ASPE REPORT

Characteristics of Part D Drugs in Shortage

Prepared by
The Office of the Assistant Secretary for Planning and Evaluation (ASPE)
At the U.S. Department of Health and Human Services

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Executive Summary

The Inflation Reduction Act (IRA) requires drug manufacturers to pay a rebate to the federal government if they raise the price of covered drugs under Medicare Part D faster than the rate of inflation. The rebate may be reduced or waived in several circumstances, such as if a drug is listed as currently in shortage on the Food and Drug Administration (FDA)'s shortage list, if there is a severe supply chain disruption of certain generics or biosimilars, or if certain generics are likely to be in shortage.

In this Report, we matched a sample of Part D drugs and biological products that had price changes between January 2011 and October 2023 to FDA's January 2023 list of drug shortages database. Then we analyzed price changes that occurred before and after the shortage, overall and by select drug characteristics of interest. This analysis is illustrative, it can help identify whether drugs in shortage were particularly likely, pre-IRA, to have price changes and the characteristics of drugs that were most impacted by shortages and high price increases. These drugs may be more likely to be eligible for reduced or waived rebates under the new IRA provisions.

For purposes of this analysis, we analyzed a Part D[1] drug and biological product if it met the following criteria: 1) it was primarily dispensed in the "retail" channel using IQVIA data; 2) it had a price change at any time between January 2011 and October 2023 as identified in AnalySource data; 3) it was not classified by AnalySource as a multi- source generic; 4) it was not a low expenditure drug, i.e., the average annual expenditure per drug per enrollee in 2021 exceeded $100 as determined using CMS Part D dashboard data; and, 5) it was found in FDA's January 2023 Drug Shortage Database. We defined a Part D drug and biological product as having a high price increase if it had a price increase that exceeded the rate of inflation at any given time (month-year) before and after it was listed in shortage.

Our results point to key product characteristics that are associated with ongoing shortages of Part D drugs and biological products with high price increases. We found that a small (1.6 percent) sample of Part D drugs and biological products were listed in FDA's list of current shortages in January 2023 and that many of these drugs (53 percent) were associated with a price increase that was considered high, i.e., exceeded the rate of inflation. The majority of Part D drugs and biological products with high price increases were small molecule drugs, generics, and products that had been approved longer than 11 years. Among those drugs with high price increases, the duration of shortages also varied by drug characteristics and the average price increase before a product was listed in FDA's shortage database varied from 6 to 19 percent. These results help provide an assessment of drug shortages and price changes prior to implementation of the IRA's inflation rebates.

The estimates presented in this Report have not been used to develop the inflation rebates program guidance. In addition, this Report may not necessarily align with how CMS will implement the inflation rebate guidance. For example, there are differences in how ASPE and CMS define rebatable drugs or biological products, the timeline used to assess the inflation rebates, and the level of aggregation from the NDC to the active ingredient level. For

[1] Medicare covers retail prescription drugs purchased through pharmacies and by mail order through Part D and drugs and biological products that are provided in physicians' office and hospital outpatient departments through Part B.

more details on how CMS will implement this policy, please see Medicare Part D Drug Inflation Rebates Paid by Manufacturers Final Guidance.[2]

KEY POINTS

- Certain covered Part D rebatable drugs or biological products may be eligible for the IRA's rebate reductions or waivers if they are listed as currently in shortage in FDA's drug shortage, or are likely to be in shortage, or in cases of severe supply chain disruptions.
- We found that 1.6 percent (32 of 1,999 NDCs) of Part D drugs and biological products on the market between January 2011 and October 2023 experienced a drug shortage, and 53 percent (17 of 32 NDCs) of them had high price increases, meaning they could have been potentially eligible for a reduction or waiver under the IRA's inflation rebate provisions.
- We found that the Part D drug and biological products with high price increases that could have been potentially eligible for the IRA reduction or waiver, were small molecule drugs, generics, and older drugs.
- The therapeutic class of Part D drugs and biological products most commonly associated with current shortages and high price increases was alimentary tract and metabolism.
- The majority (88 percent) of Part D drugs and biological products with a high price increase did not have a known cause of the shortage listed in the FDA Drug Shortage Database. The only known cause of shortage, listed for 12 percent of shortages, was an "increase in demand".
- The average duration of shortages varied by drug characteristics. Among Part D drugs and biological products currently in shortage and with high price increases, small molecule drug, generics, non-injectables, and older drugs all had the longer shortage duration (up to 3 years).
- Among Part D drugs and biological products currently in shortage and with a high price increase, the price increases ranged from 3 to 9 percent—with the largest price increase occurring 7 quarters *before* the drug was officially listed in the FDA Drug Shortages Database. The price change 7 quarters after a drug was officially listed in shortage ranged from 5 to 8 percent.

[2] Centers for Medicare and Medicaid Services. (2023). Medicare Part D Drug Inflation Rebates Paid by Manufacturers: Revised Guidance, Implementation of Section 1860D-14B of the Social Security Act. https://www.cms.gov/files/document/medicare-part-d-inflation-rebate-program-revised-guidance.pdf

Introduction

The Inflation Reduction Act (IRA) requires drug manufacturers to pay inflation rebates for nearly all covered drugs under Medicare Part D that experience price increases above inflation for each applicable period (a 12-month period beginning each October 1) (called "Part D rebatable drugs and biological products).[3] Part D rebatable drugs and biological products exclude multi-source generic drugs and low spend drugs (i.e., less than $100 per enrollee per year in 2023, adjusted for inflation in future years).[4] The IRA has special provisions to allow the Centers for Medicare & Medicaid Services (CMS) to reduce or waive these rebates for certain drugs and biological products under three cases: (1) for a Part D rebatable drug that is described as currently in shortage on a FDA drug shortage list under section 506E of the Federal Food, Drug, and Cosmetics (FD&C Act) at any point during the applicable period; (2) for a generic Part D rebatable drug or biosimilar when CMS determines there is a severe supply chain disruption during the applicable period, such as that caused by a natural disaster or other unique or unexpected event; and (3) for a generic Part D rebatable drug when CMS determines that without such a reduction or waiver in the rebate, the drug is likely to be described as in shortage on the FDA drug shortage list during a subsequent applicable period. CMS' final Part D[5] rebate guidance defined a severe supply chain disruption to mean "a change in production or distribution that is reasonably likely to lead to a significant reduction in the U.S. supply of a generic Part D rebatable drug or biosimilar by a manufacturer and significantly affects the ability of the manufacturer to fill orders or meet expected demand for its product in the United States for at least 90 days." To mitigate potential spillover effects, the definition in the guidance does not include disruptions that can be controlled by a manufacturer, such as routine maintenance, failure to comply with good manufacturing practice requirements, or insignificant changes made in the manufacturing process for a drug, as long as the manufacturer expects to resume operations within 90 days.

