Analyzing the Impact of Policies to Exclude Certain Orphan Drugs from the Drug Price Negotiation Program of the Inflation Reduction Act

HMA

EXECUTIVE SUMMARY

Orphan drugs treat rare diseases—conditions that affect fewer than 200,000 people annually in the United States. With an estimated 10,000 rare diseases identified, many of which are life-threatening, more than 30 million Americans have a rare disease.[1] Only 5 percent of rare diseases have a treatment that has been approved by the Food and Drug Administration (FDA).[2] The federal government grants orphan drugs special status to provide drug companies incentives to research and manufacture treatments with high development costs but very small patient populations and limited ability to recoup the cost of investigation and production.

The Inflation Reduction Act of 2022 (IRA) excluded certain orphan drugs from Medicare's new price negotiations, but only if they are approved to treat a single rare disease. However, some patient advocates, medical providers, policymakers, and drug manufacturers believe that all orphan drugs used to treat exclusively rare diseases merit protection. Members of Congress introduced the Optimizing Research Progress Hope And New (ORPHAN) Cures Act in 2023 and reintroduced it in 2024. This legislation calls for extending the price negotiation exclusion to orphan drugs that treat more than one rare disease.[3]

Health Management Associates, Inc. (HMA) was engaged to determine how many orphan drugs the ORPHAN Cures Act might affect and the percentage of Medicare Part B and Part D spending that is attributable to these drugs. Using that information, we estimated how the legislation would affect federal spending, applying the same assumptions and methodology that the Congressional Budget Office (CBO) uses in a 10-year budget score.

WE ANALYZED 8,842 DRUGS AND FOUND THE FOLLOWING:

Only

82 (0.9%)

orphan drugs would be covered by the ORPHAN Cures Act (i.e., have more than one orphan indication and no non-orphan indications).

These drugs accounted for

5.4%

of drug spending and

3.2%

of drug and medical spending in Medicare Parts B and D in 2022.

[1] US Food and Drug Administration. FDA Rare Disease Innovation Hub. Available at: https://www.fda.gov/industry/medical-products-rare-diseases-and-conditions/fda-rare-disease-innovation-hub.

[2] US Government Accountability Office. Rare Disease Drugs: FDA Has Steps Underway to Strengthen Coordination of Activities Supporting Drug Development. November 18, 2024. Available at: https://www.gao.gov/products/gao-25-106774.

[3] The ORPHAN Cures Act was originally introduced in 2023 in the US House of Representatives by Reps. John Joyce, MD (R-PA), and Wiley Nickel (D-NC) and in the Senate by Sens. John Barrasso, MD (R-WY), and Tom Carper (D-DE).

Drugs included in the price negotiation program are selected from a list of the top 50 negotiation eligible drugs with the highest Medicare expenditures. When we analyzed the list of the 50 drugs with the greatest drug spending in 2022, we found that most (86%) were either non-orphan drugs, or orphan drugs that had at least one non-orphan indication. Only 8% (n=4) were orphan drugs with more than one orphan indication and no non-orphan indications.

Using this information on drug spending for orphan drugs with more than one non-orphan indication, we projected that if ORPHAN Cures were enacted, one product would be excluded from negotiation during the scoring window, resulting in a cost of $810 million over 10 years.

We also compiled information on which products would be affected by the ORPHAN Cures Act provision that delays the start of the "clock" for determining the eligibility of previously orphan-only drugs until their first non-orphan indication receives FDA approval. We determined that two products meet the criteria to benefit from this policy during the current scoring window, and estimate that this provision would cost the federal government an additional $280 million over the 10-year scoring window.

Considering both policies together, we estimate the ORPHAN Cures Act will cost $1.09 billion over 10 years, or less than 1 percent of the $179 billion in savings CBO has estimated will emerge from the IRA's drug negotiation provision. Changes to ORPHAN Cures, such as delaying the implementation date, could reduce the cost of the policy.

