Insight

Drug Pricing Regulation in the U.S., UK, and EU: Assessing Trade-offs

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Executive Summary

- In an effort to lower drug costs, the Inflation Reduction Act requires the Centers for Medicare & Medicaid Services to negotiate directly with drug manufacturers on specific products to reduce Medicare Part D reimbursement; a recent study found that these provisions are likely to significantly reduce manufacturer investment in research and development of new medicines.
- The United Kingdom and European Union member states are pursuing similar strategies to reduce spending in their procurement and reimbursement of medicines – potentially with similar problematic outcomes.
- U.S. policymakers should consider the trade-offs inherent in these strategies, among them reduced availability of new and innovative products and patient access to critical therapies, as well as potentially higher long-term costs.

Introduction

In an effort to lower drug costs, the Inflation Reduction Act (IRA) requires the Centers for Medicare & Medicaid Services (CMS) to negotiate directly with drug manufacturers on specific products to reduce Medicare Part D reimbursement; a recent study found that these provisions are likely to significantly reduce manufacturer investment in research and development (R&D) of new medicines. Most important, the expected reduction in Medicare reimbursement for certain products will likely have long-term reimbursement repercussions for manufacturers across the multi-payer U.S. market. Already, manufacturers have actively modified their investment strategies in developing new and innovative products to offset the cost of potentially being included in future IRA negotiations.

On August 29, 2023, the Department of Health and Human Services announced the first 10 drugs selected for negotiation with the negotiations expected to occur in late 2023 and early 2024. CMS must offer an initial maximum fair price for the selected drugs to the manufacturers by February 1, 2024. The negotiated prices will be effective beginning in 2026 and are expected to be below 40 to 70 percent of the average manufacturer's price. If selected manufacturers do not participate, they face two choices: a maximum 95 percent excise tax or removal of their product from government coverage in several programs including Medicare and Medicaid. At this time, most of the drugs selected are neither specialty medications (which are used to treat rare, complex, and chronic health conditions), nor do they have high out-of-pocket costs for Part D beneficiaries.[i] A University of Chicago study found that the IRA provisions will likely reduce manufacturer investment by 29 to 60 percent in R&D from 2021 to 2039, which translates into 167 to 342 fewer new drug approvals during that period.

The United Kingdom (UK) and European Union (EU) are pursuing similar strategies to reduce spending in their

procurement and reimbursement of medicines – potentially with similar problematic outcomes. The UK government is considering requiring drug manufacturers to pay significantly higher manufacturer rebates for the next five-year agreement. Under the last agreement, manufacturers paid higher than expected rebates of 15 percent in 2022 and 26.5 percent in 2023. So far, one manufacturer has pulled an anti-cancer drug from the UK market due to concerns over long-term financial sustainability. The EU has proposed new legislation that would reduce manufacturer patent exclusivity from ten to eight years. Yet if a drug manufacturer can launch a new product across all 27 EU member states within two years, it will receive back two years of patent exclusivity – a goal that would be extraordinarily difficult to meet and would likely reduce launches of new medicines.

U.S. policymakers should consider the trade-offs inherent in these strategies, among them reduced availability of new and innovative products, lower patient access to critical therapies, and potentially higher long-term costs as manufacturers shift their investments away from innovative products likely to fall under increased regulatory oversight.

United States

Regulatory Background

The IRA aims to reduce the cost of prescription drugs for seniors through two key provisions. First, the law established an out-of-pocket maximum of $2,000 a year for Medicare beneficiaries. Second, CMS will set a maximum fair price that Medicare will pay for negotiated products – yet in its first round of drug selection it chose products that are among the most commonly used rather than those with very high prices. An IQIVIA study found that under 6 million, or just 10 percent, of Medicare beneficiaries will experience drug savings, with most of them saving less than $300 a year on prescription costs.

Moreover, some have argued that the IRA incentivizes manufacturers to invest in costly biologics, typically covered under Medicare Part B, instead of small molecule drugs, typically covered under Part D, for two key reasons. The first is that biologics are exempted from negotiations for 13 years as compared to nine years for small molecule drugs. The second is that only two Part B drugs – Keytruda (pembrolizumab) and Opdivo (nivolumab) – are projected to be subject to IRA negotiation in 2028.