CMS described the intent of the rebate reduction or waiver as a means to provide a period of financial relief for manufacturers who are experiencing the negative impacts of external circumstances.[6] CMS also stated that this policy should not create an incentive that could lead to the misuse of the reporting process established under 506E of the FD&C Act, nor should it allow manufacturers to intentionally maintain their drugs or biological products in shortage for the purpose of avoiding a rebate.

CMS considers a drug to be in shortage if it appears on the FDA drug shortage list[7] and has at least one National Drug Code (NDC)-11[8] with its shortage status as "current" on the shortage list during an applicable period. Drugs with a shortage status of "discontinued," "to be discontinued," or "resolved" are not eligible for a reduction or waiver. Shortages can occur for many reasons, including manufacturing quality issues, an increase in demand,

[3] U.S. Congress. (2022). H.R.5376 - Inflation Reduction Act of 2022 enacted as P.L. 117-169. https://www.congress.gov/bill/117th-congress/house-bill/5376/text

[4] The IRA delineates that the $100 be adjusted by the percentage increase in the U.S. Bureau of Labor Statistics (BLS) Consumer Price Index for all Urban Consumers (CPU-U).

[5] Centers for Medicare and Medicaid Services. (2023). Medicare Part D Drug Inflation Rebates Paid by Manufacturers: Revised Guidance, Implementation of Section 1860D-14B of the Social Security Act. https://www.cms.gov/files/document/medicare-part-d-inflation-rebate-program-revised-guidance.pdf

[6] Centers for Medicare and Medicaid Services. (2023). Medicare Part D Drug Inflation Rebates Paid by Manufacturers: Revised Guidance, Implementation of Section 1860D-14B of the Social Security Act. https://www.cms.gov/files/document/medicare-part-d-inflation-rebate-program-revised-guidance.pdf

[7] Food and Drug Administration. Drug Shortages. https://www.fda.gov/drugs/drug-safety-and-availability/drug-shortages

[8] An NDC-11 is made up of three parts: the first five digits indicate the manufacturer or the labeler; the next four digits indicate the ingredient, strength, dosage form and route of administration; and the last two digits indicate the packaging. The FDA assigns the manufacturer portion of the code; the manufacturer supplies the rest.

supply chain disruptions from natural disasters or other unexpected events, or product discontinuation.[9] Since 2012, manufacturers have been required to notify FDA of a permanent discontinuance in the manufacture of covered drugs and biological products or an interruption in the manufacture of covered drugs and biological products if it is likely to lead to a meaningful disruption in the supply of such products.[10] Manufacturers are also required to report certain reasons for the discontinuance or interruption. These reasons are mainly related to disruptions in supply.[11] Consistent with section 506E of the FD&C Act, FDA maintains publicly available lists of drugs and biological products that FDA has determined to be in shortage in the United States.

Rebate reductions will vary depending on how a rebatable drug or biological product qualifies for the reduction, by the type of product, and the duration of the shortage. Specifically, Part D rebatable drugs that are neither plasma-derived products nor single-source generic drugs may be eligible for a 25 percent rebate reduction in the first year of a shortage, a 10 percent reduction in the second year of a shortage, and a 2 percent reduction in subsequent years of a shortage. Part D rebatable plasma-derived products and single-source generic drugs are eligible for a 75 percent rebate reduction in the first year of a shortage, a 50 percent reduction in the second year of a shortage, and a 25 percent reduction in subsequent years of a shortage. Part D rebatable biosimilar biological products and single-source generic drugs are eligible for a 75 percent rebate reduction for one year when there is a severe supply chain disruption, with the option to request an extension for an additional year. Part D single-source generic drugs are also eligible for a 75 percent reduction for one year when there is likely to be a shortage, with the option to request an extension for an additional year. Price increases are calculated based on the Average Manufacturer Price (AMP) as reported in the Medicaid Drug Rebate Program for the rebatable drug or biological product. Estimation of the potential rebate reductions is outside the scope of this Report.

In this Report we examine the following research questions:

- What is the share of Part D drugs and biological products that are currently in shortage?
- Among those Part D drugs and biological products that are currently in shortage, what share have exhibited high price increases?
- What are the product characteristics (small molecule vs biological product; brand vs generic; injectable vs oral; newer vs older drugs; therapeutic class) of the Part D drugs and biological products in shortage and with high price increases?
- What is the average duration of shortages of Part D drugs and biological products with high price increases? How does duration of shortages vary by product characteristics?
- Among Part D drugs and biological products with high price increases, what is the median price increase before and after the shortage starts?

Understanding the answers to these research questions can help identify the characteristics of drugs that were most impacted by shortages and high price increases. These drugs may be more likely to have reduced or waived rebates under the new IRA provisions.

[9] U.S. Food and Drug Administration. (2020). Report | Drug Shortages: Root Causes and Potential Solutions. https://www.fda.gov/drugs/drug-shortages/report-drug-shortages-root-causes-and-potential-solutions

[10] Section 506C of the FD&C Act.

[11] While some manufacturers may report shortages due to "increases in demand," FDA does not have the statutory authority to require notifications for such types of shortages.

For this Report, we matched a sample of Part D drugs and biological products that had price changes between January 2011 and October 2023 to FDA's January 2023 database of drug shortages. Then we analyzed price changes that occurred before and after the shortage, overall and by select drug characteristics of interest.

Data and Methods

Primary Dispensing Location as a Proxy for Certain Part D Drugs and Biological Products: Medicare offers prescription drug coverage through its Part D program. Part D drugs are typically outpatient prescription drugs or drugs distributed in "retail" settings that are self-administered. To identify drugs that would typically be paid for under Medicare Part D, we gathered information on the primary dispensing location of drug and biological products in our sample using the IQVIA National Sales Perspective (NSP) dataset. IQVIA NSP contains NDC-11 level data on the sales and volume of extended units sold from manufacturers and wholesalers to chain and independent pharmacies, hospitals, mail order pharmacies, clinics, chain or food stores, home health care, long term care facilities, and other health care settings. We classified drugs and biological products as "retail" if they were dispensed in chain and independent pharmacies, chain stores, food stores, or by mail order, and as "nonretail" for all other settings. Because a drug can be dispensed in both retail and nonretail settings, to determine the primary dispensing location, we calculated the percent of total sales and total volume[12] in each setting during the period of analysis. A drug was determined to be dispensed in the retail setting if the percent of sales or the percent of volume in the retail setting exceeded 90 percent of total sales or total volume during 2017-2022. We removed duplicate NDCs from the sample. This classification is a proxy measure for Part D drugs and as such it is an imperfect measure that may exclude drugs that are sold in retail settings or have low volume of sales.

Part D Dashboard Low Expenditure Drugs: We used the CMS Medicare Drug Dashboard's Medicare Part D Spending by Drug (data downloaded November 30, 2023)[13] to identify Part D low expenditure drugs and biological products. This database includes the brand name, generic name, and total spending information from 2017 to 2021. We defined a drug as low expenditure if overall average annual spending per enrollee in 2021 was $100 or less. After dropping duplicates, this selection resulted in 438 brand name drugs. We dropped 137 records that included products such as swabs, syringes, vitamins and alcohol pads, which are not rebatable products.