INTRODUCTION

Since the Inflation Reduction Act of 2022 (IRA) was enacted, patient groups, medical providers, and other stakeholders have raised concerns about the law's impact on research and development of new drugs, particularly those used to treat rare diseases. This Issue Brief summarizes the results of research that Health Management Associates, Inc. (HMA) conducted on behalf of Alexion, AstraZeneca Rare Disease, to consider the role of orphan drugs in IRA negotiations and to analyze the budgetary impact of legislation that would exempt orphan drugs that treat only rare diseases from price negotiation requirements.

The National Institutes of Health has identified approximately 10,000 rare diseases, and the US Food and Drug Administration (FDA) estimates that more than 30 million Americans have a rare disease

RARE DISEASES AND ORPHAN DRUGS

A rare disease is defined as a health condition that affects fewer than 200,000 people in the United States each year. Though each rare disease has a small patient population, the National Institutes of Health has identified approximately 10,000 rare

diseases, and the US Food and Drug Administration (FDA) estimates that more than 30 million Americans have a rare disease, yet the FDA has approved treatments for only about 5 percent of them.

Many rare diseases are life-threatening and treatments for these conditions are challenging to develop because of their complexity and the difficulty of establishing the necessary evidence that treatments are safe and effective. Clinical trials can be difficult and expensive to conduct given the low number of potential patients living in disparate areas of the country. These barriers disincentivize pharmaceutical manufacturers from developing rare disease treatments.

In response, Congress passed the bipartisan Orphan Drug Act of 1983, which added incentives to spur development of rare disease therapies. Drug manufacturers may apply for orphan drug designation for a medicine being developed. If granted, the company may receive tax credits to defray the cost of clinical trials, have the fees required under the Prescription Drug User Fee Act waived, and receive extended market exclusivity, meaning that generic competition is delayed.

Treatments designated as orphan drugs fall into several categories:

- **Drugs that treat just one rare disease.** Very few patients are eligible to receive these therapeutics because only a small set of people have that same condition. An example is a drug that the FDA recently approved for treatment of Huntington's Disease.
- **A drug that treats more than one rare disease.** Occasionally, an orphan drug may effectively treat more than one rare disease. With additional testing, and after undergoing the same rigorous regulatory processes, the FDA may approve a single drug to treat more than one rare disease indication. More patients are eligible to receive this drug, but still the total population eligible for treatment is relatively small because each disease the drug treats is uncommon. For example, one drug treats patients with neuromyelitis optica spectrum disorder (NMOSD), an autoimmune disease of the nervous system, a chronic neuromuscular autoimmune disease called generalized myasthenia gravis (gMG), the kidney disease atypical hemolytic uremic syndrome (aHUS), and the blood disorder paroxysmal nocturnal hemoglobinuria (PNH).
- **A drug that treats one or more rare disease(s) but also is used to treat a more common disease.** For example, one drug has received FDA approval for 40 different indications, some of which are for rare diseases, and others are for commonly seen cancers.

Although there are drugs in each of these three categories, experts estimate that 95% of rare diseases still lack an FDA approved treatment.

THE INFLATION REDUCTION ACT, DRUG PRICE NEGOTIATIONS, AND THE ORPHAN CURES ACT

The IRA was enacted in 2022. Among its provisions, the legislation allows Medicare to negotiate a maximum fair price for certain prescription medications prescribed to Medicare beneficiaries. Similar to the Orphan Drug Act, the IRA recognizes the special role that orphan drugs play and the disincentives that orphan drug manufacturers face by excluding orphan drugs with a single indication from the pricing negotiations.

