



## REPORT TO CONGRESS

# Impact of Drug Shortages on Consumer Costs

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U.S. Department of Health and Human Services  
Office of the Assistant Secretary for Planning and Evaluation

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## Office of the Assistant Secretary for Planning and Evaluation

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The Assistant Secretary for Planning and Evaluation (ASPE) advises the Secretary of the U.S. Department of Health and Human Services (HHS) on policy development in health, disability, human services, data, and science; and provides advice and analysis on economic policy. ASPE leads special initiatives; coordinates the Department's evaluation, research, and demonstration activities; and manages cross-Department planning activities such as strategic planning, legislative planning, and review of regulations. Integral to this role, ASPE conducts research and evaluation studies; develops policy analyses; and estimates the cost and benefits of policy alternatives under consideration by the Department or Congress.

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## Executive Summary

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Prescription drug shortages are an ongoing concern in the United States (U.S.). While prior analyses explore the frequency of drug shortages in the U.S., little is known about the extent to which U.S. shortages impact consumer costs and healthcare systems. Drug shortages impact consumer costs in various ways. Consumers may incur increased costs in the form of higher out-of-pocket costs, higher insurance premiums, and adverse health outcomes as a result of a drug shortage. Healthcare systems also incur costs to manage or mitigate drug shortages.

ASPE developed this report to compile findings from a study conducted by the RAND Corporation (hereafter referred to as the RAND Report) and to outline existing and potential tools to address cost disparities and shortages of drugs.

Using an extract from the Food and Drug Administration drug shortage database linked to 2016-2020 national prescription sales data from IQVIA, the key findings are:

- **Drug shortages impact consumers through reduced sales and/or increased prices.** The average drug shortage affects at least a half a million consumers; more than two thirds of those impacted were consumers ages 65 to 85 (32 percent), 55 to 64 (24 percent) and 45 to 54 (17 percent).
- **Drug shortages impact consumers' ability to fill their prescriptions.** After a shortage, there was an observed decline in sales volume of between 28 percent and 35 percent compared to the year before the drug entered a shortage. The reduction in volume of generic drug fills was larger (median of 37.6 percent) compared to brand-name drugs experiencing a shortage (median of 30.4 percent).
- **Drug shortages lead to higher drug prices.** Analysis of the data showed a 16.6 percent increase in the price of drugs in shortage, driven mostly by an increase in the price of generics (14.6 percent). In some cases, the increase in the price of substitute drugs was at least three times higher than the price increase of the drug in shortage.

The report highlights potential policies that could be pursued to address cost increases when there are shortages and to ensure sufficient supply of generic drugs.

# ASPE Summary

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## I. Introduction

Congress directed the Secretary of Health and Human Services (HHS), acting through the Assistant Secretary for Planning and Evaluation (ASPE), to submit a report addressing the following:

*The Committee remains concerned about the shortage of prescription drugs, including generic drugs, in times of international crisis, disaster, or manufacturing shortages. Generic drugs account for 90 percent of prescriptions consumed in the U.S. The Committee directs the Secretary to conduct a study on increased costs to consumers due to shortages of prescription drugs, including generic drugs. The study should outline policy options to address cost disparity when there are shortages in the generic version of life-saving drugs, as well as policy options to ensure sufficient supply of generic drugs. In addition, the study should evaluate how many Americans have faced shortages of their medications.*

In response, ASPE developed this report to compile findings from a study conducted by the RAND Corporation (the RAND Report) and to outline tools and policy options to address cost disparities and shortages of drugs [1]. The RAND Report was conducted at the direction of ASPE to gather and analyze data on the following questions: 1) how many Americans face drug shortages? 2) what types of costs do consumers incur related to drug shortages? 3) how have trends in these costs varied over time? 4) are there differences in shortage costs for generic versus brand shortage drugs, between dispensing locations, or across consumers with different characteristics? 5) what policy options can address drug shortages? The RAND Report examined these questions using findings from the published literature and analysis of data on pharmaceutical sales data for a sample of drugs reported to be in shortage as of March 2020.

This ASPE report and the RAND Report do not include: 1) a national estimate on the number of Americans facing shortages of their medication; 2) estimated costs for the full range of costs to consumers such as out-of-pocket costs, or costs associated with shortage-related changes in health outcomes; 3) trend data on the full range of costs to consumers. HHS does not have access to the appropriate data to adequately examine these questions.

## II. Background

Prescription drug shortages are a persistent public health problem in the United States. The U.S. Food and Drug Administration (FDA) listed 43 new and 86 unresolved shortages of active ingredients during 2020 [2]. FDA considers information provided by manufacturers as well as market sales data on specific products (e.g., the market share of the forms in disruption, manufacturers' inventory, monthly rate of demand, manufacturing schedules, and changes in ordering patterns of the products of interest) to

determine whether the overall market demand is not being met by the manufacturers of the product and whether the drug should be included in its drug shortage list.

Shortages have implications for the healthcare systems and pharmacies that purchase, store, and dispense drugs and for the patients who rely on the availability of drugs to treat and prevent disease. Prior studies have described the impact of drug shortages on the quality and safety of healthcare, patient outcomes, and labor costs to manage or prevent shortages.