Drug Pricing and Product Characteristics: The primary data source used for drug pricing and product characteristics was AnalySource.[14] Manufacturers report their price changes at the NDC-11 level to independent databases known as pricing compendia. These vendors aggregate the information for purchasers, such as wholesalers, pharmacies, and hospitals under subscription licenses. AnalySource is one such pricing compendia database that reports daily price changes at the NDC level with other product information, such as labeler name, form (oral versus injectable), product type (brand vs generic), multi-source or single-source status, dosage, and strength. In AnalySource, price is defined as the Wholesale Acquisition Cost (WAC) of a given product at the package unit level. WAC does not represent actual transaction prices and does not include discounts, rebates, or other reductions in price.[15] WAC is also a national drug price that does not vary based on health insurer. The sample included all drugs with price changes between January 1, 2011, and October 31, 2023.[16] This period was

[12] Volume is assessed using the "extended units" variable in IQVIA NSP. "Extended units" are the number of tablets, capsules, milliliters, ounces, etc. of a product shipped in each unit. This number is calculated by multiplying the number of eaches by the product size.
[13] Centers for Medicare & Medicaid Services. (2023). Medicare Part D Spending by Drug. https://data.cms.gov/summary-statistics-on-use-and-payments/medicare-medicaid-spending-by-drug/medicare-part-d-spending-by-drug/data
[14] AnalySource: Premier Drug Pricing Services. https://www.analysource.com/contact/#premier
[15] These data sources are different than what CMS will use to calculate the inflation rebates.
[16] This is not the same period for which rebates will be calculated and applied by CMS.

selected to ensure we had pricing information before and after the oldest (February 2, 2012) and most recent (December 27, 2022) shortages in the FDA Drug Shortage Database. By default, the NDCs included in this sample were active NDCs over the period of analysis; NDCs were excluded if they were inactive or discontinued NDCs, and NDCs that did not exhibit a price change during the period of study were excluded because they are not in the AnalySource data. We then calculated price increases during the study period, before and after a shortage. We defined a 'high price increase' as the percentage change in price exceeding the inflation rate associated with the month-year in which the price changed occurred based on the U.S. Bureau of Labor Statistics Consumer Price Index for all Urban Consumers CPI-U.[17] We removed duplicate NDCs from the sample. This sample was further refined to identify only Part D drugs and biological products.

A drug may have multiple price changes before or after it is listed in shortage. Drugs may also appear in the data for shorter or longer periods of time before or after they go into shortage. For instance, some drugs had up to 10 price changes before a shortage but only one price change post-shortage. The period (in quarters) between price changes also varied. To facilitate comparison, we examined price changes over time, 7 quarters before and 7 quarters after the shortage started.

Drug Shortages: Another dataset was the publicly available FDA's Drug Shortages Database (downloaded January 21, 2023).[18] The FDA's Drug Shortages Database includes products whose demand or projected demand for the drug within the United States exceeds the supply of the drug, as determined by FDA. This dataset includes information that is self-reported by manufacturers about drugs in shortage, including the reason for the shortage, start date of the shortage, initial posting date of the shortage designation, date of updates to the shortage status, status of the shortage (current, resolved, discontinued), active pharmaceutical ingredient, therapeutic class, product form, and manufacturer name. The database defines a shortage to be at the active ingredient and route of administration level. Thus, for each shortage, there could be multiple NDCs listed in the FDA Drug Shortages Database. The NDCs in the FDA Drug Shortage Database are either NDC-11s or NDC-10s. The FDA Drug Shortages Database is a static snapshot that does not include all historically resolved shortages, so our results are only reflective of the shortages that were ongoing or resolved as of the download date, January 21, 2023.

We reformatted the NDCs in the FDA Drug Shortages Database to be consistent with the NDCs in AnalySource, i.e., everything was converted to an NDC-11. We dropped duplicate records and records where the NDC or date information was incomplete. We also standardized values in certain data fields that had variations in spelling and created categories for the following variables: reason for the shortage, therapeutic class, and product form. To define the length of a shortage, we calculated duration of a shortage as the difference in days between the start date of the shortage (when the manufacturer reports the shortage to FDA), and the end date, where available. For shortages where the end date was not available, i.e., the shortage is unresolved, we used our download date (January 21, 2023) as a proxy for the end date. This implies that for current shortages, duration denotes the number of days the shortage has been ongoing as of the download date.

Selection for Analysis: We analyzed a Part D drugs and biological product if it met the following criteria: 1) it was primarily dispensed in the "retail" channel using IQVIA data; 2) it had a price change between January 2011 and

[17] For example, consider a case where the price of a drug changed from 211.09 on January 1, 2021 to 221.64 on January 1, 2022. The percentage change in price for this case was 4.9% ((221.64-211.09)/211.09*100). This price increase was determined to be below inflation. The inflation rate for January 2022 was 7.5%, which used the CPI-U for January 2021 (261.58) and January 2022 (281.15), i.e., 100*(281.15-261.58)/261.58.

[18] U.S. Food and Drug Administration. FDA Drug Shortages. https://www.accessdata.fda.gov/scripts/drugshortages/default.cfm

October 2023 as identified in AnalySource data; 3) it was not classified by AnalySource to be a multi-source generic; 4) was not a low expenditure drug, i.e., the average expenditure per drug per enrollee in 2021 exceeded $100 as determined using CMS Part D dashboard data; and 5) it was listed in FDA's January 2023 Drug Shortage Database. We defined a Part D drug and biological product as having a high price increase if it had a price increase that exceeded the rate of inflation at any given time before or after it was listed in shortage.

Methodology: We matched 32,734 NDCs from AnalySource to IQVIA NSP data from 2017 through 2022, the period for which we had access to IQVIA NSP data. After removing records that did not meet the selection criteria, e.g., not a low expenditure drug, not a muti-source drug, etc., the sample included 1,999 NDCs. We then matched this list of 1,999 NDCs to FDA's Drug Shortage Database, which resulted in matching 67 NDCs. We excluded 1932 NDCs that were not matched to FDA's Drug Shortage Database.[19] Among the 67 NDCs that were matched to FDA's Drug Shortage Database, 32 were listed as "currently in shortage", 14 as "discontinued" and 21 as "shortage resolved". The sample of Part D drugs and biological products with a high price increase included 48 NDCs (17, 10, and 21 NDCs were listed as "currently in shortage", "discontinued", and "shortage resolved", respectively).

