ASPE REPORT

Characteristics of Part B Drugs in Shortage

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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 certain Medicare Part B drugs faster than the rate of inflation. The rebate may be reduced or waived in several circumstances, including if a drug is listed as currently in shortage on the Food and Drug Administration (FDA)'s shortage database or for a biosimilar biological product when there is a severe supply chain disruption.

In this Report, we matched a sample of Part B drugs and biological products that had price changes between January 2011 and October 2023 with the 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 included a drug and biological product in the analytical sample using the following criteria: 1) it was a drug found in the CMS Medicare Part B drug dashboard at any time from 2017 to 2021; 2) it had a price change between January 2011 and October 2023 as identified in AnalySource data; 3) it was listed as currently in shortage in FDA's January 2023 Drug Shortage Database; 4) it was identified as a sole-source drug based on AnalySource's data; and 5) it was not a low expenditure drug, i.e., the average expenditure per drug per user in 2021 exceeded $100. We defined a Part B drug and biological product with high price increases if it was a Part B drug and biological product, as defined previously, and 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 B drugs and biological products with high price increases. We found that a small (3 percent) number of Part B drugs and biological products in the sample were listed in FDA's list of current shortages in January 2023 and that most of these drugs (78 percent) were associated with a price increase that was considered high, i.e., exceeded the rate of inflation. The majority of Part B drugs and biological products with high price increases were small molecule drugs, injectables, 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 4 to 35 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 more details on how CMS will implement this policy, please see Medicare Part B Drug Inflation Rebates Paid by Manufacturers Final Guidance. [1]

[1] Centers for Medicare and Medicaid Services. (2023). Medicare Part B Drug Inflation Rebates Paid by Manufacturers: Revised Guidance, Implementation of Section 1847A(i) of the Social Security Act. https://www.cms.gov/files/document/medicare-part-b-inflation-rebate-program-revised-guidance.pdf.

KEY POINTS

- Certain covered Part B 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 database or, for biosimilars, if there is a severe supply chain disruption.
- We found that 3 percent (144 of 5,028 NDCs) of Part B drugs and biological products on the market between January 2011 and October 2023 experienced a drug shortage, and 78 percent (113 of 144 NDCs) of them had high price increases, i.e., price increases above inflation, meaning they could have been potentially eligible for a reduction or waiver under the IRA's inflation rebate provisions.
- We found that Part B drug and biological products with high price increases that could have been potentially eligible for the IRA reduction or waiver, were small molecule drugs, injectables, and drugs that had been approved longer than 11 years.
- The therapeutic classes of Part B drugs and biological products associated with most current shortages and high price increase were nervous system and hospital solutions.
- Almost two-thirds (63 percent) of Part B drugs and biological products with high price increases did not have a known cause of the shortage listed in the FDA Drug Shortage Database. Among those that had a known cause, 23 percent, 12 percent, and 2 percent were because of an "increase in demand," sourcing issues, and quality issues, respectively.
- The average duration of shortages varied by drug characteristics. Among Part B drugs and biological products currently in shortage and with high price increases, small molecule drugs, generic drugs, injectables and older drugs all had longer shortage durations (3 years) compared to biological products, brand drugs, oral drugs, and newer drugs (about 2 years).
- Among Part B drugs and biological products currently in shortage and with high price increases, the price increases ranged from about 4 to 35 percent--with the largest price increase occurring 5 quarters *before* a drug was officially listed in the FDA Drug Shortages Database. The price change 8 quarters *after* a drug was officially listed as being in shortage ranged from 7 to 10 percent.

Introduction

Medicare Part B[2] program spending in 2021 was $33 billion (about 27 percent) of Medicare drug spending, with annual spending growing, on average, at 9.2 percent over 2008-2021.[3] The IRA requires drug manufacturers to pay inflation rebates for certain Part B single-source drugs and biological products, including biosimilars, with prices that increase faster than the rate of inflation over a calendar quarter (called Part B rebatable drugs). Part B rebatable drugs exclude multi-source drugs, generic drugs, qualifying biosimilar products, low spend drugs (i.e., less than $100 per user per year in 2023 and adjusted for inflation in future years)[4] and preventive Part B vaccines.[5] The IRA has special provisions to allow the Centers for Medicare & Medicaid Services (CMS) to reduce or waive these rebates under two circumstances: (1) when a Part B rebatable drug is described as currently in shortage on the shortage lists authorized under section 506E of the Federal Food, Drug, and Cosmetic Act (FD&C Act) at any point during the calendar quarter; or (2) for a biosimilar biological product when the Secretary determines there is a severe supply chain disruption during a calendar quarter, such as that caused by a natural disaster or other unique or unexpected event.[5]

CMS' final Part B[6] 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 Part B rebatable biosimilar biological product 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 reduction or waiver of the rebate as a means to provide a period of financial relief for manufacturers who are experiencing the negative impacts of external circumstances. 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 drug or biological product in shortage for the purpose of avoiding a rebate. [7]

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

[3] Nguyen X. Nguyen, T. Anders Olsen, Steven H. Sheingold, and Nancy Delew. Medicare Part B Drugs: Trends in Spending and Utilization, 2008 2021. Washington, DC: Office of the Assistant Secretary for Planning and Evaluation, U.S. Department of Health and Human Services. June 2023.

