the potential to transform the way pharma conducts HEOR and Market Access research through its ability to analyze and summarize large amounts of data, extract insights, and provide institutional memory to new team members. TGaS Advisors, a Division of Trinity Life Sciences, is conducting a longitudinal study with

Payer Perspectives

Please assess on a scale of 1-10, the anticipated use of AI technology to facilitate your coverage access decision making in the next few years.

Rating:
1 = Not being used at all
10 = Always used

U.S. Payer Perception of Impact:

5/10

Ex-US Payer Perception of Impact:

5/10

Further Reading

Priced Out: Generic Therapy Price Competition and Drug Shortages

Read Now >

> We have a team trying to work with automated PA process, build into physicians' records, and extract previous treatments with different drugs. I thought we'd be way ahead of where we are 10 years, but I think AI offers a huge opportunity but for whatever reason has not yet succeeded.
>
> **U.S. National MCO Payer Medical Director**

pharmaceutical leaders to gather insights on their current awareness, perceptions and use of Generative AI. According to this study, specific applications in the HEOR and Market Access space include developing content for dossiers and product value messaging, summarizing and synthesizing HTA decisions, developing access rationales, and predicting access outcomes.

> We anticipate that for pharmacological or clinical advice, artificial intelligence will help and facilitate the work.
>
> **Ex-Spain Payer Advisor**

Although utilization of AI for HEOR and Market Access research is still in its infancy, U.S. payers surveyed in this report express openness to the potential leveraging of AI for reimbursement approvals based on qualifying prior authorization criteria and highlight that other AI applications are already being explored at their institutions. Despite a high willingness to adopt AI, however, payers underscored their hesitancy around AI's use for automating denials, which they wished to review manually in order to ensure accurate coverage decisionsThis concern was especially pertinent in light of a recent federal class action lawsuit against Cigna for their use of AI in automating denials in July 2023. Cigna's PxDx (i.e., procedure-to-diagnosis) system was used to refuse around 300,000 pre-approved claims over a two-month period in 2022 after allegedly only 1.2 seconds spent on average looking at each claim.[100] Thus, despite early exploration of AI at plans, AI is still unlikely to see widespread use within the field due to remaining logistical and legal considerations. As for ex-U.S. countries, particularly in Germany, the use of AI to facilitate the assessment and pricing of drugs over the long-term (e.g., by calculating p-values and hazard ratios) was mentioned as an area for potential AI application.

Conclusion

Evolution of the pricing and market access landscape, especially as related to cost containment policies alongside other trends outlined within this white paper, should play a key role in informing strategies for bringing new innovative technologies to market in the following year.

- New drug modalities and combination therapies are anticipated to continue increasing in the coming years due to increased reimbursement policy incentives and continued innovation within the Cell and Gene Therapy space.

- Continued need for thoughtful evidence generation to support strategic pricing, access and reimbursement will remain critical as payers continue to acknowledge its importance in their decision-making.

- Resource allocation strategies for product launches should increasingly focus on protecting value within EU and U.S. markets while opportunistically seeking growth opportunities beyond these markets given new cost containment policies.

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The pharma-biotech landscape is rapidly evolving, creating a range of challenges for manufacturers who need to generate evidence, communicate value, and optimize their products' pricing and access.

Trinity's Evidence, Value, Access and Pricing team team has unparalleled experience across geographies and therapeutic areas. We work across the product lifecycle, addressing needs at a global and local level.

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