We conducted our analysis at the NDC level, meaning that each drug was defined as a unique 11-digit NDC. This also means that a drug shortage was defined by an NDC being in shortage.[20] For example, a tablet and capsule shortage of the same drug would count as two different shortages. The advantage of this approach is that we can identify important characteristics about the products involved in shortages, including that some drug forms may be more likely to be in shortage (e.g., injectables may be more likely to go into shortage than tablets), and that there may be variation in price changes and duration of the shortage depending on form differences. The disadvantages of this approach are that we do not capture a broader range of products that may also be affected by the shortages, such as close substitutes, and in circumstances where all dosage-form-strength combinations of a drug experience a shortage, these larger drug groups are not considered together and could affect the number of "drugs" experiencing a shortage.

As noted above, all analyses in this Report were conducted at the NDC level. When CMS calculates inflation rebates, it will aggregate NDCs to the active ingredient level, so it is likely that the exact count of NDCs subject to an inflation rebate waiver or reduction in this analysis will be different than CMS' assessment.

Results

Characterizing the Drugs in the Sample

Our analysis showed that, as of January 21, 2023, out of 1,999 Part D NDCs, 32 drugs and biological products (1.6 percent) were currently in shortage, 14 drugs and biological products (0.7 percent) were discontinued, 21 drugs and biological products (1.1 percent) had a resolved shortage, and 1,932 drugs and biological products (97 percent) were not associated with any shortage (Table 1). Among the 32 drugs currently in shortage, 17 of them (53 percent) were associated with a high price increase (Table 1), thereby making them potentially subject to inflation rebates. While discontinued drugs and drugs with resolved shortages are not subject to inflation

[19] The NDCs that were not matched included products such as syringes, which are not considered rebatable, or other non-retail products which are not in scope of this study.

[20] Because we define rebatable drug and biological products at the NDC level, our counts of shortages will not correspond to the counts of shortages in other studies (e.g., U.S. Food and Drug Administration. Drug Shortages: Root Causes and Potential Solutions, October 2019, updated February 2021. Available at https://www.fda.gov/drugs/drug-shortages/report-drug-shortages-root-causes-and-potential-solutions), which analyzed shortages by defining a drug as a unique combination of active ingredient(s), route of administration, and dosage form, rather than defining a shortage at the NDC level.

reductions or waivers, the majority of these, 71 percent of discontinued drugs and biological products and 100 percent of drugs and biological products that had a resolved shortage, also had high price increases.

Table 1. Number of Part D Drugs and Biological Products by Shortage Status*

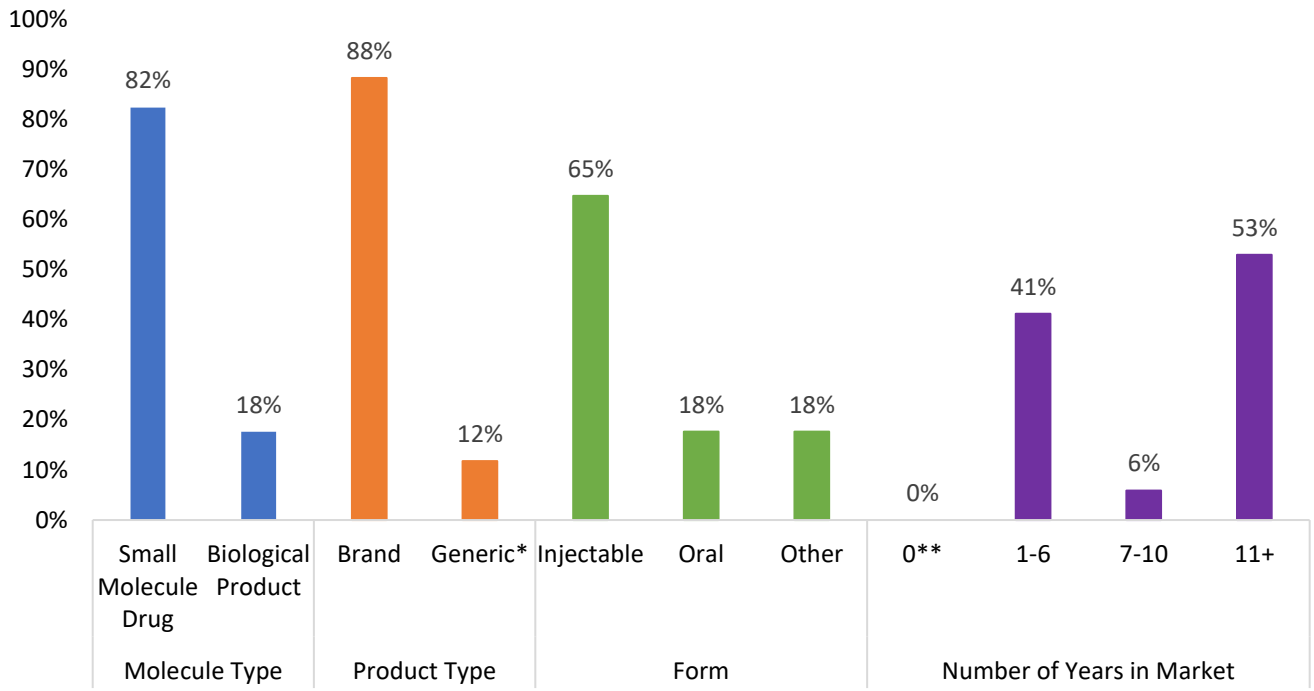
Shortage Status	Any Price Change*	High Price Increase**	
	(N=67)	(N=48)	%
Currently in shortage	32	17	53%
Discontinued	14	10	71%
Shortage resolved	21	21	100%
Total drug products on shortage list	67	48	72%
Total drug products not on shortage list	1932	N/A	N/A
Total drug products	1999	N/A	N/A

*Notes: "N/A" indicates not applicable. Price changes above inflation were determined relative to the start of a shortage. The "%" columns show row percentages. * Sample meets the following criteria: 1) it was primarily dispensed in the "retail" channel using IQVIA data; 2) it had a price change between January 2011 and October 2023 as identified in AnalySource data; 3) it was not classified by AnalySource as a multi-source generic; 4) was not a low expenditure drug, i.e., the average expenditure per drug per enrollee in 2021 exceeded $100 as determined using CMS Part D dashboard data; and 5) it was listed in FDA's January 2023 Drug Shortage Database. ** High price increase Is defined as a price change that exceeds the rate of inflation on the month/year in which the price changed occurred at any point during the period of analysis.*
Source: ASPE analysis of AnalySource (January 1, 2011-October 31, 2023), CMS Medicare Drug Dashboard's Medicare Part D Spending by Drug (2017-2021), FDA Drug Shortage Database, as of January 21, 2023, and IQVIA NSP (2017-2022).

Figure 1 shows the breakdown of Part D drugs and biological products listed as currently in shortage and with high price increases by drug characteristics. Most Part D products meeting these criteria were small molecule drugs (82 percent);biological products comprised 18 percent. A much larger share were brand name drugs (88 percent) than generics (12 percent). The most common forms were injectables (65 percent) followed by oral (18 percent) and "other" (18 percent).[21] Finally, the majority of Part D drugs and biological products listed as currently in shortage and with high price increases had been on the market for more than 11 years (53 percent).