[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] 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

[6] Centers for Medicare and Medicaid Services. (2023). Medicare Part B Drug Inflation Rebates Paid by Manufacturers: Revised Guidance, Implementation of Section 1847A(i) of the Social Security Act. https://www.cms.gov/files/document/medicare-part-b-inflation-rebate-program-revised-guidance.pdf.

[7] Centers for Medicare and Medicaid Services. (2023). Medicare Part B Drug Inflation Rebates Paid by Manufacturers: Revised Guidance, Implementation of Section 1847A(i) of the Social Security Act. https://www.cms.gov/files/document/medicare-part-b-inflation-rebate-program-revised-guidance.pdf.

CMS considers a drug to be in shortage if it appears on the FDA drug and biological shortage lists[8] and has at least one National Drug Code (NDC)-11[9] with its shortage status as "current" on the shortage list during an applicable period or calendar quarter. 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, supply chain disruptions from natural disasters or other unexpected events, or product discontinuation.[10] 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.[11] Manufacturers are also required to report certain reasons for the discontinuance or interruption. These reasons are mainly related to disruptions in supply.[12] 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 the type of product, and the duration of the shortage. Specifically, Part B rebatable drugs that are not plasma-derived products 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 B rebatable plasma-derived products 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 B rebatable biosimilar biological products 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. Price increases are calculated based on either the Average Sales Price (ASP) or the Wholesale Acquisition Cost (WAC) from the Healthcare Common Procedures Coding System (HCPCS) code used 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 B drugs and biological products that are currently in shortage?
- Among those Part B drugs and biological products that are currently in shortage, what share have exhibited high price increases and thus are potentially eligible for inflation rebates?
- 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 B drugs and biological products in shortage and with high price increases?
- What is the average duration of shortages of Part B drugs and biological products with high price increases that may be potentially eligible for inflation rebates? How does duration of shortages vary by product characteristics?
- Among Part B drugs and biological products with high price increases, what is the median price increase before and after the shortage starts?

[8] Food and Drug Administration. Drug Shortages. https://www.fda.gov/drugs/drug-safety-and-availability/drug-shortages
[9] 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.
[10] 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
[11] Section 506C of the FD&C Act.
[12] 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.

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.

For this Report, we matched a sample of Part B 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. As noted above and in the section below, ASPE's methodology differs from the CMS definition in various ways due to data limitations.

Data and Methods

Part B Dashboard Drugs: We used the CMS Medicare Drug Dashboard's Medicare Part B Spending by Drug report (data downloaded November 30, 2023) to identify the sample of Part B drugs and biological products used in our analysis.[13] The database contains Healthcare Common Procedure Coding System (HCPCS) codes, brand name, generic name, total annual spending, and average annual spending per drug per beneficiary for 2017 to 2021.

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 versus generic), multi-source or single-source status, HCPCS codes, product approval dates, dosage, and strength. In AnalySource, price is defined as the 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. WAC is a national drug price that does not vary based on health insurers. The sample included all drugs with price changes between January 1, 2011, and October 31, 2023.[15] This period was 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, 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 a percentage change in price exceeding the inflation rate associated with the month-year in which the price change occurred based on the U.S. Bureau of Labor Statistics Consumer Price Index for all Urban Consumers CPI-U.[16]

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

[13] Centers for Medicare & Medicaid Services. (2023). Medicare Part B Spending by Drug. https://data.cms.gov/summary-statistics-on-use-and-payments/medicare-medicaid-spending-by-drug/medicare-part-b-spending-by-drug/data

[14] Analysource: Premier Drug Pricing Services. https://www.analysource.com/contact/#premier

[15] This is not the same period for which rebates will be calculated and applied by CMS.

[16] 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.

10 price changes before a shortage but only one price change post-shortage. The period (in quarters) between price changes also varies. To facilitate comparison, we examined price changes over time, 8 quarters before and 7 quarters after the shortage started.