Healthcare systems spend resources to manage or mitigate shortages, which have been estimated to be at least \$359 million per year for labor resources and \$200 million per year to purchase alternative treatments [3, 4]. Besides the costs to the healthcare system, patients or consumers may incur direct costs to purchase new or alternative treatments, which may be exacerbated by international crisis, disaster or other external factors. Patient health outcomes may also be impacted when a shortage results in abandonment of therapy, medication errors, delays, cancellations or changes in necessary medical treatment.

Recent studies show an increase in prices of prescription drugs that are in shortage compared to those that are not in shortage (non-shortage drugs) [5]. The rising prices of prescription drugs under shortage suggests that the impacts of shortages on some consumers can be significant.

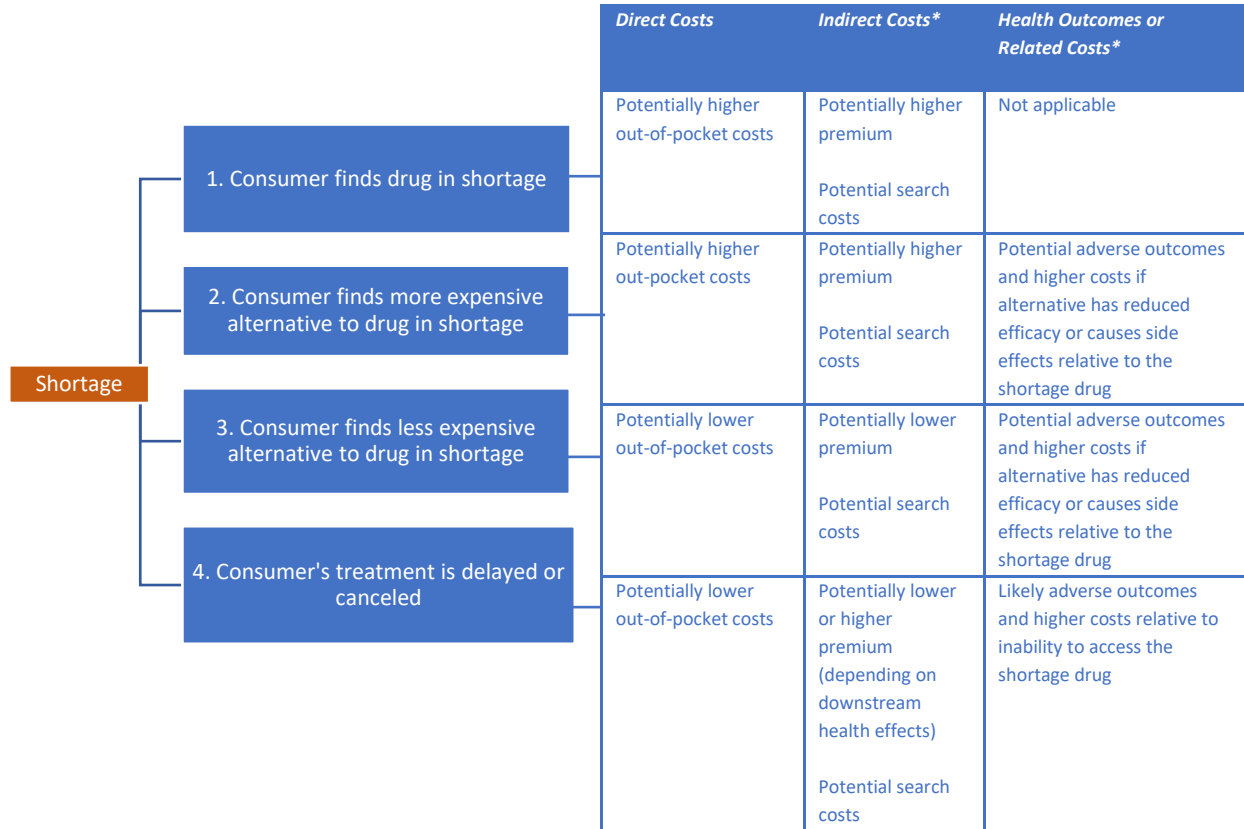
### III. Types of Consumer Costs Associated with Drug Shortages

#### Types of Consumer Costs

Drug shortages affect consumers in different ways. Figure E.1 illustrates the potential impact of drug shortages on consumers which varies by how consumers' medical needs are met when a drug goes into shortage. The types of associated costs include direct costs, indirect costs, and costs associated with adverse health outcomes and related care.

Direct costs are defined as out-of-pocket costs associated with filling shortage and substitute drugs. In response to a drug shortage, consumers may face higher costs in time and effort, such as contacting additional pharmacies and traveling farther distances; these are considered indirect costs. Changes in health outcomes and related care due to shortages (e.g., delays in treatment, receiving a suboptimal substitute, or not receiving treatment at all) can also lead to higher consumer costs and healthcare spending. The implications of drug shortages on consumer costs and health can be more severe when there are few close substitutes for drugs used to treat serious conditions. Increased spending on medical care can lead to higher insurer and payer expenses, leading to higher premiums. Consumers more likely to be affected by drug shortages are those without drug or medical coverage and those with relatively less generous coverage—for example those with high deductibles or co-insurance. (For a detailed description of the framework and types of costs see section 2 of the RAND Report.)