[21] Other form includes drugs such as topicals, ophthalmic, suppositories, patches and aerosols.

Figure 1. Characteristics of Part D Drugs and Biological Products Currently in Shortage and with High Price Increases (N=17)



*Notes: N=17. Other form includes drugs such as topicals, ophthalmic, suppositories, patches and aerosols. *There are no authorized generics in our sample of rebatable drugs and biological products. **This category includes drugs without marketing date information or drugs with a marketing date after January 2023.*
Source: ASPE analysis of AnalySource (January 1, 2011-October 31, 2023), CMS Medicare Drug Dashboard's Medicare Part D Spending by Drug (2017-2021), FDA Drug Shortage Database, as of January 21, 2023, and IQVIA NSP (2017-2022).

Table 2 presents the percent of Part D drugs and biological products based on select drug characteristics of interest. Among all small molecule drugs in shortage, 88 percent had a high price increase while 19 percent of biological products in shortage had a high price increase. Only 2 generic drugs were in shortage and both had a high price increase. In contrast, of the 30 brand drugs in shortage, 15 (50 percent) had high price increases. Forty-eight percent of injectable drugs and biological products in shortage, compared with 75 percent of oral drugs and biological products in shortage, exhibited high price increases. Finally, among all Part D drugs and biological products in shortage, a higher percentage of new drugs and biological products (1-6 years on the market, 88 percent) exhibited high price increases compared to older drugs and biological products (11+ years on the market, 47 percent).

Table 2. Characteristics of Part D Drug and Biological Products Listed as Currently in Shortage

	Status	Any Price Change[2]	High Price Increase[3]	
		(N=32)	(N=17)	%
Molecule	Small Molecule Drug	16	14	88%
	Biological Product	16	3	19%
Product Type	Brand	30	15	50%
	Generic[1]	2	2	100%

	Status	Any Price Change[2]	High Price Increase[3]	
Form	Injectable	23	11	48%
	Oral	4	3	75%
	Other	5	3	60%
Number of Years in Market	0[4]	0	0	0%
	1-6	8	7	88%
	7-10	5	1	20%
	11+	19	9	47%
Total number of NDCs		32	17	53%

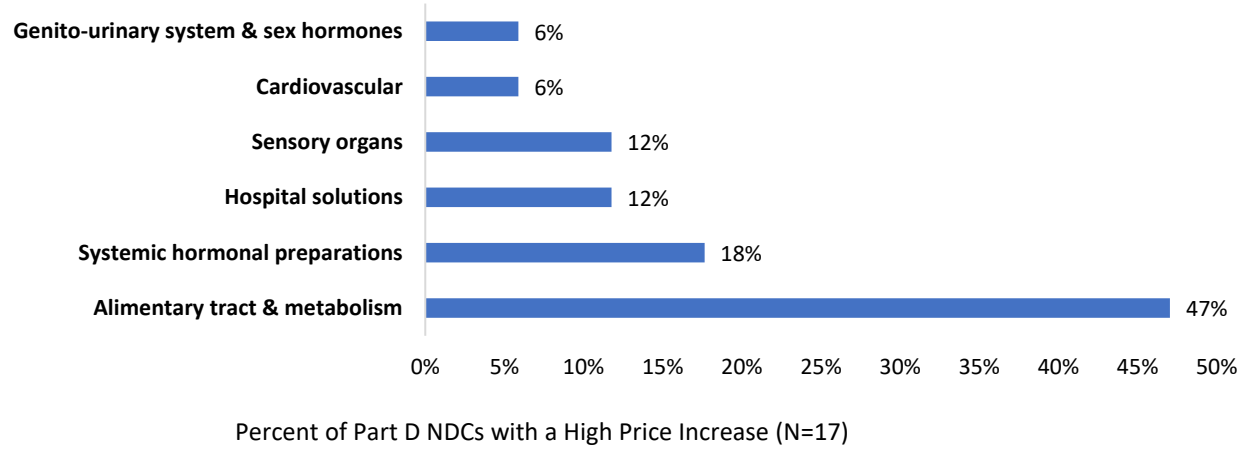
Notes: 1. There are no authorized generics in our sample of rebatable drugs and biological products. 2. Sample meets the following criteria: 1) it was primarily dispensed in the "retail" channel using IQVIA data; 2) it had a price change between January 2011 and October 2023 as identified in AnalySource data; 3) it was not classified by AnalySource as a multi-source generic; 4)was not a low expenditure drug, i.e., the average expenditure per drug per enrollee in 2021 exceeded $100 as determined using CMS Part D dashboard data; and 5) it was listed in FDA's January 2023 Drug Shortage Database. 3. High price increase is defined as a price change that exceeds the rate of inflation on the month/year in which the price changed occurred at any point during the period of analysis.4. This category includes drugs without marketing date information or drugs with a marketing date after January 2023. Other form includes drugs such as topicals, ophthalmic, suppositories, patches and aerosols.

Source: ASPE analysis of AnalySource (January 1, 2011-October 31, 2023), CMS Medicare Drug Dashboard's Medicare Part D Spending by Drug (2017-2021), FDA Drug Shortage Database, as of January 21, 2023, and IQVIA NSP (2017-2022).

Most Common Therapeutic Classes Associated with Shortages and High Price Increases

Figure 2 shows that among Part D drugs and biologicals products listed as currently in shortage and with high price increases, the therapeutic classes most commonly represented were alimentary tract and metabolism (47 percent), systemic hormonal preparations (18 percent), hospital solutions and sensory organs (12 percent each), and finally genito-urinary system & sex hormones and cardiovascular (6 percent each). Using the proxy measure to identify retail drugs in this analysis, our analysis included two drugs classified as hospital solutions which are generally non-retail drugs and are unlikely to be considered Part D rebatable drugs or biological products.

Figure 2. Therapeutic Class of Part D Drugs and Biological Products Listed as Currently in Shortage and with High Price Increases*



*Notes: N=17. Therapeutic class is based on the Anatomical Therapeutic Chemical (ATC) classification system where the active substances are divided into different groups according to the organs or system on which they act and their therapeutic, pharmacological and chemical properties. Drugs classified in the nervous system class include analgesics and anesthetics; drugs in the hospital solutions category include IV and injection solutions; drugs in the sensory organs include ophthalmologicals. * Sample meets the following criteria: 1) it was primarily dispensed in the "retail" channel using IQVIA data; 2) it had a price change between January 2011 and October 2023 as identified in AnalySource data; 3) it was not classified by AnalySource as a multi-source generic; 4) was not a low expenditure drug, i.e., the average expenditure per drug per enrollee in 2021 exceeded $100 as determined using CMS Part D dashboard data; 5) it was listed in FDA's January 2023 Drug Shortage Database; and 6) had a high price increase. ** High price increase Is defined as a price change that exceeds the rate of inflation on the month/year in which the price changed occurred at any point during the period of analysis.*
Source: ASPE analysis of AnalySource (January 1, 2011-October 31, 2023), CMS Medicare Drug Dashboard's Medicare Part D Spending by Drug (2017-2021), FDA Drug Shortage Database, as of January 21, 2023, and IQVIA NSP (2017-2022).