Drug Shortages: To identify drug shortages, we used the publicly available FDA's Drug Shortages Database (downloaded January 21, 2023).[17] 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, date of updates to the shortage status, status of the shortage (current, resolved, discontinued), active pharmaceutical ingredient, therapeutic class, product form, NDC 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 of Drugs for Analysis: We included a drug in our analytical sample if it met the following criteria: 1) it is a drug found in CMS Medicare Part B drug dashboard at any time during 2017-2021; 2) it had a price change between January 2011 and October 2023; 3) it was listed in FDA's January 2023 Drug Shortage Database; 4) it is identified as a sole-source drug based on AnalySource's data; and 5) it is not a low expenditure drug, i.e., the average expenditure per drug per user in 2021 exceeds $100. We defined a Part B drug and biological product as having high price increases 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 Part B dashboard data (n=617) to the AnalySource data by HCPCS codes which resulted in matching all but 66 of 617 HCPCS codes. We excluded from our sample HCPCS codes that were not matched to AnalySource, which included vaccines and other products which are not considered to be rebatable.[18] A HCPCS code may be associated with multiple NDCs. Once the Part B dashboard data were merged with the AnalySource data, the sample was refined further to include NDCs that met the following criteria: it was identified as a sole-source drug based on AnalySource's data and it was not a low expenditure drug, i.e., the average expenditure per drug per beneficiary in 2021 exceeded $100 as indicated in the Part B dashboard. This matched sample included 5,028 NDCs. We then matched this list to FDA's shortage database; 222 NDCs were found in the list and their status included, "currently in shortage (144 NDCs)," "discontinued (18 NDCs)," and "shortage resolved (60 NDCs)." We excluded 4,806 NDCs that were not matched to FDA's Drug Shortage

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

[18] The unmatched records included HCPCS codes with the following prefices: 900, A95, J06, J08, J10, J24, J25, J27, J34, J70, and J73, J75, J85, J90, J92, P90, Q01, Q41, and Q51.

Database. Among the 222 NDCs, we identified NDCs with a high price increase as defined above. The sample of Part B drugs and biological products with high price increases included 184 NDCs (113, 12, and 55 NDCs were listed as "currently in shortage", "discontinued" and "shortage resolved", respectively). NDCs that could not be matched between all three data sources were not included in the analysis.

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 (a "drug product") being in shortage.[19] 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 5,028 Part B NDCs, 144 drugs and biological products (2.9 percent) were currently in shortage, 18 drugs and biological products (0.4 percent) were discontinued, 60 drugs and biological products (1.2 percent) had a resolved shortage, and 4,806 drugs and biological products (96 percent) were not associated with any shortage (Table 1). Among the 144 drugs currently in shortage, 113 drugs and biological products (78 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 reductions or waivers, the majority of these, 67 percent of discontinued drugs and biological products and 98 percent of drugs and biological products that had a resolved shortage, also had high price increases.

[19] Because we define Part B 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.

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

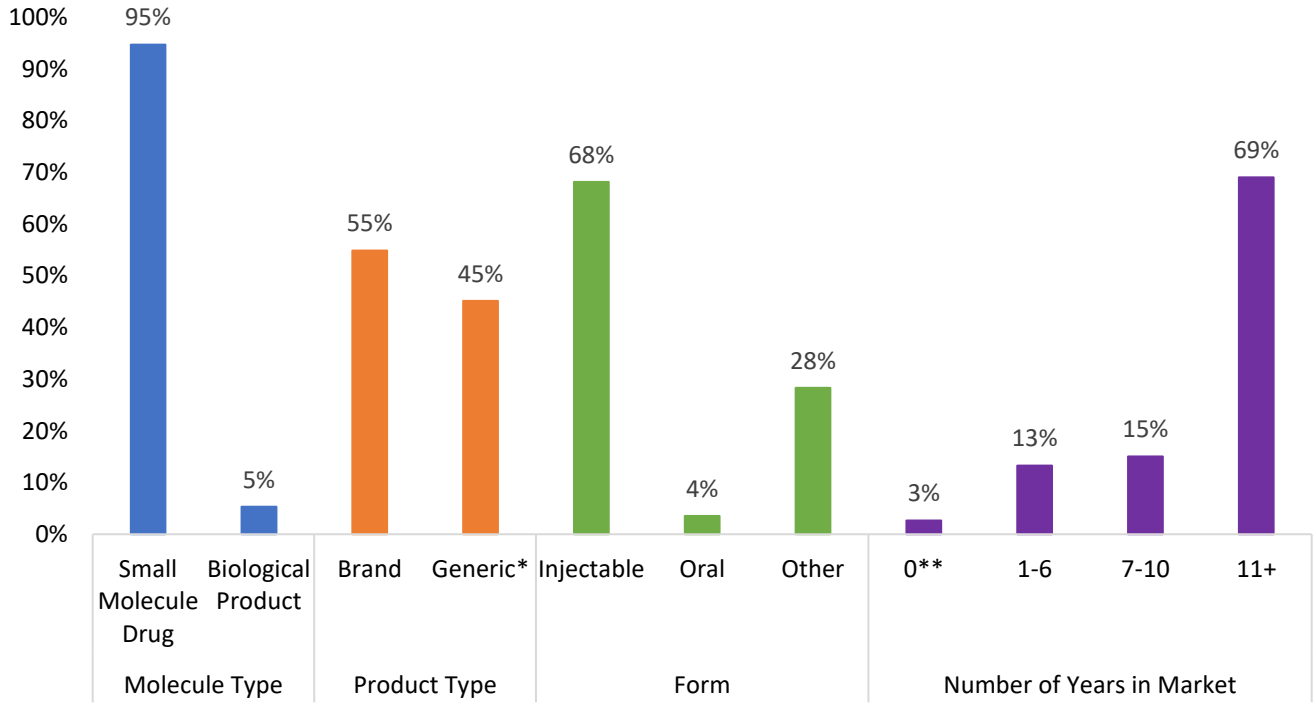
Shortage Status	Any Price Change*	High Price Increase**	
	N	N	%
Currently in shortage	144	113	78%
Discontinued	18	12	67%
Shortage resolved	60	59	98%
Total drug products on shortage list	222	184	83%
Total drug products not on shortage list	4086	N/A	N/A
Total drug products	5028	N/A	N/A