Manufacturers of orphan drugs, patient advocates, and other stakeholders have expressed concern that the IRA price negotiation program's orphan drug protections are too limited and stifle the development of new drugs or research into the expanded ability of existing drugs to treat other rare conditions. Specifically, stakeholders support the Optimizing Research Progress Hope And New (ORPHAN) Cures Act, which would extend the IRA's orphan drug protections in two ways. First, the legislation excludes orphan drugs with more than one orphan indication and without any non-orphan indications from price negotiation. Second, it delays negotiation eligibility for orphan drugs that lose the exclusion because a non-orphan indication has been approved. The ORPHAN Cures Act was originally introduced in 2023 in the US House of Representatives by Reps. John Joyce, MD (R-PA), and Wiley Nickel (D-NC) and in the Senate by Sens. John Barrasso, MD (R-WY), and Tom Carper (D-DE).[4] ORPHAN Cures was reintroduced in February 2025 for the 119th Congress's consideration.

Similar to the Orphan Drug Act, the IRA recognizes the special role that orphan drugs play and the disincentives that orphan drug manufacturers face by excluding orphan drugs with a single indication from the pricing negotiations.

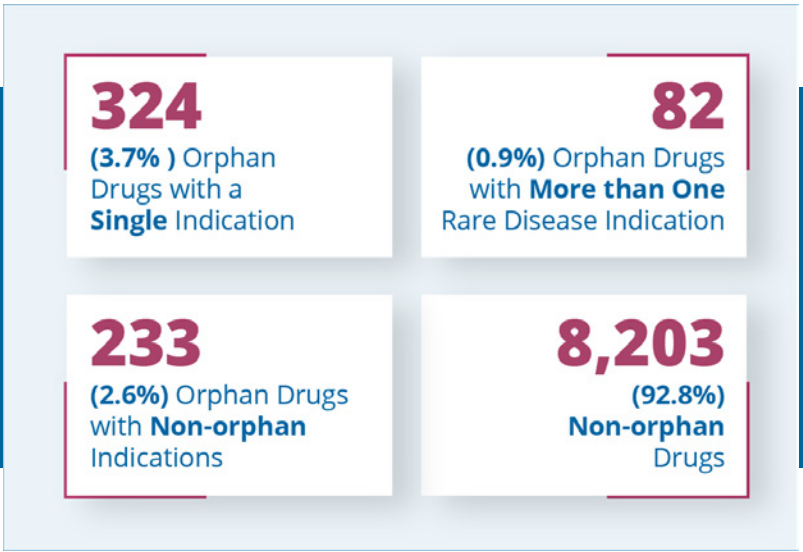
HMA was engaged to examine Medicare claims data to determine how much of Medicare's spending on drugs and healthcare services are attributable to orphan drugs with single and more than one rare disease indication. In addition, HMA was asked to estimate the budgetary effects of the ORPHAN Cures Act. Specifically, we were asked to apply our understanding of the methodology and expected assumptions that Congressional Budget Office (CBO) uses to analyze how the agency might score the bill's effect on the federal budget.

[4] Cosponsors included: Reps. Donald G. Davis (D-NC), Kevin Hern (R-OK), Scott H. Peters [D-CA], Gus M. Bilirakis (R-FL), Josh Gottheimer (D-NJ), Lloyd Smucker (R-PA), Mariannette Miller-Meeks (R-IA), Shri Thanedar (D-MI), Mary Sattler Peltola (D-AK), Brian K. Fitzpatrick (R-PA), William R. Keating (D-MA), and Richard Hudson (R-NC) and Sens. Roger Marshall (R-KS) and Ted Budd (R-NC).

ORPHAN DRUG SPENDING 2018-2022

We looked at Medicare spending in Medicare Parts B and D from 2018 through 2022 and examined claims for 8,842 drugs, which we sorted into the following four categories:

- A total of **324 (3.7%)** orphan drugs had a single orphan indication. These drugs are currently excluded from IRA price negotiation.
- A total of **82 (0.9%**) orphan drugs had more than one rare disease indication, and no non-orphan indications. These medications would be exempt from IRA negotiations if the Orphan Cures Act were enacted into law.
- A total of **233 (2.6%)** orphan drugs had at least one non-orphan indication.