Key Problem: Gross Versus Net Spending

In August 2023, CMS selected the first 10 drugs based on Medicare gross spending from June 2022 through May 2023. Yet as CMS' calculation of the net price, or the actual amount paid after these concessions are applied, did not account for rebates and other discounts, these products may already be fairly priced. Moreover, most of the products selected for the first round of negotiations are not specialty or high-cost products, but rather medications used to treat diabetes or reduce the risk of blood clots. Of the 10 products selected, KFF found that "Six of the 10 selected drugs (Entresto, Eliquis, Farxiga, Januvia, Jardiance, and Xarelto) are more commonly placed on a preferred brand tier in 2023, with a median copayment of $47 per month – an out-of-pocket amount that is fixed rather than being a percentage of the drug's list price." Medicare beneficiaries already have the ability to pay for these products, as exhibited by the sheer number of prescriptions filled.[ii] Furthermore, KFF found that Part D beneficiaries pay the most out-of-pocket for nonpreferred or specialty drugs.[iii]

CMS did exclude from its calculation single-source drugs with existing brand competition or impending generic competition, as well as drugs designated as "orphan, low-spend Medicare drugs, and plasma-derived products." [iv]

Yet these limited exclusions are reducing the incentivizes for drug manufacturers to expand the number of orphan drugs that have one or more indication as well as invest in clinical trials for future products at risk of negotiation.

Outlook for the Orphan Drug Exclusion

The IRA may disincentivize manufacturers from investing in new and innovative products for medications that can be utilized by a limited population. The Food and Drug Administration (FDA) defines an orphan drug as "as a drug intended to treat a condition affecting fewer than 200,000 persons in the United States, or which will not be profitable within 7 years following approval by the FDA." Currently, the IRA exempts orphan drugs with a single approved indication.

To avoid future IRA selection, manufacturers will likely focus on single-indication orphan drugs or abandon them altogether. For example, Alnylam Pharmaceuticals did not proceed with a phase 3 clinical trial of a therapeutic treatment for Stargardt disease, a rare genetic eye condition that leads to central vision loss. Cleveland Clinic estimates that 30,000 to 200,000 people with Stargardt disease are located in the United States.

According to a 2023 study "FDA approved 282 novel orphan drugs from 2003 to 2022 [and within the same period]…the FDA approved 152 separate follow-on indications." It is likely that manufacturers will move away from investing in treatments for these smaller, less lucrative populations. This manufacturer-led reduction in investment will likely slow research into medicines for rare diseases.[v] In September 2023, Representatives John Joyce (R-PA) and Wiley Nickel (D-NC) introduced the Optimizing Research Progress Hope And New Cures (ORPHAN Cures) Act to address concerns around the IRA's impact on follow-on investment into orphan drug development.

United Kingdom

Regulatory Background

The United Kingdom is undergoing a lengthy negotiation between government and industry on the next iteration of its Voluntary Scheme for Branded Medicines Pricing and Access. This proposed scheme is expected to mandate hefty rebates in line with manufacturers' rebates provided in 2022 (15 percent) and 2023 (26.5 percent). Drug manufacturers already must sell their products at a competitive price to secure regulatory approval and inclusion on the British National Formulary. The UK has two drug pricing schemes: a voluntary program, in which the majority of manufacturers participate, and a statutory program.

Key Problem: Utilization Limitations

A recent review of the proposal highlights a key policy challenge: If branded products exceed a set growth in total sales, the manufacturer must pay an additional financial penalty.[vi] These terms were also part of the last five-year agreement. While manufacturers in the United States tend to increase their rebates or price concessions based on additional volume, manufacturers in the UK are penalized if their products experience a sudden increase over expected use.[vii] The authors highlight that "volatile and rising payment percentages create uncertainty for the pharmaceutical industry around the value that governments place on the health benefits obtained through branded medicines and the compensation that government will offer for that value." For small- and medium-sized companies, this upward pressure on future price concessions would be hard to predict, especially (as the authors note) as trends in prescribing and changes in composition can vary in high-

price classes such as oncology and immunotherapies.[viii]

Outlook for QALYs

For a drug to gain approval in the UK, the National Institute for Health and Care Excellence (NICE) must conduct a cost-effectiveness assessment. NICE uses the quality-adjusted life year (QALY) to measure the benefits of the medicines in terms of a single year of perfect health. NICE explains that QALYs are weighted based on a patient's remaining years of life based on a particular treatment or intervention. In general, interventions that cost less than "£20,000 per QALY gained are considered to be cost effective" as the current threshold ranges between £20,000 and £30,000 – with some exempted products approved with thresholds of £50,000 per QALY or more for end-of-life treatments or highly specialized technology. QALYs are notoriously controversial as recent report from the London School of Economics called for NICE to lower the QALY to £15,000.[ix] Yet, setting too low a threshold may create new restrictions or disincentivize manufacturers from pursuing new medicines or technologies.