**Figure E. 1: Consumer Responses to Shortages and Associated Costs**



Notes: Figure E.1 adapted and revised from Figure 2.1 of the RAND Report. \*Indicates that the response will be delayed from when the shortage occurred. Search costs are defined as the time and resources that consumers spend to locate the shortage drug. N/A = not applicable.

## Empirical Evidence of Consumer Costs from Drug Shortages

### Direct Costs

A review of the literature revealed limited estimates of direct costs associated with drug shortages. One study reported an increase in annual out-of-pocket costs of between \$167 and \$716 when a drug to treat anemia went into shortage and as a consequence 6.6 percent of patients had to switch to an alternative treatment [6]. Another study found that drug list prices increased by 20 percent in the 11 months after the shortage began, compared with 9 percent when there was no shortage [5]. Other studies found that payments by insurers increased between 4.3 and 14.2 percent on average from drug

shortages [7, 8]. The review of the literature did not lead to estimates of direct costs of drug shortages on consumers over time.

### **Indirect Costs**

While studies have documented the increased cost of consumer time lost to mitigating drug shortages, this study did not find any empirical estimates of their magnitude [9, 10, 11].

### **Costs Associated with Adverse Health Outcomes**

Drug shortages have been reported to be associated with treatment delays or cancelations, poor medication adherence, increased length of hospitalizations, medication errors, and adverse events related to the use of alternative therapies [12, 13, 14, 15], and even deaths [16, 17]. These factors can increase the risk of experiencing an adverse or suboptimal health outcome and avoidable medical event, including death. This study did not find empirical estimates on these costs associated with drug shortages.

## **IV. Estimated Impact of Drug Shortages on Consumers**

The analysis used an extract from the FDA drug shortage database listing ongoing or recently resolved drug shortages as of March 2020. The FDA drug shortage database was linked to 2016-2020 IQVIA's National Sales Perspective data containing estimates of drug-specific monthly volume and payments to manufacturers. The data were also linked to IQVIA's Total Patient Tracker data to obtain estimated counts of unique patients with fills for specific pharmacy-dispensed drugs. Using the linked data, RAND compared the volume and price of drugs listed in the FDA shortage database during the 12-months before and after the start of a shortage.<sup>1</sup> We summarize the findings below.

### **Drug Shortages Impact a Substantial Number of Consumers**

Drug shortages can impact a substantial number of consumers. For the sample of drugs examined, on average, there were more than half a million consumers (652,100) filling monthly prescriptions to meet their medical needs before a drug entered a shortage. Twelve months after the shortage, there was a 10.8 percent reduction in the number of consumers filling monthly prescription fills.

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<sup>1</sup> The change around the shortage start month uses 12-month pre and post-periods. The pre and post periods exclude a ten-month washout period centered on the month in which the shortage began. The washout period allows for uncertainty in the shortage start month. Please see the RAND Report for additional details on the data and methodology, as well as sensitivity analysis conducted.



The impacts on consumers also differed by age groups. Consumers aged 65 to 85 years represented about one-third of consumers filling monthly prescriptions before a drug went into shortage; after a shortage there was an 9.3 percent decline in consumers filling prescriptions in this age group. In contrast, prescription fills for consumers aged 45 to 54 experienced the largest decline (14 percent) after a drug shortage and they represented 17 percent of consumers filling up prescriptions before the drug went into shortage. There was no observed difference in prescription fill rates by gender before or after drugs went into shortage (not shown).

**Table E.1. Estimated Reduction in the Number of Consumers Filling Prescriptions After A Shortage, by Age Groups**

Consumer Age Group	Consumers Filling Prescriptions Before A Shortage		Percentage Reduction in The Number of Consumers Filling Prescriptions After a Shortage
	Total (thousands)	Percent	
<b>0-17</b>	43.3	7%	-0.5%
<b>18-24</b>	20.2	3%	-5.4%
<b>25-44</b>	51.0	8%	-9.8%
<b>35-44</b>	71.9	11%	-10.6%
<b>45-54</b>	112.0	17%	-14.0%
<b>55-64</b>	154.3	24%	-11.8%
<b>65-85</b>	206.2	32%	-9.3%
<b>Unknown age</b>	1.3	0.2%	-15.0%
<b>Total</b>	652.1	100%	-10.8%

*Notes: Table E.1 adapted from Table 4.4 of the RAND Report. Analysis of IQVIA data for a sample of 30 primarily retail pharmacy-dispensed shortage drugs. The estimated reduction was measured around the shortage start month. The change around the shortage start month uses 12-month pre and post-periods. The pre and post periods exclude a ten-month washout period centered on the month in which the shortage began. The washout period allows for uncertainty in the shortage start month.*

### **Drug Shortages Impact Consumers’ Ability to Fill their Prescriptions**

The decline in the number of consumers filling prescriptions of drugs in shortage was usually accompanied by a decline in volume of prescription fills. Volume declined between 27.8 percent and 35.4 percent across shortage drugs around the start of a shortage.

Shortage drugs dispensed primarily through retail pharmacy settings had relatively larger reductions in volume (median of 66 percent) compared with shortage drugs dispensed primarily through hospitals (55 percent) or other settings (e.g., clinics or other) (29 percent). The reduction in volume of generic drugs in shortage was higher (median of 37.6 percent) compared to brand-name drugs in shortage (median of 30.4 percent).

