Inflation Reduction Act: Global Implications for Pricing and Reimbursement

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INTRODUCTION

- The Inflation Reduction Act (IRA) 2022, signifies a pivotal change in the United States (US) healthcare policy, profoundly impacting the pharmaceutical sector. By emphasizing the need to lower prescription drug prices and enhance access to vital medications, the IRA implements a series of cost-control measures designed to improve affordability for patients and savings for payers.[1]
- IRA not only aims to ease the financial strain on consumers but also establishes a new framework for drug pricing and reimbursement.
- The implications of the IRA are poised to extend beyond the US, influencing pharmaceutical industries in Europe and other regions as well. As the IRA reshapes the landscape of drug pricing and accessibility, its effects will likely resonate globally, prompting changes in how pharmaceutical companies operate and engage in pricing and reimbursement discussions.

OBJECTIVES

- To describe the potential direct and indirect impacts of IRA on pharmaceutical industry globally, concentrating on alterations in pricing strategies, market access, and research and development trends. We will assess how these developments might reshape the industry's approach to innovation and their potential long-term implications for drug availability and patient care. This research aims to offer meaningful insights for industry stakeholders and policymakers as they adapt to the changing landscape influenced by the IRA.
- To identify potential opportunities for pharmaceutical manufacturers concerning IRA.
- To assess future health economics and outcomes research trends for upcoming treatment options.

METHODS

- Desk research was conducted for policy analysis and to identify previous policy analyses.
- MEDLINE, and International Society for Pharmacoeconomics and Outcomes Research (ISPOR) were searched in a targeted manner to identify published literature on impacts of IRA .

RESULTS

Summary of IRA price negotiation conditions[2]

Eligibility for price negotiation	Eligibility for exclusion	Eligibility for renegotiation
Top 50 expensive Part B and Part D medicines	• Small biotech drugs (<1% of total expenditure for Medicare Part D and Part B, and >=80% of the Medicare expenditure for manufacturer) until 2028 • Products of the manufacturer are acquired after 2021 by another manufacturer or, in the case of an acquisition, before 2025.	• Selected drug (excluding vaccines) with extended-monopoly having 75% market for 11 - 16 years • Long-monopoly drugs having 65% market for at least 16 years. • Standard monopoly drugs having a 40% market.
Approved or licensed under section 505(j) or section 351(a), and not listed as the reference product for a 351(k) product or application	• Biologics that are named reference products for a product approved or under approval in the 351(k) filing • Biologics that are selected in special Social Security Plan for which 106% of the Maximum Fair Price (MFP) will be applicable for such drug and a year during such period	If a selected drug receives a new indication or there is a material change in the factors considered by the Secretary in setting the initial negotiated price.
Single source drugs post 9 years of US Food and Drug Administration (FDA) approval	• Plasma derived products • New formulations include extended-release, higher concentration and change of route of administration of a qualifying drug	A selected drug's negotiated price (or as renegotiated when applicable) will remain in place until a generic or biosimilar is launched, in which case the selected drug's MFP would terminate at the start of the first year that begins 9 months after the generic or biosimilar has entered the market
Single source biologics post 13 years of FDA approval	Drugs below expenditure of $200 million annually (total Part B and Part D)	
Drugs designated for >1 rare disease or condition	Drugs with single orphan drug designation with indication only for the same	

Timeline of price negotiation[2]

2024	2025	2026	2027	2028	2029
Removal of 5% coinsurance for Part D catastrophic coverage	Adds $2,000 out-of-pocket cap in Part D and other drug benefit changes	Negotiated price of 10 Medicare part D drugs	Negotiated price of 15 Medicare part D drugs	Negotiated price of 15 Medicare part B and D drugs	Negotiated price of 20 Medicare part B and D drugs

Impact of IRA (Figure 1)

1. Impact on research and development

The impact of IRA on research and development is yet to be determined. The views and research on this demonstrate some contradiction.

I. A 2024 model described that small companies (<$7 billion in revenue) are leading innovation by carrying out more than 50% clinical developments, originating 67% of new drugs, sponsoring 64% of late-stage clinical trials and 40%–69% of new drug approvals. The research and development (R&D) of these small companies is not driven by revenue, rather than investment, stock options and market condition unlike large companies' revenue utilization. The model analyzed three different scenarios of predicted revenue decline for large and small companies and concluded that overall, the effect of revenue decline may lead to per year 0.45 to 4.52 lesser number of drugs. Therefore, IRA was anticipated to have little to moderate effect on R&D and drug launches as the small companies continue leading clinical development.[3]