European Union

Regulatory Background

In April 2023, the EU released draft pharmaceutical legislation.[x] The draft legislation proposes to reduce innovator manufacturer market exclusivity for new products from ten to eight years unless the manufacturer can supply new medicines across all 27 member states within two years. For manufacturers, this requirement is difficult to meet because member states must price and reimburse new medicines before they are made available in their jurisdiction. EU member states' ability to price and reimburse innovative medicines varies widely depending on the national robustness of individual health care systems. For example, the *Financial Times* reported that Germany, Austria, and Denmark had 100 new drug approvals between 2015 to 2017 that were launched by 2018, while Latvia only had 11 new medicines brought to market in that period.

Key Problem: Patent Exclusivity

The proposed reduction in patent exclusivity time as related to equitable access may disincentivize certain manufacturers for bringing new and innovative products to market.[xi] Eli Lilly's chief executive David Ricks said that under a draft plan to cut market exclusivity protection from ten to eight years, it might not be worth the industry pursuing treatments for chronic diseases or cancer trials. A recent industry report on patient wait indicators found that "For medicines that have completed the reimbursement process, early trends…suggest that about a quarter of the delays to patient availability are due to delays in company filing and the rest (75 percent) occur as the product goes through national pricing and reimbursement processes." Manufacturers may not launch a new product if they are aware that certain EU member states struggle to meet certain pricing and reimbursement deadlines.

Outlook for Access

In March 2023, European Commissioner of Health and Food Safety Stella Kyriakides stated in a speech that her focus was on "the three As – Accessibility, Availability, Affordability," when describing the aims of the draft pharmaceutical legislation. Currently the EU Transparency Directive sets a 180-day limit for which medicines should become available after pricing and reimbursement decisions – but meeting this time frame can be challenging for smaller manufacturer as well as certain member state payers. According to a 2020 industry report,

"the average time to reimbursement for innovative treatments across EU and European Economic Area countries continues to be as long as 504 days, ranging from 127 days in Germany to over 823 days in Poland." For manufacturers, the ability of specific member states to complete the pricing and reimbursement process can vary dramatically. In terms of market structures, pricing and reimbursement vary across the EU states penalizing manufacturers could reduce investment from larger firms as well as disincentivize small to mid-size manufactures as patent exclusivity is now tied to equitable access.

Conclusion

The United States, UK, and EU member states are undertaking pharmaceutical reforms to address patient access and costs without considering longer-term negative impacts from increased regulatory scrutiny. Moreover, government payers are attempting to set prices or market conditions that will ultimately reduce or delay new therapies and treatments. These regulations are likely to put pressure on the fragile global drug supply chain as small- to mid-size manufacturers reevaluate their ability to participate in specific markets for certain therapies.

Pharmaceuticals can be expensive, but setting new regulations that penalize manufacturers for factors outside their control is unlikely to create a robust and dynamic marketplace. Coupled with a decline in reimbursement from government payers, manufacturers are likely to change the composition of the products they bring to market, ultimately delaying patient access to the newest innovative therapies.

U.S. policymakers should consider the trade-offs inherent in these strategies, such as reduced availability of new and innovative products and patient access to critical therapies. These strategies could also drive up long-term costs, as manufacturers may choose to invest in developing new and costly biologics rather than cheaper small molecule drugs most at risk of future IRA negotiation.

[i] In 2023, KFF found that "In 2023, three of the 10 selected drugs – the rheumatoid arthritis drug Enbrel, the cancer drug Imbruvica, and the psoriasis drug Stelara – are placed on the specialty tier in virtually all Part D plans that cover these drug."

[ii] The first 10 products may account for a large share of total Medicare spend but are not the products patient cannot afford and typically are the preferred brand for Medicare Part D plans (or these products would not have been dispensed at such a large volume.)