## Drug Shortages Can Lead to Higher Drug Prices

The impact of drug shortages on consumer costs was examined by analyzing changes in trade level prices or prices paid by pharmacies, which for brevity we refer as “prices.” This implies that trade level prices reflect the changes in drug prices that consumers would experience when a drug goes into shortage. For insured consumers, it further assumes that the prominent cost-sharing structure is that of co-insurance. The results show an observed increase in price between 7.2 percent and 16.6 percent twelve months after a shortage occurs. Retail dispensed drugs in shortage had larger increases in price (14 percent) compared to those dispensed in the hospital (1 percent) or other types of (5 percent) distribution. Generic drugs in shortage had larger increase in prices (median of 14.6 percent) compared with brand-name drugs (median of 0 percent).

## Changes in Volume and Price: A Case Study of Five Drugs

Table E.2 presents changes in volume and price for five drugs and their substitutes. Table E.2 shows that changes in volume and price varied by the type of drug in shortage, the number of alternative treatments available, and the cause of the shortage. Among these case studies, unexpected changes in demand or supply with few substitutes available seemed to have the greatest impact on the price of substitute drugs. Consider the case of belatacept, a drug used to prevent organ rejection and with few alternatives available, and which experienced a shortage due to an increase in demand in October 2016. The increase in demand of belatacept can be seen in the resulting increase in volume of 46.4 percent over the 12 months following the shortage. In the 12 months following the shortage the average price of alternative drugs for belatacept increased more than the price of belatacept (18.1 percent vs 5.7 percent); the corresponding change in volume was an increase of 3.8 percent for the alternative drugs. By contrast, the shortage of asparaginase, due to manufacturing and capacity constraints in March 2017, resulted in an increase in the price of alternative drugs of 73.7 percent, while the price of asparaginase decreased by 45 percent. The extent to which quality is reflected in price suggests that the manufacturing issues that resulted in the shortage could explain part of the decrease in price of asparaginase. The price of alternative drugs decreased in the cases of cardidopa-levodopa, heparin, and valsartan where there were more options available, and the reasons for the shortage involved a discontinuation, voluntary recall, and a hurricane, respectively.

These five case studies illustrate the complexities associated with drugs in shortage and subsequent changes in volume and prices. Changes in prices or volume depend on various factors including, the indication for use, reason for the shortage (increase in demand, supply chain disruption, or manufacturing quality), the number of substitutes available, the number of manufacturers involved in the shortage, and the healthcare setting in which the drug is primarily administered or dispensed.

**Table E. 2. Changes in Volume and Prices 12 Months After Shortages:**

**A Case Study of Five Drugs**

Active Ingredient of Drug in Shortage (Start of Shortage)	Therapeutic Category	Reason for Shortage (Extent <sup>4</sup> )	Available Substitutes	Shortage Drug		Substitute Drugs	
				Volume	Price	Volume	Price
<b>asparaginase<sup>1</sup> (October 2016)</b>	Hematology	Manufacturing issues and capacity constraints (Single manufacturer)	pegaspargase	20.10%	-44.90%	1.6%	73.7%
<b>belatacept<sup>1</sup> (March 2017)</b>	Transplant	Increased demand (Single manufacturer)	abatacept, tacrolimus, cyclosporine	46.4%	5.7%	3.8%	18.1%
<b>cardidopa-levodopa<sup>2</sup> (September 2017)</b>	Neurology	Discontinuation (Multiple manufacturers)	Oral solid ropinirole, pramipexole, and cabergoline	4.1%	6.5%	-10.6%	-27.7%
<b>Heparin<sup>1,3</sup> (November 2017)</b>	Hematology	Hurricane (Multiple manufacturers)	Desirudin, Lepirudin, and Bivalirudin	-32.4%	-12.2%	36.2%	-54.5%
<b>valsartan<sup>1</sup> (August 2018)</b>	Cardiovascular	Voluntary product recall due to safety concerns (Multiple manufacturers)	losartan, olmesartan, telmisartan, irbesartan, and candesartan	-52.0%	35.9%	169.2%	-30.6%

Notes: Table E.2 adapted from Appendix C of the RAND Report. Analysis of IQVIA data. The estimated reduction was measured around the shortage start month. The change around the shortage start month uses 12-month pre and post-periods. The pre and post periods exclude a ten-month washout period centered on the month in which the shortage began. The washout period allows for uncertainty in the shortage start month. 1. As of December 4, 2021, this shortage was ongoing. 2. This drug has been discontinued. 3. As of August 6, 2020, Heparin has been listed in the Food and Drug Administration’s List of Essential Medicines. 4. Extent refers to how many manufacturers were involved in the shortage.