*Notes: The "%" columns show row percentages. * This sample meets the following criteria: 1) Includes a drug found in CMS Medicare Part B drug dashboard; 2) it is identified as a sole-source drug based on AnalySource's data; 3) it is not a low expenditure drug (the average expenditure per drug per beneficiary in 2021 exceeds $100); 4) it is listed in FDA 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 change 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 B Spending by Drug (2017-2021), and FDA Drug Shortage Database as of January 21, 2023.

Figure 1 shows the breakdown of Part B drugs and biological products listed as currently in shortage with high price increases by drug characteristics. Most Part B products meeting these criteria were small molecule drugs (95 percent); biological products comprised 5 percent. A much larger share were brand name drugs (55 percent) than generics (45 percent). The most common forms were injectable products (68 percent), followed by other (28 percent) and oral drugs (4 percent, these products are rarely paid for through Part B).[20] Finally, the majority of Part B drugs and biological products listed as currently in shortage and with high price increases have been on the market for more than 11 years (69 percent).

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

Figure 1. Characteristics of Part B Drugs and Biological Products Listed as Currently in Shortage and with High Price Increases (N=113)



*Notes: N=113. "Other" form products include ophthalmic solutions. *There are no branded generics subject to inflation rebates in our sample of Part B drugs and biological products. **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 B Spending by Drug (2017-2021), and FDA Drug Shortage Database as of January 21, 2023.

Table 2 presents the percent of Part B drugs and biological products based on select drug characteristics of interest. Among all small molecule drugs in shortage, 95 percent had a high price increase while 19 percent of biological products in shortage had a high price increase. More generic drugs in shortage had a high price increase, 96 percent, compared to brand drugs in shortage, 68 percent. Seventy five percent of injectable drugs and biological products in shortage compared with 67 percent of oral drugs and biological products in shortage exhibited high price increases. Finally, among all Part B drugs and biological products in shortage, a higher percentage of new drugs (based on the number of years in the market, 100 percent) exhibited high price increases compared to older drugs and biological products (76 percent).

Table 2. Characteristics of Part B Drugs and Biological Products Listed as Currently in Shortage