Reasons for Drug Shortages

FDA collects information from drug manufacturers on the cause of drug shortages as required by statute. The FDA Drug Shortages Database is based on information from numerous sources, including information from drug manufacturers through FDA's Direct NextGen Portal, which is set up to capture required fields (as established by statute) as well as other information that is optional or voluntary. For instance, while some manufacturers may voluntarily report other causes of a shortage beyond those required by statue, such as those due to an increase in demand, this is not a requirement. As a result, the FDA Drug Shortage Database has a lot of entries missing information for some key fields such as the "cause of shortage." In our data, 69 percent of shortages did not have an identified or known cause. The data may be missing because the information is not known, because release of this information would exacerbate a shortage, or because the information is required to be withheld from release because it is confidential commercial information. FDA uses the self-reported information submitted as the starting point to assess the nature of the shortage and the underlying reason for it, however the publicly available database is not always updated with the subsequent information learned by FDA. For example, it is possible for a manufacturer to select "Other" as the cause of the shortage, after which FDA may learn during its assessment that the underlying reason is a manufacturing quality issue. This change may not be reported in the publicly available database. Consequently, our results may be misaligned with FDA studies that conclude that 62 percent of drugs that went into shortage between 2013 and 2017 were associated with manufacturing or product quality problems.[22,23] Table 3 provides a breakdown of the publicly known cause of drug shortages among Part D drugs and biological products listed as currently in shortage by price change. This table does not include discontinued and resolved shortages because these drugs and biological products are not eligible for rebate waivers and reductions; the cause for these shortages was either "Unknown" or "Other unspecified" in all cases.

Table 3 shows the reasons for shortages among Part D drugs and biological products with any price change and for each reason it presents the percent that was associated with a high price increase. Although the sample size is small (33 with any price change, and 17 with a high price increase), Table 3 shows that the percent of drugs and biological products with price changes varied by cause of shortages. The only known cause for shortages was a demand increase (4 out of 32 NDCs, or 13 percent) of which 2 drugs and biological products (50 percent) had high price increases. The most common cause of shortages was for drugs and biological products in shortage due to an unspecified reason (59 percent) of which 9 drugs and biological products (47 percent) had high price increases. There were 9 Part D drugs and biological products for which the cause of the shortage was

[22] U.S. Food and Drug Administration. Frequently Asked Questions About Drug Shortages, April 6, 2023. https://www.fda.gov/drugs/drug-shortages/frequently-asked-questions-about-drug-shortages
[23] U.S. Food and Drug Administration. Drug Shortages: Root Causes and Potential Solutions, 2019. February 21, 2020.

unknown, and of 6 these had a price increase (67%). The highest percentage of Part D drugs and biological products with high price increases was for shortages with an unknown cause (67 percent).

Table 3. Reasons for Current Shortages of Part D Drugs and Biological Products with Price Changes

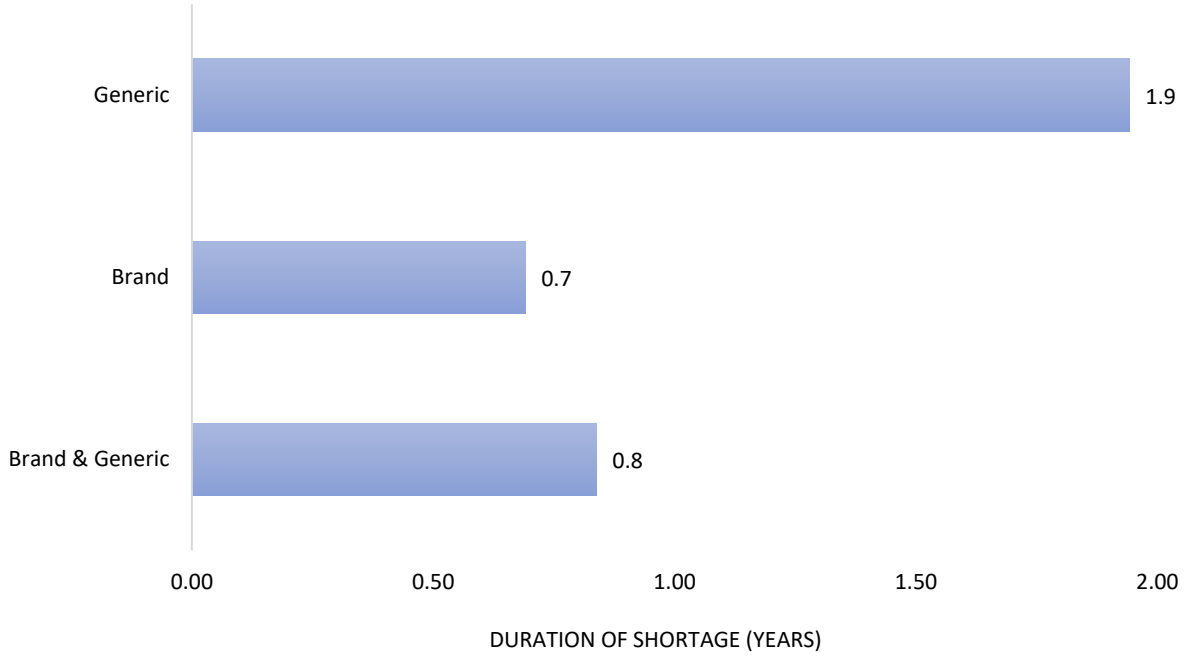
Cause of Shortage	Any Price Change*	High Price Increase**	
	N	N	%
Demand Increase	4	2	50%
Other unspecified	19	9	47%
Unknown	9	6	67%
Sourcing Issues	0	0	0%
Manufacturing Quality Issues	0	0	0%
Total	32	17	53%

*Notes: Price changes above inflation are determined relative to the start of a shortage. The "%" columns show row percentages. * Sample meets the following criteria: 1) it was primarily dispensed in the "retail" channel using IQVIA data; 2) it had a price change between January 2011 and October 2023 as identified in AnalySource data; 3) it was not classified by AnalySource as a multi-source generic; 4) was not a low expenditure drug, i.e., the average expenditure per drug per enrollee in 2021 exceeded $100 as determined using CMS Part D dashboard data; and 5) it was listed in FDA's January 2023 Drug Shortage Database. ** High price increase Is defined as a price change that exceeds the rate of inflation on the month/year in which the price changed occurred at any point during the period of analysis.*
Source: ASPE analysis of AnalySource (January 1, 2011-October 31, 2023), CMS Medicare Drug Dashboard's Medicare Part D Spending by Drug (2017-2021), FDA Drug Shortage Database, as of January 21, 2023, and IQVIA NSP (2017-2022).