**V. Tools to Address Drug Shortages**

**Existing Tools**

Various actions, including Executive Order 13588 on Reducing Prescription Drug Shortages from 2011, the enactment of the Food and Drug Administration Safety and Innovation Act in 2012, the Further Consolidated Appropriations (CREATES) Act of 2020, the Coronavirus Aid, Relief, and Economic Security Act of 2020, and the Inflation Reduction Act (IRA) of 2022 provide the basis for some of the tools available to address drug shortages. These tools include:

- Requiring manufacturers of certain drugs and active pharmaceutical ingredients (APIs) to notify FDA and provide information on permanent discontinuation of manufacturing and interruptions in manufacturing that are likely to lead to meaningful disruption in supply in the U.S.,
- Requiring FDA to prioritize and expedite the review of certain applications and inspections, as appropriate,
- Requiring manufacturers of certain drugs or of any API or any associated medical devices used for preparation or administration included in those drugs to develop, maintain, and implement, as appropriate, a redundancy risk management plan, [18] and
- Requiring registrants of drug establishments to report annually on the amount of each listed drug that they manufactured, propagated, compounded, or processed for commercial distribution. [19]

In addition, FDA has taken the following steps, among others, to prevent or mitigate shortages [20], including:

- Working with manufacturers willing and able to increase production of certain drugs in shortage,
- Expediting inspections and reviews of submissions to increase supply of products in shortage,
- Reviewing requests for extensions of expiration dating as well as working with manufacturers to determine whether there are data to support extending expiration dates of certain drugs in shortage,
- Exercising temporary regulatory flexibility for sources of medically necessary drugs, and
- Issuing emergency use authorizations, under a public health emergency, for certain therapeutic treatments and patients.

Furthermore, outsourcing facilities under section 503B of the Federal Food, Drug, and Cosmetic Act (FD&C Act) may legally compound drug products that are identical or nearly identical to FDA-approved products that appear on FDA's drug shortage list.

Finally, the Centers for Medicare & Medicaid Services (CMS) is working to implement new IRA authorities that allow the Secretary to negotiate prices for certain high expenditure, single source Medicare Part B or Part D drugs, lower the cost for insulin, and cap out-of-pocket costs under Medicare Part D prescription drug coverage at \$2,000 per year by 2025. The new authorities would disincentivize price increases of some alternative treatments by requiring manufactures to pay a rebate to the government when manufacturers increase the price for covered drugs faster than the rate of inflation. The IRA would provide financial relief to certain manufacturers of drugs affected by shortages or supply chain disruptions by reducing or waiving rebate amounts. See Appendix for additional details and related implementation plans.

## Potential Tools

In this section we discuss other tools that may be considered to address drug shortages and ensure sufficient supply of drugs.

### **Promote and Expedite Market Entry or Faster Approval of Generic Drugs**

Due to market consolidation, some of the drugs that go into shortage have no or few alternative substitutes available, which may further limit the supply of drugs when a drug goes into shortage. FDA's 2019 Drug Shortages Report provided recommendations to "evaluate existing regulatory frameworks and further expedite application reviews and facility processes to accelerate the entry of generics and API suppliers." [21] Exclusivity (i.e., the period of time after approval of certain qualifying drugs during which FDA is prohibited from approving certain competing products) and patent protection provide manufacturers incentives to invest in drug development and thereby increase the supply of drugs. However, often generic drug manufacturers submit applications to the FDA in advance of patent expiration or in anticipation of resolution of a patent dispute. These generic drugs, even if approved, may not be able to enter the market until the patent or exclusivity period expires or is found invalid, which can be a lengthy process before they reach consumers. [22] In other cases, patent infringement risks [23] or insufficient labeling information on brand name drugs such as the name and amount of ingredients needed to duplicate generic drugs could disincentive generic market entry. One of FDA's legislative proposals in Fiscal Years 2023 and 2024 proposes amending legislation pertaining to 180-day patent challenge exclusivity provisions to specify that FDA can approve subsequent applications unless a first applicant begins commercial marketing of the drug to ensure that the exclusivity last 180 days and not multiple years as it occurs under the current law. [24, 25] Further, other legislative proposals for Fiscal Year 2024 seek amendments to create a safe harbor for patent infringement for certain generic drug manufacturers marketing a drug with "skinny labeling", and to require drug manufacturers to disclose full information about the name and amount of ingredients in the product's labeling. [25]

Manufacturers can extend the length of patent protection and exclusivity in multiple ways (e.g., applying for restoration of patent term elapsed during the clinical trial and regulatory review period, receiving additional exclusivity for conducting trials in certain populations or obtaining "secondary" patents covering the drug's manufacturing methods). Shortening the period or narrowing the eligibility criteria for exclusivity would encourage timely marketing of competing products, and could in the short term improve competition in the pharmaceutical market. Similarly, providing full ingredient information that is already available could reduce delays and costs associated with gathering that information in order to meet the requirements for generic approval. Studies have shown that drug prices decline when generic drugs enter the market, [26, 27] so increased availability of generic options could reduce the price of drugs. Modifying the regulatory and statutory framework surrounding patent protection and exclusivity would require legislative support, coordination with multiple regulatory agencies, as well as

implementation and training costs. Because manufacturers' decisions to enter a market are based on future market profits and anticipated costs to bring a drug to market, reducing the duration of marketing exclusivity or patent protections could in the long term reduce profits and discourage research and development of new drugs. The reduction in the pipeline could impact the availability of drugs that may be needed to treat future diseases or conditions.

The Drug Price Competition and Patent Term Restoration Act of 1984 (Hatch-Waxman Amendments) established the existing approval pathway for generic products and includes provisions that involve exclusivities related to new drug applications and certain follow-on applicants and patents. Consequently, implementation of changes to regulations pertaining to follow-on drug approvals and patents would involve FDA and the USPTO. Further, because changes in exclusivity may have impacts on market competition matters covered by the Sherman Act or state-specific unfair competition laws, changes to the approval pathway or patents may also involve coordination with FTC. Implementation of this approach could occur by changing the statutory authorities that impact FDA alone, or in coordination with FDA and USPTO and FTC.