II. Another 2021 model predicted that the IRA price negotiations will cause a $663 billion reduction in private R&D spending in oncology between 2022 and 2039. This could lead to 135 fewer new cancer drug approvals. If this scenario persists, globally there would be similar effects as biologics mostly get approved and marketed in the US first.[4]

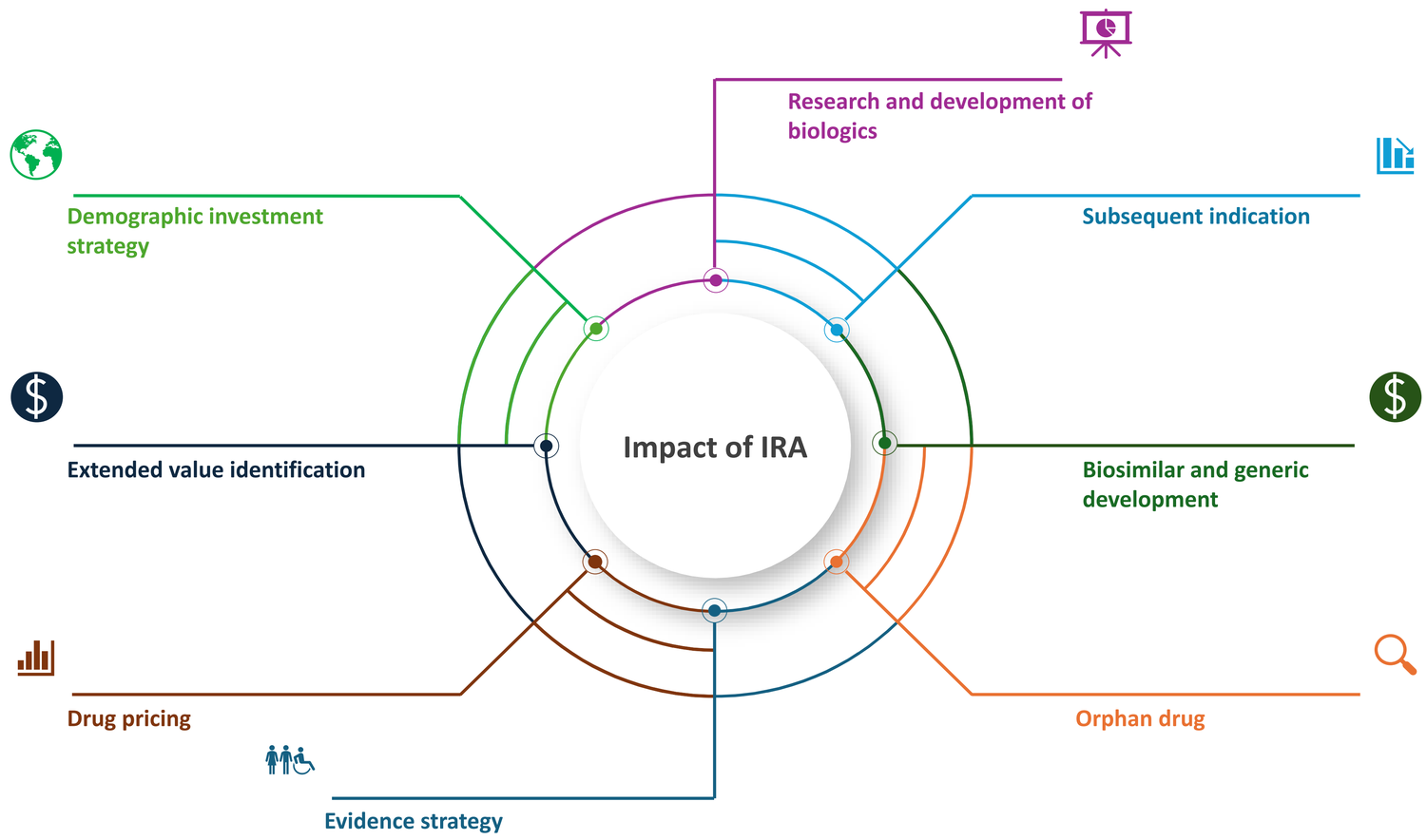
2. Impact on subsequent indication

A 2024 study reported the timeframe of approval for first subsequent indication since first approval ranges from 0.7- 5.7 years (median). Second subsequent indication 2.1-7.6 years (median) and furthermore time from third indication onwards. Close to 33% drugs were approved in their most recent indication after they would be eligible for Drug Price Negotiation Program (DPNP).

I. Launch delay: Companies may delay the first launch in case of close completion of clinical trials for second indication to delay the DPNP timeframe for maximizing value proposition. As a result, globally the availability of those drugs would get further delayed.