Estimated Duration of Shortages

Figure 3 presents the estimated duration of current shortages by product type among Part D drugs and biological products listed as currently in shortage and with high price increases. The data show that the average duration of shortages was more than 2 times longer for generic Part D drugs and biological products compared with branded drugs and biological products (1.9 years versus 0.7 years, respectively). This analysis shows the importance of understanding product characteristics of drugs in shortage and how these characteristics may be associated with the duration of a shortage.

Figure 3. Estimated Duration of Shortage by Drug Product Type: Part D Drugs and Biological Products Listed as Currently in Shortage and with High Price Increases*[24]



*Notes: * Sample meets the following criteria: 1) it was primarily dispensed in the "retail" channel using IQVIA data; 2) it had a price change between January 2011 and October 2023 as identified in AnalySource data; 3) it was not classified by AnalySource as a multi-source generic; 4) was not a low expenditure drug, i.e., the average expenditure per drug per enrollee in 2021 exceeded $100 as determined using CMS Part D dashboard data; and 5) it was listed in FDA's January 2023 Drug Shortage Database. ** High price increase Is defined as a price change that exceeds the rate of inflation on the month/year in which the price changed occurred at any point during the period of analysis. The range duration was (1.94, 2.79), (0.69, 2.69), and (0.84, 2.79) years for "Generic", "Brand", and "Brand & Generic", respectively.*
Source: ASPE analysis of AnalySource (January 1, 2011-October 31, 2023), CMS Medicare Drug Dashboard's Medicare Part D Spending by Drug (2017-2021), FDA Drug Shortage Database, as of January 21, 2023, and IQVIA NSP (2017-2022).

Table 4 presents some of the information from Figure 3 in tabular form, plus additional information on the average duration of shortages by other product characteristics. Generally, the average duration of current shortages tended to be longer for small molecule drugs (1.0 years), generics (1.9 years), orals (1.2 years), and older drugs (1.1 years). Part D drugs and biological products listed as currently in shortage and with high price increases that fell under hospital solutions and sensory organs had the longest shortages (between 1.6 and 1.8 years).

[24] The median and the mean are similar, so for ease of presentation, we only present means for the remainder of this Report.

Table 4. Estimated Duration of Shortages by Product Characteristics of Part D Drugs and Biological Products with Price Changes

Description		Any Price Change[2]		High Price Increase[3]	
		Average Duration (in years)	Std. Error	Average Duration (in years)	Std. Error
Molecule	Small Molecule Drug	1.0	(0.2)	1.0	(0.2)
	Biological Product	0.02	(0.01)	0.01	(0.0)
Product Type	Brand	0.4	(0.1)	0.7	(0.2)
	Generic[1]	1.9	(0.8)	1.9	(0.8)
Form	Injectable	0.3	(0.1)	0.5	(0.1)
	Oral	1.2	(0.6)	1.0	(0.9)
	Other	1.1	(0.5)	1.9	(0.5)
Number of Years in Market	0[4]	N/A	N/A	N/A	N/A
	1-6	0.6	(0.1)	0.6	(0.1)
	7-10	0.1	(0.1)	0.3	N/A
	11+	0.6	(0.2)	1.1	(0.4)
Therapeutic Class	Alimentary tract & metabolism	0.6	(0.2)	0.9	(0.3)
	Cardiovascular	0.9	(0.9)	0.05	N/A
	Genito-urinary system & sex hormones	0.3	N/A	0.3	N/A
	Hospital solutions	1.6	(0.5)	1.6	(0.5)
	Sensory organs	1.8	(0.9)	1.8	(0.9)
	Systemic hormonal preparations	0.01	(0.0)	0.01	(0.0)

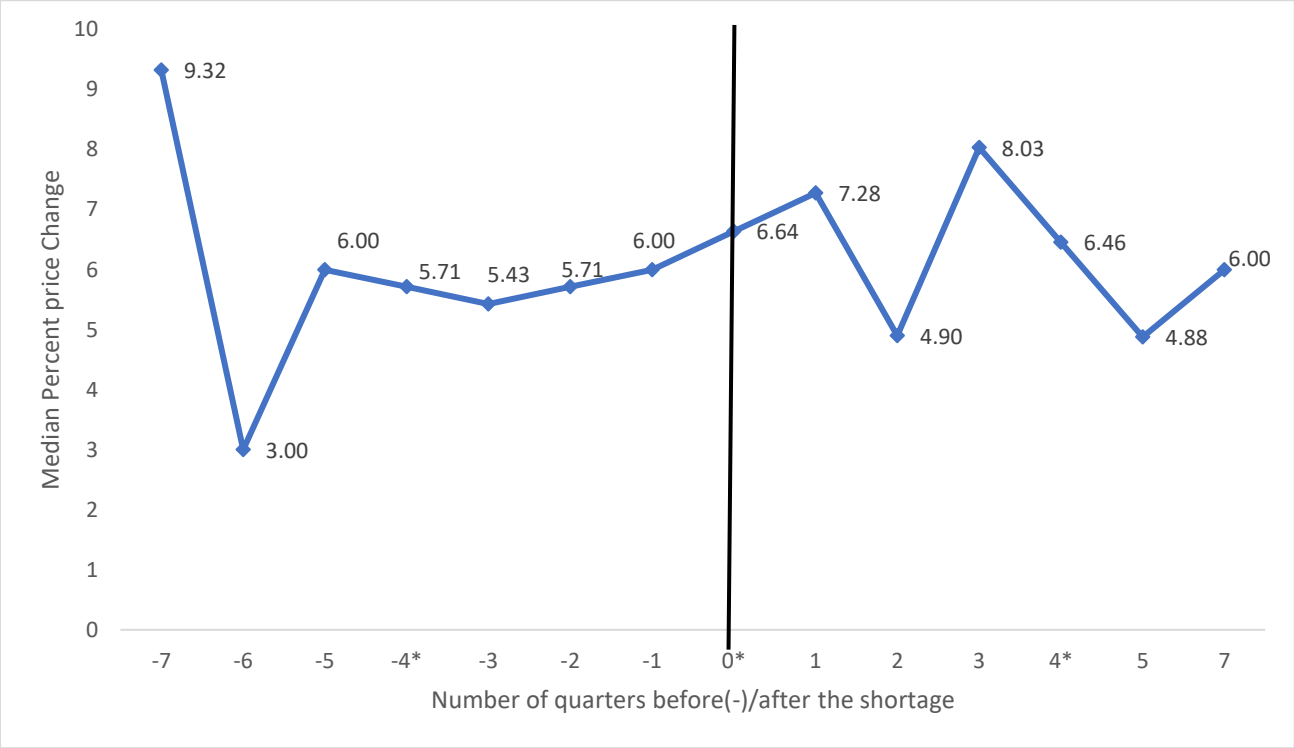
Notes: These categories are mutually exclusive of each other: all drugs are either small molecule drug or biological product, brand or generic, oral or injectable, etc. N/A denotes records for which there were no observations, or the statistic cannot be computed due to sample size; the "High Price Increase" column is a subset of the "Any Price" column. 1. There are no branded generics subject to inflation rebates in our sample of rebatable drugs and biological products. 2. Sample meets the following criteria: 1) it was primarily dispensed in the "retail" channel using IQVIA data; 2) it had a price change between January 2011 and October 2023 as identified in AnalySource data; 3) it was not classified by AnalySource as a multi-source generic; 4) was not a low expenditure drug, i.e., the average expenditure per drug per enrollee in 2021 exceeded $100 as determined using CMS Part D dashboard data; and 5) it was listed in FDA's January 2023 Drug Shortage Database. 3. High price increase Is defined as a price change that exceeds the rate of inflation on the month/year in which the price changed occurred at any point during the period of analysis.4. This category includes drugs without marketing date information or drugs with a marketing date after January 2023.
Source: ASPE analysis of AnalySource (January 1, 2011-October 31, 2023), CMS Medicare Drug Dashboard's Medicare Part D Spending by Drug (2017-2021), FDA Drug Shortage Database, as of January 21, 2023, and IQVIA NSP (2017-2022).