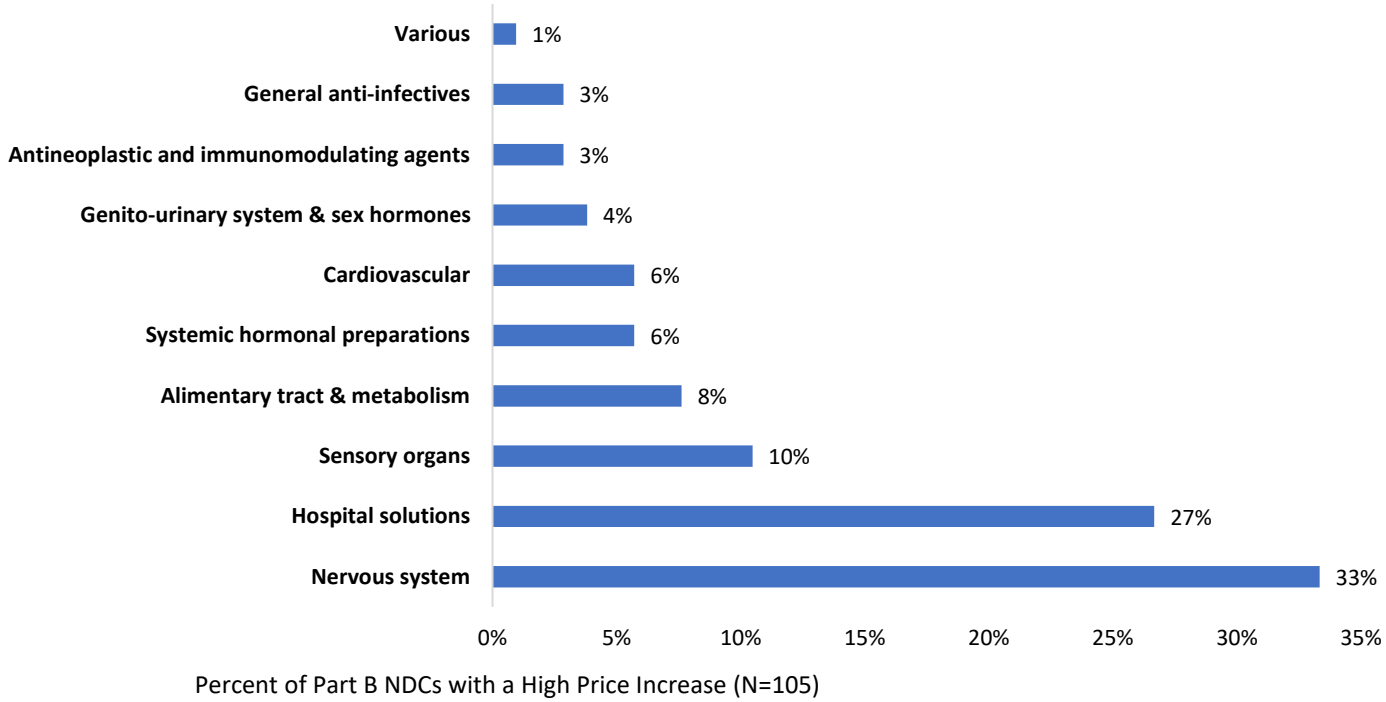
	Description	Any Price Change[2]	High Price Increase[3]	
		(N=144)	(N=113)	%
Molecule Type	Small Molecule Drug	113	107	95%
	Biological Product	31	6	19%
Product Type	Brand	91	62	68%
	Generic[1]	53	51	96%
Form	Injectable	102	77	75%
	Oral	6	4	67%
	Other	36	32	78%
Number of Years in Market	0[4]	3	3	100%
	1-6	18	15	83%
	7-10	21	17	81%
	11+	102	78	76%
Total		144	113	78%

Notes: 1. There are no authorized generics in our sample of Part B drugs and biological products. 2. This sample meets the following criteria: 1) Includes a drug found in CMS Medicare Part B drug dashboard; 2) it is identified as a sole-source drug based on AnalySource's data; 3) it is not a low expenditure drug (the average expenditure per drug per beneficiary in 2021 exceeds $100); 4) it is listed in FDA 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 change 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 B Spending by Drug (2017-2021), and FDA Drug Shortage Database as of January 21, 2023.

Most Common Therapeutic Classes Associated with Current Shortages and High Price Increases

Figure 2 shows that among Part B drugs and biological products listed as currently in shortage and with high price increase, the therapeutic classes most commonly represented were nervous system (33 percent), hospital solutions (27 percent), sensory organs (10 percent), and alimentary tract and metabolism (8 percent). Drugs classified in the class of nervous system drugs include analgesics and anesthetics; drugs in the hospital solutions category include intravenous and injection solutions; and drugs in the sensory organs include ophthalmics.

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



Notes: 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 ophthalmics. The total sample size (N=105) excludes 8 observations with missing ATC information. This sample meets the following criteria: 1) Includes a drug found in CMS Medicare Part B drug dashboard; 2) it is identified as a sole-source drug based on AnalySource's data; 3) it is not a low expenditure drug (the average expenditure per drug per beneficiary in 2021 exceeds $100); 4) it is listed in FDA Drug Shortage Database; 5) 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 change 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 B Spending by Drug (2017-2021), and FDA Drug Shortage Database as of January 21, 2023.

Reasons for Drug Shortages

FDA collects information on drug shortages from manufacturers as required by statute. The FDA Drug Shortages Database is based on information from numerous sources, including information submitted by drug manufacturers through FDA's Direct NextGen Portal, which is set up to capture required fields (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 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, release of this information would exacerbate a shortage, or the information is required to be withheld from release because it is confidential commercial information. FDA uses the self-reported information 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 and for FDA to learn during its subsequent assessment that the underlying reason is a manufacturing quality issue, without the change being 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.[21,22] Table 3 provides a breakdown of the publicly known cause of drug shortages among Part B 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.