### **Explore Lengthening Drug Expiration Dates**

An approach that could be adopted to help increase the supply of drugs is lengthening drug expiration dates. This approach proposes legislative authority to require, when likely to prevent or mitigate a shortage, that an applicant evaluate, submit data to the FDA, and label a product with the longest expiration date that FDA agrees is scientifically justified. [24] Currently when shortages occur, FDA works with applicants who on a voluntary basis agree to conduct studies or provide evidence to support extending the expiration dates to help alleviate the shortage. Based on stability data provided by the manufacturers and reviewed by FDA, recent examples include drugs such as heparin, epinephrine, and propofol where the data supported the extension of use to be a year longer than labeled. [28, 29]<sup>2</sup> Studies that have examined testing and stability of certain marketed drugs have shown that the stability period can be highly variable, and suggest that more data can support longer expiration dates. [30, 31, 32] Due to this variability, extending the expiration date would involve additional costs for those manufacturers that do not already conduct periodic testing and systematic evaluation. In addition, there could be government costs associated with preparing and issuing guidance or other information that would reduce the uncertainty of the regulatory process and evidence necessary to support longer drug expiration dates. The potential cost savings from the current process, where this is done on an ad-hoc basis, could offset the overall cost. Further, there could be cost savings by reducing wastage or disposal of drugs by healthcare providers, hospitals, nursing homes, and agencies managing the strategic national stockpile who otherwise dispose of these drugs due to legal restrictions and liability concerns.

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<sup>2</sup> FDA regulations (21 CFR 211.166 as well as related sections 211.137 and 211.160) require drug applicants to provide stability testing data with a proposed expiration date. However, the proposed expiration date may not reflect the actual long-term stability of the drug. This legislation has been proposed in the President's Fiscal Years 2023 and 2024 budget and in FDA's Drug Shortages Task Force report [33].

Implementation of on the proposed approach to lengthen drug expiration dates through approvals for an expiration date extension or requiring the longest possible expiration date supported by the data could occur through new legislative authority. [20, 33] FDA currently works with applicants, who participate on a voluntary basis, to determine if there is evidence to extend the expiration dates of certain products. Issuing guidance to encourage applicants to conduct more studies to support lengthening the expiration date may not result in wide-spread adoption of this practice because without new legislation such guidance would be non-binding. Development of such policy would involve the usual procedure of seeking input from affected stakeholders which may include providers, consumers, and researchers.

### **Improve Drug Supply Chain Data Collection and Reporting**

A set of tools to improve data collection and reporting from FDA-regulated components of the pharmaceutical supply chain could improve FDA data analytics and capacity related to monitoring and surveillance activities and in turn ensure the supply of drugs. Legislative proposals in Fiscal Year 2024 [25] seek legislation amendments to expand notification requirements to include notifying FDA of an increase in demand, to require certain facilities to create, submit and maintain Site Master Files about the firm's quality management policies, to require labeling to include the original manufacturer and supply chain information, and to enhance the drug manufacturing amount information and reporting requirements.<sup>3</sup>

Currently, FDA gathers some information from manufacturers that shed light on anticipated disruptions to the supply chain. However, the information that FDA receives is limited and does not provide a comprehensive understanding of important vulnerabilities in the supply chain. Collecting additional data such as notifications when a shortage is expected due to an increase in demand, manufacturing volume, and original manufacturer and supply chain information could enhance FDA's visibility into the supply chain. These data would also help develop better surveillance and modeling methods or other tools that can help to more quickly identify potential shortages and to help target resources and outreach efforts more efficiently and more proactively. [34]

Although it may be expected that manufacturers may have some of this information available, such information may be too fragmented and inconsistently captured across the supply chain to be readily transmitted and analyzed, or to be of good quality. [35] There might be government costs to create standardized procedures and collect standardized data. Given the potential for information that may be considered trade secrets, the government might also incur costs to establish infrastructure and systems to securely share, store and handle the data. The anticipated volume of data may result in additional government investments in analytic capability. To implement this approach, industry would bear the cost of complying, which would vary based on the firm's existing processes and capabilities.

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<sup>3</sup> The President's 100 Day Supply Chain Review noted critical sources of data such as distribution data on prescription drugs and certain biologics, requiring manufacturers to notify FDA of an increase in demand and requiring that the labeling of API and finished product labeling include original manufacturers. [20]

Implementation of this approach could occur through a combination of efforts that involve changes in FDA legislative authority, regulations or guidance, and coordination with affected stakeholders. Alternatively, FDA may issue guidance to encourage reporting but participation would be voluntary.

## **VI. Conclusion**

This report responds to the request from Congress for ASPE to examine consumer costs due to shortages of prescription drugs. The report found that drug shortages typically impact consumer costs through higher prices of drugs in shortage and their substitutes, as well as through reduced access to drugs. The report found that in some cases the increase in the price of substitute drugs can be substantially higher than increases in the price of the drug in shortage, that the price increases for generic can be larger in comparison to the price increases for brand-name drugs, and that shortages impact a substantial number of consumers. Higher manufacturer prices could translate into higher consumer costs through higher out-of-pocket costs or higher overall drug spending and potentially higher premiums in the future. Potential policy tools discussed in this report such as those to ensure sufficient supply of drugs can improve visibility and resilience of the drug supply chain, and enhance the availability and affordability of critical drugs for consumers. Analysis of the range of potential policy tools points to careful consideration of the unintended consequences to develop cost-effective policy that works out as intended.