II. Impact on late developments: Companies may ditch late development for subsequent indication if DPNP schedule is close or would have already happened. A 2024 study reported that 78% of pediatric indications were post approval subsequent indication starting on average 4.6 years [SD:3.2] post first approval and with average duration of 4.1 years [SD:2.8]. In addition to this, 95% of post approval trials included patients aged ≥65 years. This may lead to decreased treatment options for children and the older population.[5]

Figure 1: Impacts of IRA on pharmaceutical industry



Impact of IRA *continued*..

3. Biosimilar and generic pricing in US and global impact

I. Unlike in Europe, the IRA does not restrict biosimilar and generic pricing in the US, instead, it offers incentives for biosimilars, **attracting investment in these areas**.[1]

II. The dominant strategy of blocking biosimilar product entry by originator biologics manufacturers may shift to a coexisting strategy as IRA offers a 2-year delay in negotiation in case of high likelihood of biosimilar entry. **IRA may catalyze the already growing biosimilar industry globally.**

III. However, a potential downside to this is, a highly negotiated price may dilute the value proposition of the upcoming biosimilar resulting in exit or not-launching.

IV. Increased investment in biosimilar would naturally have a positive impact on **patients' access around the world with access to effective biosimilar options**. Global pharmaceutical giants are already advancing their biosimilar businesses such as:

a. Sanofi partnered with China's JHL biotech to commercialize rituximab biosimilar in China.[7]

b. Pfizer has developed a strong portfolio of biosimilars, including biosimilar versions of **REMICADE®** (infliximab) with sales of $2.5 billion in 2022.[8]

c. Novartis prior sinning-off Sandoz generated net sales of $9.2 billion in 2022 including $4.9 billion in Europe and $1.8 billion in the US from Sandoz .[9]

4. Impact on orphan drugs

Reports have suggested that the IRA orphan drug carve-out disincentivizes secondary indications, as multiple indications would lead to loss of orphan status, making it eligible for price negotiation. It is predicted that any extra indication would have to produce a minimum of a 40% increase in revenue to offset the losses due to price negotiation.[10]

I. A 2024 article suggested that **multiple indication of orphan drug designation in same disease area may get considered by Centers for Medicare & Medicaid Services (CMS) for orphan drug exemption**. We may need to look out for **CMS's decision in 2025 price negotiation on TAGRISSO® (osimertinib) as its four indications are for specific Non-small cell lung cancer (NSCLC) mutations** and revenue is projected to cross $1.2 billion.[11]

II. As an effect in the US companies may prefer to go for **multiple indication in same disease state for orphan designation** and the **treatment may not be reimbursed for other disease indications that are approved and marketed in ex-US markets.**

5. Evidence strategy

I. The DPNP negotiation post 9-13 years of approval, gives manufacturer scope to conduct comparative effectiveness studies to demonstrate superiority than therapeutic comparators.

II. Real-world studies in large population including Medicare population may give edge to the manufacturer for effective value demonstration. As IRA does not devalue the life gain in vulnerable population, manufacturers may also consider including elderly, terminally ill, and disabled population for better value demonstration on these population subgroups. This may result into **increased inclusion of vulnerable population leading to treatment access to those patients**[12]

6. Drug pricing

I. The two-way blockade of high-priced and price increase higher than inflation rate, from IRA, may lead to **high launch prices of drugs** as manufacturers will aim for maximizing profit before price negotiation. This may cause ripple effect **to global pharmaceutical pricing with high launch prices**. The downside of this also could be, that Health technology assessment (**HTA)** agencies **may demand for additional discounts based on the already garnered profits of the drug in HTA markets**.

II. Post DPNP negotiation, Europe and other HTA markets may take reference pricing of reduced US drug prices, and **eventually reducing drug prices**.

III. Manufacturers may **hike price of generics and biosimilars to cover the impact of price negotiation on biologics.**

7. Extended value identification

I. Considering the global focus on drug price control, exploring benefits beyond the Quality adjusted life years (QALYs) may become helpful to understand the long-term values of a drug.

II. ISPOR value flower identifies non-traditional values of a drug including reduction in uncertainty, real option value, scientific spillover and etc. However, most of these values are difficult to quantify yet and not typically accepted by payers.

III. ICER acknowledges the possible merit of these values in a cautious way and recommends these to be used with deliberation on broad cost-effectiveness threshold range.[13] The need to quantify and appropriately measure the extended value of a drug is ever evolving to get a rounded overview of potential benefits.[13]

8. Demographic investment strategy

I. There is a growing notion that the pharmaceutical industry might focus investing on ex-US countries. Instead, **companies might aim to maximize returns within the first 10-13 years of a drug's launch as IRA discussion starts post this period**.