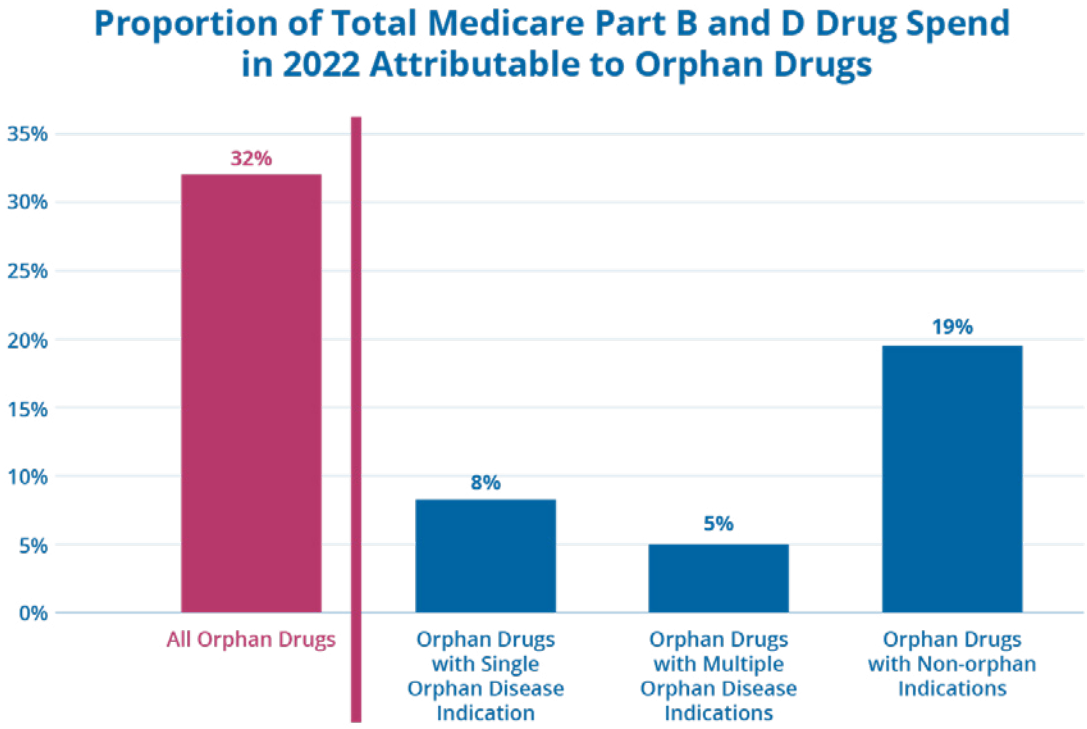
- A total of **8,203 (92.8%)** drugs with no orphan indication.

Once we had categorized the prescription drugs, we analyzed claims data from the Virtual Research Data Center (VRDC), which contains all (100%) Medicare Part B and D claims from 2018 through 2022. We identified claims with and without the drugs to calculate Medicare's spending on each type of drug. We also calculated total Medicare Part B and D spending to determine the percentage of Medicare spending attributable to each drug category.

We found that orphan drugs comprised approximately one-third (32.4%) of Part B and Part D drug spending in 2022. When we looked at Part B and Part D total spending (drugs and medical care), spending on orphan drugs was 19.4 percent of the total.