## **VII. Appendix: Additional Tools for Consideration**

For purposes of this section, a tool may be a policy, law, or other action that could be under implementation, or could be considered for implementation with the appropriate authority. We also discuss potential stakeholders affected as well as intended and unintended consequences of implementing each tool. The discussion is intended to lay out key considerations in the understanding, formulation and development of each tool, and should not be construed to reflect a particular position by the Department or its components, unless otherwise stated. Further, HHS or its components may not have the appropriate authority to implement the tools discussed in this section. Where relevant, we discuss potential pathways, e.g., new legislative authority, issuance of guidance, etc., to implement such tools, but it should not be construed as a request for legislative or departmental action.



## Food and Drug Administration

### Establish A Quality Management System Rating

One of the main root causes of shortages is that the market does not recognize and reward mature quality management and, as a result, many problems related to quality manufacturing result in shortages. [36, 21] Mature quality management systems focus on performance and outcomes that affect customers and patients. They involve continual improvements in infrastructure, risk management practices, business continuity plans, communication in the manufacturing process for more robust oversight and earlier identification of potential supply chain disruptions.

In competitive markets, information can play a key role to incentivize firms to distinguish themselves in other attributes, e.g., service, quality of product, other than price. For example, posting restaurant hygiene ratings or scores has shown to improve restaurant owners' incentives and resulted in improvements in hygiene and reduction in foodborne illnesses [37, 38] Another initiative to promote robust and mature quality management systems may be advanced by the establishment and dissemination of a measure such as a rating, that captures a firms' level of quality management maturity. Such an initiative would increase information to stakeholders, which would then incentivize firms to improve their quality systems and ensure there is adequate supply of needed pharmaceuticals. Quality maturity management (QMM) information could also be used to inform contracting, purchasing and inventory decisions, which may result in greater transparency in pricing decisions.

FDA has proposed the development of a rating system that could incentive drug manufacturers to achieve QMM at their facilities, and that "could inform regulators and purchasers about the performance and robustness of drug manufacturing facilities and give patients increased confidence about the performance in the availability of drugs." [39] This recommendation has also been made in the President's 100 Day Supply Chain Review. [20]

FDA has recently completed a pilot in which FDA contractors developed assessment frameworks based on QMM concepts that were used to assess firms. Implementation of this initiative at a wide scale could occur through development of standards developed by industry or FDA. Industry standards are voluntary agreements that establish requirements for products, practices or operations in medical products and may not necessarily align with the regulatory objectives of FDA to ensure products are safe, effective, and available when patients or consumers need them. For FDA to implement certain requirements, FDA might need new authority. FDA may also be able to coordinate certain activities with state or local partners, which may require establishing agreements, e.g., memoranda of understanding, or potential changes in state, local, and federal laws. Further, the novelty of this program may require drawing from expertise and input from other components of the supply chain such as purchasers, healthcare providers, manufacturers, and other experts familiar with similar programs in other industries. Implementing this initiative at a wider scale would impact the government and pharmaceutical firms. Costs to the government could involve the establishment of the rating system,

training assessors, and time to conduct quality management maturity assessments. Industry would bear the cost of upgrading quality management systems, record keeping and other activities. For firms to invest in quality management systems it is assumed that such investment will result in a good return on investment. If such investment is not profitable, firms may maintain the status quo, which has the potential to exacerbate the problem of drug shortages. Such initiative would also consider the advantages and disadvantages of disseminating ratings, in part or in full, or on a voluntary or mandatory basis, to optimally incentivize firms to improve and maintain QMMs.

### **Promote Use of Advanced Manufacturing Technologies**

Market factors, such as cost pressure, play the central role in firms' decisions to manufacture drugs and compete on the basis of price. The generic pharmaceutical market has consolidated over the last decades [40] and has increasingly outsourced its production to countries with lower labor and manufacturing costs. [41] Promoting the use of advanced manufacturing technologies<sup>4</sup> through regulation and policy could lead to efficiencies in the manufacturing process and thereby reduce production costs. Reduced costs could lead to increased profit margins, which can incentivize an increased supply of drugs in shortage. Implementation of this tool would require industry investment in research and development, equipment, personnel training, and establishment and maintenance of new processes. To keep pace with continuing innovation and deployment of these technologies, the government might incur costs to update regulations and guidance documents as well as to train staff involved in inspection and other compliance activities. Development of new technologies involves risks that influence the potential revenue for manufacturers and their decision to invest in these efforts. Known barriers in adoption of some of these technologies include insufficient funding, competing business priorities, lack of expertise, information systems, and regulatory and compliance. [42] Thus, development and adoption of these technologies assume barriers and incentives to invest in these technologies are addressed.

