IRA, PDABS, & ORPHAN DRUGS:
How Price Setting Mechanisms May Harm Patients with Rare Disorders

AIMEDALLIANCE

With growing concerns about the cost and affordability of prescription drugs, both federal and state legislators have launched initiatives to address prescription drug affordability. At the federal level, efforts include the Inflation Reduction Act (IRA), which empowers the Secretary of the Department of Health and Human Services to negotiate prescription drug prices for Medicare plans. Additionally, several states have established Prescription Drug Affordability Boards (PDABs), which are state-run entities tasked with setting price controls, such as upper payment limits, for prescription drugs deemed "unaffordable." However, as noted in Aimed Alliance's "Challenges and Alternatives PDAB Factsheet," the complexity of the current drug pricing system suggests that these well-intended efforts may not necessarily achieve the desired cost savings for consumers.

Moreover, these efforts could potentially hinder, delay, or even halt the development of treatments for certain rare or ultra-rare disorders. The resource below provides an overview of the potential impacts of PDABs and IRA negotiations on the development of treatments for rare disorders and proposes considerations and solutions that can help maintain incentives for investment and research into these conditions and treatments.

IRA Drug Negotiations	Prescription Drug Affordability Boards
Overview: The Inflation Reduction Act (IRA), signed in August 2022, requires the Centers for Medicare & Medicaid Services (CMS), to negotiate prices with drug companies for certain drugs covered under Medicare Part D (starting in 2026) and Part B (starting in 2028).[16] • The negotiated price is known as the maximum fair price (MFP).[17] • CMS announced the list of 10 drugs selected for negotiation on August 29, 2023.[18] • CMS is currently negotiating MFPs with drug manufacturers. If the two sides reach an agreement, the MFPs will be published by September 1, 2024, and take effect during 2026.[19]	Overview: Building on the momentum of the IRA negotiation process, several states have passed legislation to create PDABs. These state-run boards aim to address the costs of prescription drugs through various strategies, including implementing price controls.[20] • Upper payment limits (UPLs) are the highest allowable reimbursement rate that purchasers can provide for a prescription drug product.[21] These price controls do not dictate the manufacturer's pricing, or what a consumer pays out of pocket.[22] • Nine states have implemented PDABs. Four of these states (CO, MD, MN, WA) have the authority to establish UPLs, while the remaining five (ME, NH, NJ[i], OH[ii], and OR) do not have this authority.[23] Vermont has also passed similar legislation, granting an already existing Board the authority to regulate the cost of prescription drugs.[24]

i. New Jersey established a prescription drug affordability council.

ii. Ohio established a prescription drug affordability council.

What measures have been implemented to incentivize research and development into rare disorders and treatments?

Congress has acknowledged that the small population size of many rare disorders poses challenges in researching, investing in, and developing treatments for these conditions. Recognizing these challenges, Congress passed the Orphan Drug Act in 1983.[1] The Orphan Drug Act offers incentives to pharmaceutical manufacturers who develop Food and Drug Administration (FDA) approved drugs for rare diseases. These incentives include a seven-year period of market exclusivity, during which competing generic drugs are generally not allowed on the market, as well as significant tax credits for research and development expenses.[2]

ORPHAN DRUGS

Orphan drugs are pharmaceutical drug products developed to treat rare medical conditions, which are defined as conditions affecting fewer than 200,000 individuals within the United States.[3]

How might these new initiatives impact orphan drugs?

FEDERAL:

The IRA exempts orphan drugs from price negotiations, however, this exemption only applies to drugs that are approved to treat a single rare disease or illness.[4] If a prescription drug later receives approval for additional conditions, even if those are rare conditions, it will no longer be exempt and may become subject to the IRA negotiation process.

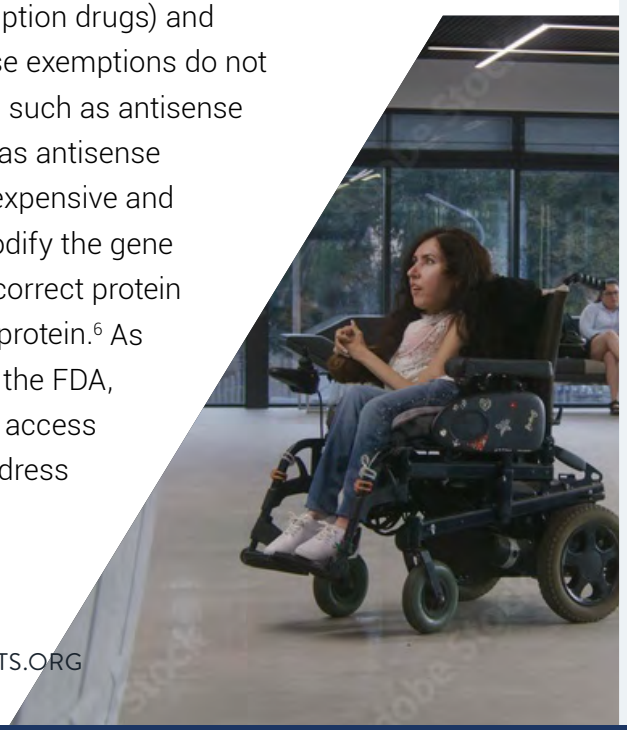
Thus, if receiving additional designations disqualifies as drug from the negotiation exemption, pharmaceutical and biotechnology companies are less incentivized to continue research on FDA-approved drugs to determine if they can treat other rare or ultra-rare conditions.[5] Ultimately, reducing ongoing and future research in treatment options for patients with rare diseases.