II. Companies may get the benefit of market exclusivity in the US due to patent protection which could be used for aggressive pricing. Cumulatively these will lead to **higher initial pricing globally.**

III. To be eligible for manufacturing subsidies and tax remissions provisioned in IRA for plants in the US companies may set up plants in the US or get in licensing agreement with US based companies. [14]

IV. For long-term profits manufacturers may focus on Europe, and China and strategize on the sales volume increase. It is worth noting that Europe is also going through its negotiation program. In light of recent developments with Joint clinical assessment (JCA) manufacturers may need to demonstrate extensive value on clinical efficacy and safety in Europe.[15]

Potential strategy for IRA negotiation

I. AbbVie's strategy for HUMIRA® (adalimumab) might offer a way to address possible revenue declines post price negotiation. Prior to the arrival of biosimilars, the company recovered its investment through competitive pricing and substantial investments in research and development, resulting in the development and marketing of RINVOQ® (upadacitinib) (for rheumatoid arthritis) and SKYRIZI® (risankizumab-rzaa) (for psoriatic arthritis), which caters to similar conditions. These medications could assist AbbVie in maintaining HUMIRA® (adalimumab)'s patient base and shifting its revenue stream to mitigate any impacts from IRA-related changes on HUMIRA® (adalimumab). RINVOQ® (upadacitinib) and SKYRIZI® (risankizumab-rzaa) are expected to generate combined sales of $21 billion by 2027.

II. While biosimilars made their debut in the U.S. in 2023, HUMIRA® (adalimumab) has encountered competition from biosimilars in international markets, such as Europe, since 2018. Despite the presence of these alternatives, AbbVie has maintained a significant portion of the market share and consistent profit. After 1 year of adalimumab biosimilars' entry into Europe, HUMIRA® (adalimumab)'s revenue although shrunk, it stayed up to $19 billion in 2019. Factors contributing to this resilience include brand loyalty, established relationships with healthcare providers, AbbVie's patient support initiatives, and innovative pricing strategies, all of which have helped preserve HUMIRA® (adalimumab)'s attractiveness to consumers.

III. Manufacturers may leverage the 9-13 years pre DPNP negotiation time for maximizing evidence from RWE and comparative studies to demonstrate superior value. They may also develop comprehensive evidence strategies for potential payer objections through the evidence strategy.

IV. Long-term values of drugs including scientific spillover, real option value, reduction in uncertainty could be explored for value demonstration.

CONCLUSION

The IRA signifies a pivotal change in the U.S pharmaceutical policy, with considerable implications for the global landscape. By allowing Medicare to negotiate drug prices, the IRA is likely to reduce revenue for pharmaceutical companies, leading them to reevaluate their pricing strategies on a worldwide scale. The impacts will include global pricing adjustments, increased focus on biosimilars, delay in launch of innovative products, and lesser number of orphan drugs. Although the true impacts of IRA are yet to be explored, the need to identify and assess the long-term value of drugs is ever increasing. The extended values from ISPOR value flower could become a starting point of discussion for evidence-based assessment of the long-term values of a drug. Furthermore, instead of solely implementing price controls, which may stifle innovation, fostering competition could effectively reduce drug prices and overall drug spending without the associated downsides. "Competition" encompasses not only pricing dynamics, particularly with generic alternatives, but also the rivalry among drugs that offer similar survival benefits but differ in safety profiles and treatment approaches. If the unintended consequence of IRA spans to lower research and development, it could restrict treatment options and hinder patients and caregivers from considering their preferences in treatment choices. Data indicates that similar policies in Europe have historically led to delayed drug launches such as the delayed launch of Hepatitis C treatment, SOVALDI® (sofosbuvir) and increased scrutiny of clinical trial data. Thus, it is crucial for industry leaders to engage in proactive scenario planning and risk assessment to mitigate potential disruptions to supply chains and market access. By investing in health economics and outcomes research (HEOR) activities, manufacturers can demonstrate the value of their products in a more competitive environment.

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Keys: *CMS, Centers for Medicare & Medicaid Services; DPNP, Drug Price Negotiation Program; FDA, Food and Drug Administration; HTA, Health Technology Assessment; ICER, Institute for Clinical and Economic Review; IRA, Inflation Reduction Act; ISPOR, International Society for Pharmacoeconomics and Outcomes Research; JCA, Joint clinical assessment; MFP, Maximum fair price; NSCLC, Non-small cell lung cancer; QALY, Quality adjusted life year; R&D, Research and development; SD, Standard deviation, US, the United States of America*

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This study was funded by PharmaQuant Insights Pvt. Ltd., India