Table 3 shows the reasons for shortages among Part B drugs and biological products with any price change and for each reason it presents the percent that was associated with a high price increase. Table 3 shows that the percent of Part B drugs and biological products with price changes varied by cause of shortage. The most common, specified cause for shortages was a demand increase (33 out of 144 NDCs, or 23 percent) of which 26 drugs and biological products (79 percent) had high price increases. The most common cause of shortages was for an "other unspecified" reason (42 percent), of which 43 drugs and biological products (72 percent) had high price increases. Manufacturing quality issues was listed as the cause of shortages of only 2 drugs, both of which experienced high price increases..

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

Cause of Shortage	Any Price Change[2]	High Price Increase[3]	
	N	N	%
Demand Increase	33	26	79%
Other unspecified[1]	60	43	72%
Unknown	33	29	88%
Sourcing Issues	16	13	81%
Manufacturing Quality Issues	2	2	100%
Total	*144*	*113*	*78%*

Notes: 1. The "Other unspecified" category includes one NDC with the cause of the shortage as "available" in the FDA Drug Shortages Database. Price changes above inflation are determined relative to the start of a shortage. The "%" columns show row percentages. 2. This sample meets the following criteria: 1) Includes a drug found in CMS Medicare Part B drug dashboard; 2) it is identified as a sole-source drug based on AnalySource's data; 3) it is not a low expenditure drug (the average expenditure per drug per beneficiary in 2021 exceeds $100); 4) it is listed in FDA 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 change 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 B Spending by Drug (2017-2021), and FDA Drug Shortage Database as of January 21, 2023.

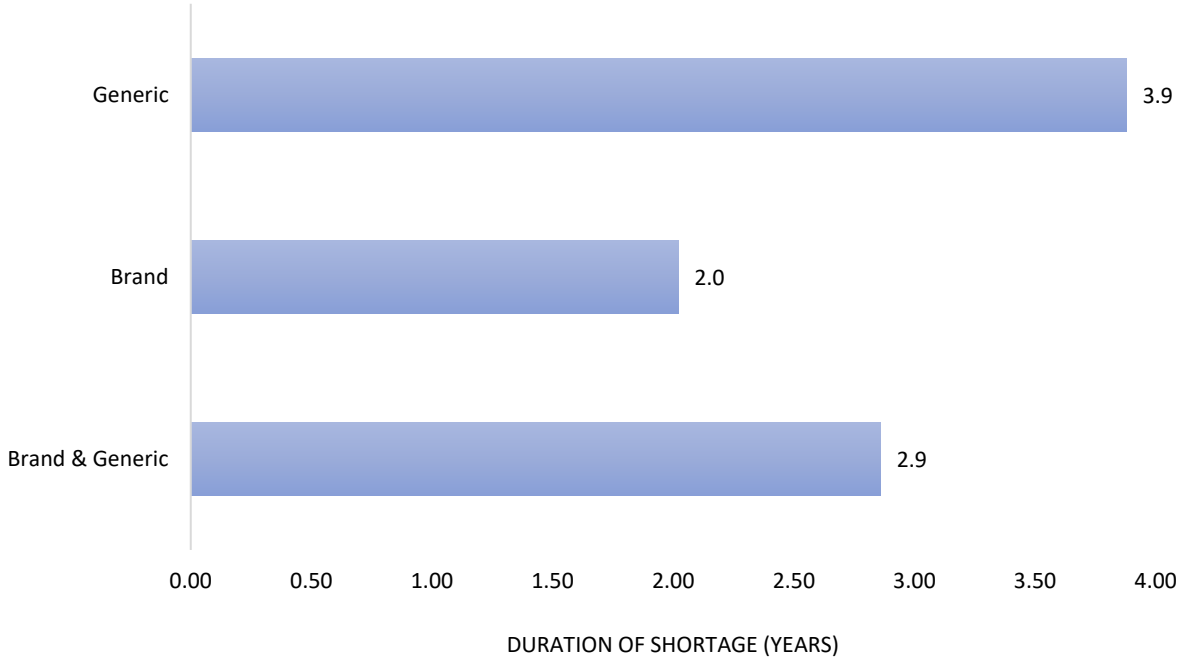
Estimated Duration of Shortages

Figure 3 presents the estimated duration of current shortages by product type among Part B drugs and biological products listed as currently in shortage and with high price increases. The data show that the average duration of shortages was nearly double for generic Part B drugs and biological products compared with branded drugs and biological products (3.9 years vs 2.0 years, respectively). This analysis shows the importance

[21] 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
[22] U.S. Food and Drug Administration. Drug Shortages: Root Causes and Potential Solutions, 2019. February 21, 2020.