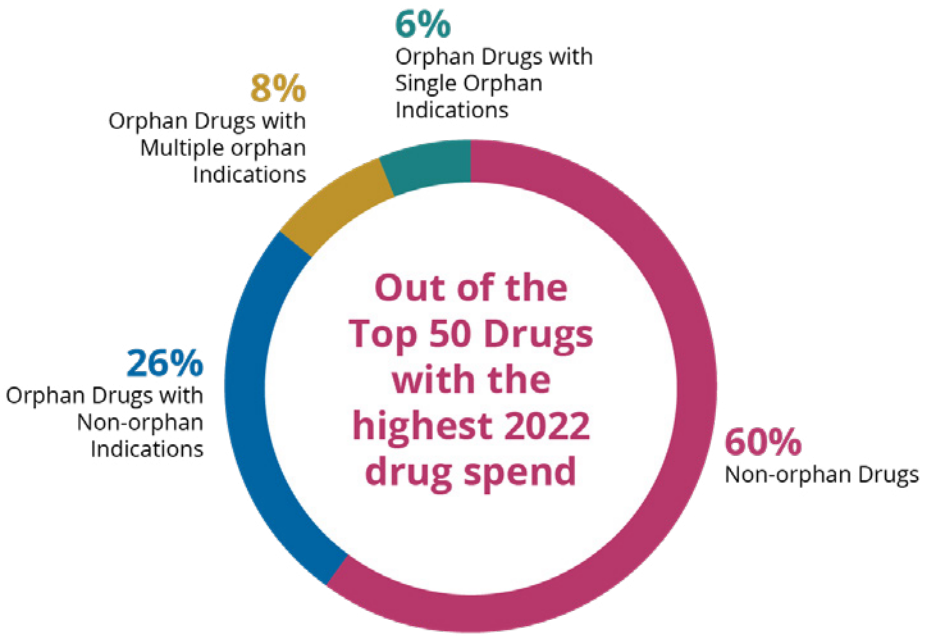
Orphan drugs play an important role in cancer care, and we found that 18 percent of orphan drug spending was directed toward oncology indications.

We then broke down these numbers by type of orphan drug. Orphan drugs with a single orphan indication—those drugs that are currently exempt from price negotiation in the IRA—constitute 7.5 percent of drug spending in Medicare Parts B and D and 4.5 percent of total B and D spending. Orphan drugs with more than one orphan indication and would be subject to the ORPHAN Cures Act constitute an even smaller portion of Medicare spending. Spending on these drugs comes to 5.4 percent of drug spending and 3.2 percent of drug and medical spending in Medicare Parts B and D.



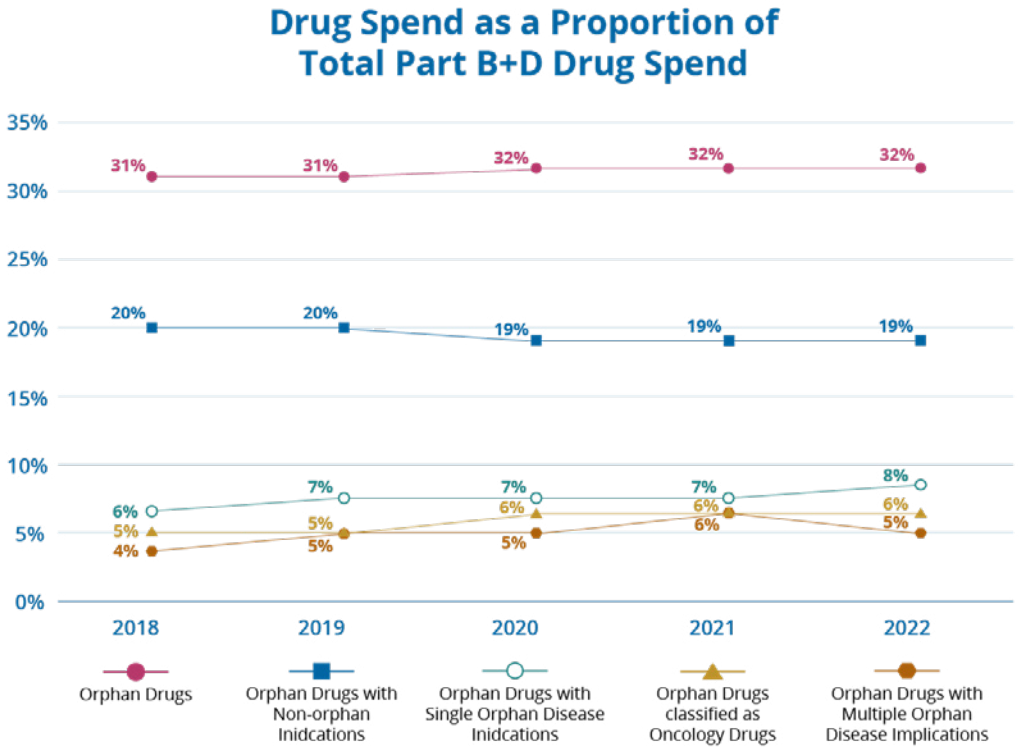
Orphan drugs with non-orphan indications, however, comprise a much more substantial portion of spending—19 percent of Part B and Part D drug spending and 11.6 percent of total Part B and Part D spending.