[iii] Stacie B. Dusetzina, Juliette Cubanski, Leonce Nshuti et all. "Medicare Part D Plans Rarely Cover Brand-Name Drugs When Generics Are Available" Health Affairs Vol. 39, No. 8, August 2020. The authors found that 84 percent of Part D plans had generic only coverage. Significantly, the IRA will not address the types of drugs currently being abandoned by Medicare Part D beneficiaries who lack a subsidy. A 2022 Health Affairs study reviewed over 17,000 new prescription claims issued between 2012 and 2018 for Part D beneficiaries. For Part D beneficiaries, who do not receive a subsidy, the authors observed a noninitiation (which means the patient did not collect medication) for "30 percent of prescriptions written for anticancer drugs, 22 percent for hepatitis C treatments, and more than 50 percent for disease-modifying therapies for either immune system disorders or hypercholesterolemia."

[iv] CMS explains that their selection criteria for the first round as…"single source drugs – that is, drugs for which at least seven years, or biologics for which at least 11 years, have elapsed between the FDA approval or

licensure of the drug or biologic, and for which there is no generic or biosimilar competition. 2. CMS excluded certain orphan drugs, low-spend Medicare drugs, and plasma-derived products. 3. CMS determined which drugs are negotiation-eligible– that is, the 50 qualifying single source drugs with the highest gross Part D covered prescription drug costs, except for small biotech drugs. 4. The negotiation-eligible drugs were ranked according to highest total gross Part D covered prescription drug costs. 5. Finally, CMS selected from the ranked list of 50 negotiation-eligible drugs up to 10 drugs with the highest total gross Part D covered prescription drug costs, after excluding any biologics that qualified for delayed selection because CMS determined there is ahigh likelihood that a biosimilar will enter the market within a specified time."

[v] It is important to note that AstraZeneca sued the Department of Health and Human Services on the regulatory parameters around the follow-on indications for orphan drugs. It was reported that the company stated the law deters continued research and development into cancer drugs (such as Lynparza) and blood disorder drugs (such as Soloiris) which have several follow-on indications.

[vi] The current 5-year agreement also requires manufacturers pay rebates based on utilization.

[vii] In the US, manufacturers can face inflationary penalties for products under Medicare Part B and Part D as directed by the IRA. Inflationary penalties are unrelated to actual drug utilization.

[viii] On October 4, 2023 the University of Oxford and Harrington Discovery Institute at University Hospitals in Cleveland Ohio announced a first of its kind transatlantic therapeutics accelerator to advance breakthrough medicines for rare diseases. The goal of the accelerator is to deliver 40 new therapies into clinical trials in the US, UK and EU markets. The accelerator will work under a non-profit/for-profit model with an anticipated budget of $250 million. The author notes that the potential for US/UK regulatory alignment post-Brexit could be beneficial for new drug development—however, reimbursement realities under the IRA and the next iteration of VPAS could slow market penetration of these products.

[ix] In short, NICE's use of QALYs is understood through the lens of supply-side economics within a fixed budget best described as viewing "new technologies that are not cost-effective, when judged against a threshold, would displace more beneficial expenditure from existing programs, with an overall negative impact on population health." Yes, monies used within a single system can be re-allocated—but the productivity of those monies being understood as higher (or more prolific) for front-line care as compared to stabilizing a patient with a long-term chronic condition with a medication may be somewhat limited in its assessment. As noted in the study above, "little attention has been given to the costs associated with setting a threshold too low, which might include a restriction of access to cost-effective new technologies and a stifling of innovation."

[x] The two general objectives of the proposed legislation are to "guarantee a high level of public health by ensuring the quality, safety and efficacy of medicinal products for EU patients" and "harmonize the internal market for the supervision and control of medicinal products and the rights and duties incumbent upon the competent authorities of the Member States."

[xi] It is important to note that the proposed legislation would reduce the number years that a marketing authorization (MA) would have basic data protection from eight to six years. Furthermore, one legal analysis argues that "The current additional 2-year market exclusivity period remains unchanged. This is the period which runs after data protection has expired and during which a generic or biosimilar product which cross refers to the relevant product, cannot be put onto the market even if an MA has been granted. This means the total minimum exclusivity will be for 6+2 years, so 8 years of exclusivity from MA grant, compared to 10 years under the current system."