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 B Drugs and Biological Products Listed as Currently in Shortage and with High Price Increases*[23]



*Notes: * This sample meets the following criteria: 1) Includes a drug found in CMS Medicare Part B drug dashboard; 2) it is identified as a sole-source drug based on AnalySource's data; 3) it is not a low expenditure drug (the average expenditure per drug per beneficiary in 2021 exceeds $100); 4) it is listed in FDA Drug Shortage Database; 5) 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 change occurred at any point during the period of analysis. The minimum duration was 0 years for each "Generic", "Brand", and "Brand & Generic". The maximum duration was 10.9 years for each "Generic", "Brand", and "Brand & Generic". Source: ASPE analysis of AnalySource (January 1, 2011-October 31, 2023), CMS Medicare Drug Dashboard's Medicare Part B Spending by Drug (2017-2021), and FDA Drug Shortage Database as of January 21, 2023.*

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 (3.0 years), generics (3.9 years), injectables (3.4 years), and older drugs (3.0 years). Part B drugs and biological products listed as currently in shortage and with high price increases that fell under the cardiovascular, nervous system and anti-infective therapeutic classes had the longest duration of shortages (about 4 years or longer).

[23] 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 B 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	2.9	(0.2)	3.0	(0.2)
	Biological Product	0.3	(0.2)	0.4	(0.3)
Product Type	Brand	1.5	(0.2)	2.0	(0.3)
	Generic[1]	3.7	(0.4)	3.9	(0.4)
Form	Injectable	2.6	(0.3)	3.4	(0.3)
	Oral	1.6	(0.5)	1.5	(0.8)
	Other	1.6	(0.2)	1.8	(0.2)
Number of Years in Market	0[4]	2.8	(1.0)	2.8	(1.0)
	1-6	1.9	(0.6)	2.3	(0.6)
	7-10	2.4	(0.4)	2.9	(0.5)
	11+	2.4	(0.3)	3.0	(0.3)
Therapeutic Class	Alimentary tract & metabolism	0.6	(0.2)	0.9	(0.3)
	Cardiovascular	3.8	(1.2)	4.5	(1.6)
	Dermatologics	0.1	(0.0)	N/A	N/A
	Genito-urinary system & sex hormones	0.3	(0.02)	0.3	(0.02)
	Systemic hormonal preparations	0.1	(0.1)	0.3	(0.3)
	General anti-infectives	4.4	(2.0)	4.4	(2.0)
	Hospital solutions	1.8	(0.3)	1.8	(0.3)
	Antineoplastic and immunomodulating agents	2.1	(1.3)	0.8	(0.2)
	Nervous system	5.0	(0.4)	5.0	(0.4)
	Sensory organs	2.0	(0.2)	2.1	(0.2)
	Various	0.9	(0.9)	2.6	N/A

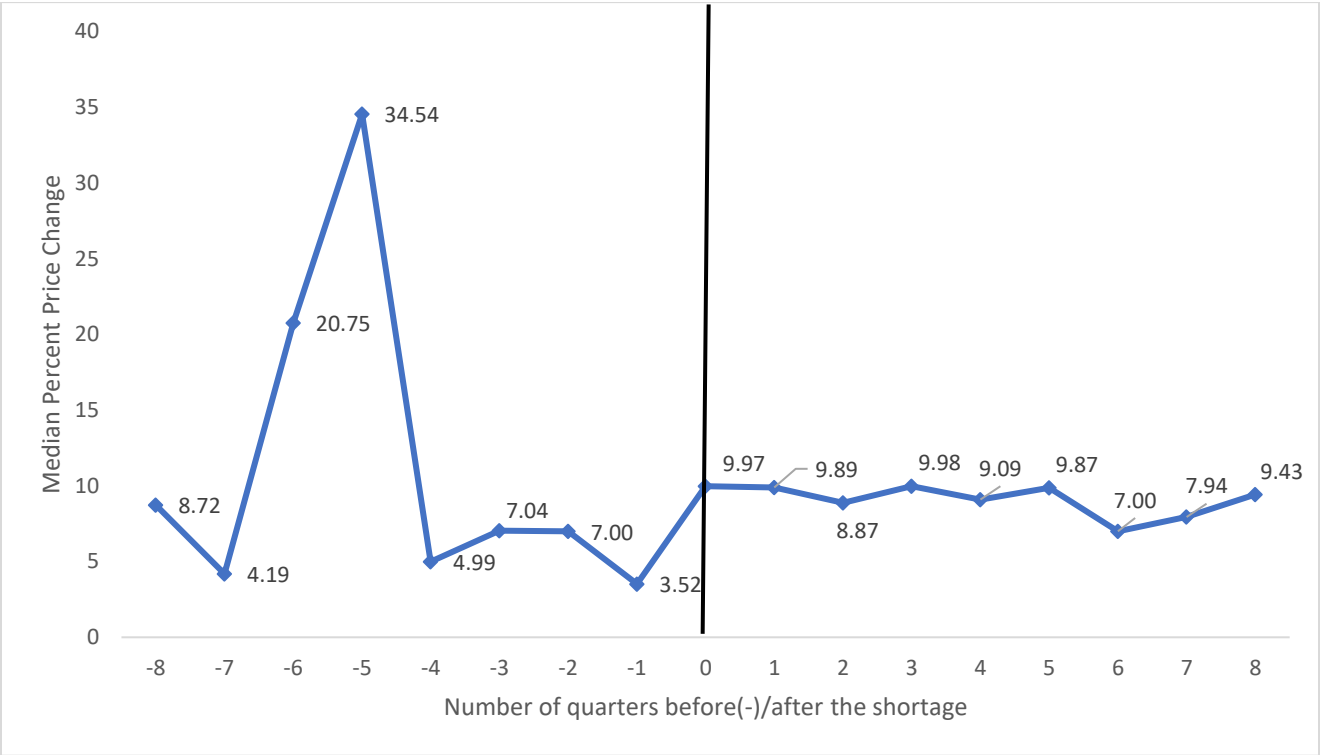
Notes: These categories are mutually exclusive of each other across rows: all drugs are either small molecule drug or biological product, brand or generic, oral, or injectable, etc. N/A denotes records for which there were no observations, or the statistic cannot be computed due to sample size; the "High Price Increase" column is a subset of the "Any Price Increase" column. 1.There are no authorized generics subject to inflation rebates in our sample of Part B drugs and biological products. 2. This sample meets the following criteria: 1) Includes a drug found in CMS Medicare Part B drug dashboard; 2) it is identified as a sole-source drug based on AnalySource's data; 3) it is not a low expenditure drug (the average expenditure per drug per beneficiary in 2021 exceeds $100); 4) it is listed in FDA 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 change 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 B Spending by Drug (2017-2021), and FDA Drug Shortage Database as of January 21, 2023.