Because the drugs included in future rounds of price negotiation under the IRA will be selected from the list of highest spending drugs, we looked at the list of the top 50 drugs with the highest combined Part B and Part D spending in 2022. Of those 50 drugs, 60 percent are non-orphans. Orphan drugs with non-orphan indications



comprised another 26 percent. Orphan drugs with a single orphan indication accounted for another 6 percent of the list. Finally, orphan drugs with more than one orphan indication constituted 8 percent of the list. These four drugs would be exempt from price negotiation under the ORPHAN Cures Act.

We also examined spending on orphan and non-orphan drugs over time and found that their proportion of total Part B and Part D drug spending from 2018 through 2022 to be very stable. Orphan drugs overall, as well as the different sub-types



(orphan drugs with a single orphan indication, orphan drugs with more than one rare disease indication, orphan drugs with non-orphan indications) only varied by 2 percent at most over the five-year span. The percentage of orphan drug spending attributable to oncology drugs also stayed at between 5 percent and 6 percent during the study period.

ESTIMATES OF FEDERAL BUDGETARY IMPACT OF THE ORPHAN CURES ACT

In assessing the budgetary effects of the ORPHAN Cures Act, we incorporated information from our understanding of how the CBO intends to score legislation that would change the products that would be eligible for drug price negotiations.[5]

After developing a baseline of federal spending, we projected spending per product across the budget window based on a blend of the overall Part D trend per CBO and the individual product trends from recent history. We then determined for each year which products we believed would become subject to negotiation and were also multi-orphan drugs, subject to the legislation. When a multi-orphan product would have been negotiated in a given calendar year, we replaced it with the next product by our projected total spending that could be subject to negotiation. We applied the published CBO savings rate per product to the new product instead of the multi-orphan product and calculated savings as the difference between the two rates. After using this process for the first year, we applied this calculation to every year in the scoring window. Finally, we adjusted for premium impacts, including the IRA's premium stabilization provisions in accordance with CBO's standard methodology.

Our model did not forecast any behavioral changes as a result of the policy. For example, we did not account for additional changes that might occur if a manufacturer of a drug that currently has a single orphan indication pursued additional orphan indications in reaction to the policy change and the additional drug spending that could occur as a result of new indication approvals by the FDA. We think that CBO would view that exercise as too speculative and unlikely to occur during the scoring window.

We also believe that CBO would not forecast any changes in market entry of new products during the scoring window as a result of this policy. If CBO were to take a position, it might conclude that this policy increases the likelihood of future drugs with multi-orphan indications being developed and achieving FDA approval. Again, we

[5] When conducting these analyses, HMA follows The Moran Company's longstanding methodology. Specifically, we apply our understanding of CBO precedents to predict how we think CBO will evaluate the budgetary impact of the legislation in question. We use our best judgment to adopt the assumptions that we think CBO would follow, with the understanding that any variance in the assumptions CBO ultimately adopts could cause our estimate to differ from theirs.

defer placing a number on this behavioral change due to both the speculative nature and because any behavioral change on market entry is likely to take many years to occur and thus have an impact outside of the scoring window.