Comparing Median Price Changes Before and After a Shortage

Figure 4 presents median price changes before and after a shortage for all Part D drugs and biological products in our sample, which is limited to drugs listed as currently in shortage and that have a high price increase at any time in the 7 quarters before or after the shortage. We also note that given the small sample size (n=32) in this analysis, results should be interpreted with caution. The x-axis represents the quarter in which median price changes occurred relative to when a shortage started; the y-axis represents the median percent change in price over the prior [month. Median price increases were largest 7 quarters before the start of a shortage. After the

start of a shortage, the median price increase ranged from about 5 to 8 percent, which with the exception of the highest price change, represented similar price changes compared to the pre-shortage period.

Figure 4. Median Percent Change in Price Before and After a Shortage Begins



*Notes: * denote periods for which there is no data and the estimates were imputed as the median of the price change from the quarter before and the quarter after.*
Source: ASPE analysis of AnalySource (January 1, 2011-October 31, 2023), CMS Medicare Drug Dashboard's Medicare Part D Spending by Drug (2017-2021), FDA Drug Shortage Database, as of January 21, 2023, and IQVIA NSP (2017-2022).

Discussion and Conclusion

We found that 1.6 percent (32 of 1,999 NDCs) of a sample of Part D drugs and biological products examined experienced a drug shortage and that 53 percent (17 of 32 NDCs) of them had a high price increase, meaning they could have potentially been eligible for a reduction or waiver under the IRA's Part D inflation rebate provisions. In a companion Part B IRA drug shortages report (see separate ASPE Report),[25] we found that the frequency of shortages among drugs covered by Part D was half that among drugs covered by Part B (1.6 versus 3 percent, respectively). We also found that the number of drugs experiencing shortages in Part D was significantly smaller than in Part B. Part D had 32 shortages and of these, 17 drugs and biological products with high price increases; in comparison, Part B had 144 shortages and of these, 113 drugs with high price increases, meaning there were 4.5 times more shortages and 6.6 times more drugs in shortage with high price increases in Part B compared with Part D. Our analysis does not exactly match the criteria that will be used by CMS and as such, there may be differences in the numbers that ASPE found and how CMS implements the inflation rebate policy.

[25] Beleche, T., Parasrampuria, S., and Adetunji, O. Characteristics of Part B Drugs in Shortage. Washington, DC: Office of the Assistant Secretary for Planning and Evaluation, U.S. Department of Health and Human Services. December 2024.

Our results show that most of the Part D drugs and biological products in shortages and with high price increases affected small molecule drugs, generics, and drugs that have been on the market for up to 6 years. These factors are similar to the characteristics of Part B drugs and biological products in shortage and with high price increases. While there was variation with respect to the types of therapeutic classes affected by shortages, most of the Part D drug and biological products fell into the alimentary tract and metabolism therapeutic class. This analysis also indicates that the duration of a shortage varied widely across drug product characteristics, with small molecule drug, generics, other, and older drugs having the longest shortages. Shortages in Part D lasted almost half as long as those in in Part B. Further, the analysis indicates a correlation between a longer duration of a shortage and price increases that exceed the rate of inflation. Finally, we also found that the greatest median increase in prices, about 9 percent, occurred seven quarters before a drug was listed on the FDA shortage list. This represents a lower median increase, and earlier in the pre-shortage period, compared to Part B drugs and biological products (35 percent median increase, 5 quarters before a shortage). However, unlike Part B, median price increases after the shortage began were about the same as the pre-shortage levels.

Our analysis does not examine specifically the characteristics of shortages associated with severe supply chain disruptions such as natural disasters, so our results cannot be generalized to these types of shortages. Future research could examine the characteristics and duration of shortages due to severe supply chain disruptions. It is possible that other factors, such as company size, number of substitutes, or number of competitors also affect the likelihood of a drug going into shortage and how the shortage is addressed. Also, the COVID-19 pandemic may have exacerbated the frequency and nature of the shortages due to significant disruptions in the supply chains which highlighted dependence on foreign suppliers. An FDA report showed that manufacturing issues are associated with at least 60 percent of shortages.[26] However, in our data, there were zero Part D drugs and biological products in shortage associated with manufacturing issues as the cause of a shortage; most causes were “Other” and “Unknown”. It is possible that this reflects differences in the information that the manufacturer initially reports to FDA and information that FDA receives as part of their response to a notification which may not get updated in the database that is released to the public. In addition, other research has suggested that the reasons for shortages of medical devices differed before and after the pandemic. [27] Further research is needed to assess whether the reasons for drug shortages have changed over time and to assess the type of information that can be shared with the public that may only be internally available to FDA.

These results help provide an assessment of drug shortages and price changes prior to implementation of the IRA’s inflation rebates.

[26] U.S. Food and Drug Administration. (2020). Report | Drug Shortages: Root Causes and Potential Solutions. https://www.fda.gov/drugs/drug-shortages/report-drug-shortages-root-causes-and-potential-solutions

[27] Beleche, T., Kuecken, M., Sassi, A., Toran, K., Galloway, E., Henry, T. Characteristics of Medical Device Shortages in the US, 2006-20. Health Affairs, 2022, 41(12):1790-1794.

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Office of the Assistant Secretary for Planning and Evaluation

200 Independence Avenue SW, Mailstop 434E
Washington, D.C. 20201

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ABOUT THE AUTHORS
Trini Beleche is a Senior Economist in the Office of Science and Data Policy in ASPE.
Sonal Parasrampuria was a Social Science Analyst and FDA portfolio lead in the Office of Science and Data Policy in ASPE when this work was completed.
Oluwarantimi Adetunji is an Economist and NIH portfolio lead in the Office of Science and Data Policy in ASPE.

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