Comparing Median Price Changes Before and After a Shortage

Figure 4 presents median price changes before and after a shortage for all Part B 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 8 quarters before or after the shortage. The x-axis represents the quarter in which the median price change occurred relative to when a shortage started; the y-axis represents the median percent change in price over the prior month. Figure 4 shows that Part B drugs and biological products exhibited the highest median price increase (35 percent) five quarters *before* the product was listed in shortage. On average, there is a price decrease right before the shortage. After the shortage starts, the median price increase ranged from about 7 to 10 percent, which was generally higher than the pre-shortage price.

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



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

Discussion and Conclusion

We found that 3 percent (144 of 5,028 NDCs) of a sample of Part B drugs and biological products examined experienced a drug shortage, and that 78 percent (113 of 144 NDCs) of them had high price increases, meaning they could have potentially been eligible for a reduction or waiver under the IRA's Part B inflation rebate provisions. In a companion Part D IRA drug shortages report (see separate ASPE Report)[24], we found that the frequency of shortages in Part B was double that of Part D (3 versus 1.6 percent, respectively). We also found

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

that the number of shortages and the number of drugs in shortage that had high price increases was significantly higher in Part B than in Part D. Part B had 144 shortages and 113 drugs and biological products with high price increases compared with 32 shortages and 17 drugs in Part D, meaning there were 4.5 times more shortages and 6.6 times more drugs with high price increases in Part B compared with Part D--this is despite there being many more drugs in Part D than in Part B. 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.

Our results show that most of the Part B drugs and biological products in shortages and with high price increases affected injectable forms. These factors are somewhat different from the drug types that are potentially most susceptible to Part D inflation rebates, which were most common among small molecule drugs, and relatively newer drugs.[24] While there was variation with respect to the types of therapeutic classes affected by shortages, most of the Part B drug and biological products listed as currently in shortage and with high price increases were in the classes of nervous system drugs and hospital solutions. This analysis also indicates that the duration of a shortage varied widely across drug product characteristics, with generics and injectables having the longest shortages, on average, between 2 and 4 years. It is important to note that shortages in Part B lasted almost twice as long as shortages in Part D.[24] Further, the analysis indicates a correlation between a longer duration of a shortage and high price increases. Finally, we also found that the median percent increase in prices reached its highest level (about 35 percent) more than year before a drug was listed onto the FDA shortage list. In contrast, the highest median price increase for part D drugs and biological products in shortage was 9%.

Our analysis does not examine specifically the characteristics of shortages associated with 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 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.[25] However, in our data, we only had a small number (n=2) of shortages of drugs and biological products that were due to manufacturing issues; 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. [26] 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. The findings point to other product characteristics that are associated with shortages of Part B drugs and biological products beyond those specified in the IRA.

[25] 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

[26] 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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