While the IRA exempts drugs from the negotiation process for the first seven years (small molecule—prescription drugs) and eleven years (large molecule—biologics), these exemptions do not address how certain rare disease treatments, such as antisense oligonucleotides (ASOs) will be treated, such as antisense oligonucleotides (ASOs). ASOs can be more expensive and time-consuming to develop because they modify the gene expression to ensure the gene produces the correct protein or stops the gene from producing the wrong protein.[6] As of 2022, only 14 ASOs had been approved by the FDA, therefore, Congress must continue to protect access to these novel treatments which may help address genetic disorders in ways other therapeutics (small molecule and biologics) cannot.

STATES:

Similarly, PDABs target the most expensive drugs that a state pays for, making high-cost orphan drugs more likely to be targeted by PDABs for review compared to other therapeutics. If a prescription drug is deemed unaffordable after review, states may implement an upper payment limit (UPL) on the drug.

In some states, if a UPL is set for a drug, the pharmaceutical manufacturer has the option to withdraw the drug from the state market. Although this concern has not yet materialized, as no state has completed the drug negotiation and UPL setting process,[9] a manufacturer's withdrawal could leave patients with rare disorders without access to their medication within that state.



Recently, ASO treatments were found effective in treating Spinal Muscular Atrophy (SMA), a condition affecting nearly one in 6,000 children.[7] Before the development of ASOs, many individuals with a severe SMA mutation did not live past the age of two.[8] The development of ASOs for this community illustrates the significant potential of investing in treatments for rare disorders and underscores the importance of ensuring continued investment, research, and access to these treatments.

How do PDABs evaluate the value of medications for rare diseases, and what implications does this have for rare disease treatments?

Some states, in reviewing drugs, utilize quality-adjusted life years (QALYs) as a measure of cost-effectiveness. QALYs quantify both the quality and quantity of life that a medical intervention can provide, aiming to assess its value in relation to its cost.[10] However, QALYs often undervalue the potential benefits for rare disease patients as they do not account for the unique and often significant improvements these drugs can provide in patients' quality of life, such as less frequent hospital visits and life-extensions.[11] Consequently, the use of QALYs in drug reviews inherently devalues the lives of people with rare diseases and disabilities.[12] Aimed Alliance affirms its long-standing opposition to the use of QALYs in drug value assessments.

How can state and federal legislators ensure that PDABs and the IRA do not negatively impact individuals living with rare disorders?

FEDERAL:

In response to concerns about the current carve-out, H.R.5539, the Optimizing Research Progress Hope And New Cures Act, has been proposed to extend the negotiation exemption to all orphan drugs, regardless of the number of orphan designations the drug receives.[13] This would mean that FDA-approved orphan drugs could continue to be exempt from the negotiation process as long as any additional designation the drug receives is also for rare diseases.[14]

The Maintaining Investments in New Innovation Act (MINI Act) (H.R. 5547/S.476) aims to support ongoing investment in treatments for rare disorders. The Act proposes exempting genetically targeted therapies, like ASOs, from Medicare negotiation for at least 11 years following market approval. Currently, these therapies are subject to negotiation after seven years. Extending the exemption to 11 years would align genetically targeted therapies with the existing exemption period for biologics.

STATES:

Colorado has proposed legislation to exempt orphan drugs from affordability reviews and the establishment of UPLs.[15] Like the IRA exemption, excluding orphan drugs from cost reviews will help ensure that individuals with rare diseases maintain access to treatments and that there is continued research and investment into these conditions.

CONCLUSION

While the IRA price negotiations and the establishment of PDABs are well-intentioned, they carry the risk of unintended negative consequences for consumers. Prescription drug manufacturers facing price negotiations or payment limits for orphan drugs may be disincentivized from seeking additional indications or continuing to market their drugs in the state. This could result in patients having access to fewer potential treatments and challenges to accessing current treatments. Without appropriate modifications to the current state and federal negotiation parameters, these cost-saving measures may inadvertently harm patients with rare diseases and lead to less treatments for these conditions.

State-By-State Treatment of Rare Disease Carveouts

Enacted PDABs	Rare Disease Provisions
Colorado	In reviewing drug affordability, the Board must consider orphan drug status. The orphan drug exemption has not yet passed. Prohibited from using QALYs or similar cost-effectiveness formulas.
Maine	None.
Maryland	None.
Minnesota	Advisory Council membership must include one member from the Rare Disease Advisory Council. **The Advisory Council consists of 18 governor-appointed individuals who provide advice to the Board on drug cost issues and represent stakeholders' views. The Council's authority is advisory only, meaning it cannot mandate actions or compel the Board to consider specific issues**
New Hampshire	None.
Oregon	Prescription drugs that are FDA-approved to treat a rare disease or condition are exempted from review. Prohibited from using QALYs or similar cost-effectiveness formulas.
Washington	Prescription drugs that are FDA-approved solely to treat a rare disease or condition are exempted from review. In reviewing drug affordability, Board must consider orphan drug status. Prohibited from using QALYs or similar cost-effectiveness formulas.

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AIMEDALLIANCE

1455 Pennsylvania Ave, NW, Suite 400, Washington, DC 20004

(202) 349-4089 • AimedAlliance.org