We also assumed that any products already selected for negotiation, which would otherwise be classified as multi-orphan products, would not be subject to the provisions of the bill. As a result, our analysis projects one product will be excluded from negotiation during the scoring window as a result of the ORPHAN Cures policy, yielding a cost of $810 million over 10 years.

We compiled information on which products would be affected by the ORPHAN Cures Act provision, which delays the start of the "clock" for determining the eligibility of previously orphan-only drugs until their first non-orphan indication receives FDA approval. We determined that two products meet the criteria to benefit from this policy during the current scoring window, pushing their eligibility to be selected for negotiation at least one year further than our data estimate of when they would otherwise be selected for negotiation.

We estimate that this provision would cost the federal government another $280 million over the 10-year scoring window. This score is sensitive to the choice of spending trends for these two products, as one product's eligibility for selection would be pushed outside the scoring window. We have chosen the midpoint of plausible upper and lower bounds for the selection year for that product, which results in the current score. If CBO assumes a softer trend line for that product, it might be negotiated later in the window and the cost of the policy reduced.

Considering both policies together, we estimate the ORPHAN Cures Act will cost $1.09 billion over 10 years, or less than 1 percent of the $179 billion in savings that CBO has estimated will emerge from the IRA's drug negotiation provision. Changes to ORPHAN Cures, such as delaying the implementation date, could reduce the cost of the policy.

Estimated Impact on Federal Spending ($ in billions)

	2026	2027	2028	2029	2030	2031	2032	2033	2034	2024-2033
CBO Original IRA Negotiation Provision Score	$(3.7)	$(8.3)	$(17.5)	$(21.0)	$(23.4)	$(24.5)	$(25.7)	$(26.9)	$(28.1)	$(179.2)
Multi Orphan Policy Delta	$ -	$ -	$ -	$ -	$ -	$ -	$.26	$.27	$.28	$.81
Clock Start Policy Delta	$ -	$ -	$.02	$.01	$.03	$.04	$.05	$.06	$.08	$.28

This study was sponsored by Alexion, AstraZeneca Rare Disease, Boston, MA.

MEDICARE CLAIMS ANALYSIS METHODOLOGY

To identify the prescription drugs used in this study, we collected information from the Centers for Medicare & Medicaid Services (CMS) Average Sales Price files, CMS Part B Drug Dashboard data from 2018 to 2022, and the Outpatient Prospective Payment System Drug Cost Statistics file from 2019 to 2024. We also included all the Healthcare Common Procedure Coding System (HCPCS) codes that start with J9. We used the FDA Orphan Drug Database to identify orphan drugs. We excluded any orphan drugs that had their orphan designation withdrawn or revoked and identified the number of orphan indications by unique generic name.

We created four different flags to categorize orphan drugs: Orphan drugs with one orphan indication only, orphan drugs with two or more orphan indications and no non-orphan indications, and orphan drugs with one or more non-orphan indications. Orphan drug indications were identified using the FDA orphan database and DailyMed, which is a resource provided by the US National Library of Medicine that lists FDA-approved indications.

For HCPCS code identification, we used several resources: CMS Part B dashboard data, the Surveillance, Epidemiology, and End Results (SEER) Cancer database, and a 2021 study by Chua et al., which provided a list of HCPCS codes for top selling orphan drugs approved to treat common diseases.[6] If we were unable to find a specific HCPCS code, we used the EncoderPro database. When a unique HCPCS code for a brand drug could not be found, we identified the HCPCS code associated with the drug's generic name.

We used the 100 percent Medicare Standard Analytic Files housed in the CMS VRDC, which contain all Medicare claims in all settings of care from 2018 to 2022.

[6] Chua KP, Kimmel LE, Conti RM. Spending for Orphan Indications Among Top-Selling Orphan Drugs Approved to Treat Common Diseases. Project Hope. *Health Affairs*. 2021;40(3):453–460. doi:10.1377/hlthaff.2020.01442

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