Implementation of this tool could occur through a combination of efforts that may involve new regulations and guidance, funding, and public-private partnerships. FDA is actively working with medical product sponsors to clarify regulatory and data requirements to support applications using advanced manufacturing technologies. For example, FDA's Office of Counterterrorism and Emerging Threats Advanced Manufacturing Program has helped FDA develop regulatory science tools and metrics, and facilitate industry adoption of emerging technologies. [43] FDA also established the Framework for Regulatory Advanced Manufacturing Evaluation Initiative to support the adoption of advanced manufacturing technologies, following recommendations from a report by the National Academies of Sciences, Engineering, and Medicine. [44, 45] The President's 100 Day Supply Chain Review also noted the potential for advanced manufacturing to improve quality and increase the resilience of the domestic manufacturing base and providing options to accommodate changing supply demands. [20]

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<sup>4</sup> Advanced technologies include technologies that enable on-demand, continuous current good manufacturing quality production of pharmaceuticals.

Additional changes to FDA's authority may be considered that can further incentivize adoption of these new technologies. For example, new regulatory authority could be considered to codify designation or expedited review of certain types of advanced manufacturing technologies. Collaboration and coordination with other U.S. government agencies, academia, research institutes and industry such as the Manufacturing USA Institutes, America Makes, VA, the National Institutes of Health (NIH), the Administration for Strategic Preparedness and Response (ASPR), and DOD, who are also involved in this area, may be necessary to improve knowledge sharing and efficiencies. Given the emerging nature of this field, government agencies could conduct pilots to gain expertise and learnings to inform the development of such program more broadly. Such decisions should consider the appropriate agency to participate, distribute and manage the resources given that some agencies have a regulatory function that may create potential conflicts of interest.

### **Evaluate The List of Essential Drugs and Establish Timelines for Regular Updates**

This tool would involve evaluating the process for developing and updating the list of essential medicines in a timely manner, and mirrors the approach in other countries.

In 1963 Cuba was the first country to launch a list of basic medicines, followed by the introduction of national lists in Tanzania (1970) and Peru (1972). However, the World Health Organization (WHO) was the first to introduce the concept of essential medicines in 1977 and to establish the notion that some medicines were more useful in addressing public health needs. [46, 47] This list has evolved over time and has moved from an experience-based to an evidence-based process including criteria such as public health relevance, efficacy, safety and cost effectiveness. The WHO list is updated every two years. More recently WHO now provides an Essential Medicines List and a List of Essential Diagnostics. [48] The most recent WHO list focuses on cancer and other global health challenges, with an emphasis on "effective solutions, smart prioritization and optimal access for patients." Unlike other countries that use the WHO list, the U.S. history of building a list of essential medicines is short. Prior to the COVID-19 pandemic, the United States did not have such a list. On August 6, 2020, President Trump issued an executive order that directed FDA to identify a list of essential medicines, among other products, that are medically necessary to have available at all times in an amount adequate to serve patient needs and in the appropriate dosage forms, to ensure that the American public is protected against emerging infectious diseases as well as chemical, biological, radiological and nuclear threats. [49]

On October 30, 2020, FDA published a list of essential drugs and devices, as well as the criteria to identify such products. [50, 51] The list includes drugs that meet the criteria of "medical countermeasure" and for which FDA anticipates will be needed to respond to future pandemics, epidemics, and chemical, biological, and radiological/nuclear (CBRN) threats. Many drugs in the list are generic sterile injectables that have been crucial to treat critical ill patients during the COVID-19 pandemic, and many were also in shortage at the time the list was published. Evidence from other countries with a longer history of creating and using a list of essential medicines suggests that there could be wide variation across countries regarding the criteria to include drugs in a list of essential medicines. [52] FDA coordinates with other federal partners on strategies to acquire the products on the

essential list, accelerating domestic manufacturing and identifying and addressing supply chain vulnerabilities. [49] There is more limited information about how industry and providers utilize the list, but comments submitted to the docket on this issue suggest that the list is used to inform anticipated provision of patient care, manufacturing and investment decisions, and selection and updates criteria of manufacturer-specific lists. [51]

In the Presidents' 100-Day Supply Chain Review, [20] HHS described ongoing efforts to gather a consortium to review the FDA Essential Medicines list, to identify those that are most critical, to estimate future needs, and to determine major drivers of drug shortages for drugs in the essential medicines list. FDA's 2019 Drug Shortages Report discussed stakeholders' comments to explore the financial incentives or reporting requirements for essential medicines. [41] Additional research, improved transparency and frequency of updates to the list of essential drugs, can help efforts to improve quality control, drug information, prescriber training, and to lower costs by simplifying procurement, supply distribution and reimbursement. [53, 54]

Implementation of this tool could occur by enhancing HHS ongoing efforts and establishing timelines for future updates. [33] Further, given the nascent nature of this list in the United States, efforts might also consider engagement with international partners to gather evidence and lessons learned from other countries and assess their applicability to the United States. Such efforts could also consider examining how the list of essential medicines in the United States overlaps with those in other countries to better understand potential supply chain vulnerabilities. Relatedly, because the list of essential drugs overlaps with agents or drugs that are classified as medical countermeasures, implementation of this policy would consider coordination with other agencies such as Federal Emergency Management Agency (FEMA) and ASPR. Other agencies to consider given their involvement in providing related services or coverage of potentially affected drugs include DOD, VA, CMS, Agency for Healthcare Research and Quality (AHRQ), Health Resources and Services Administration (HRSA) and the Indian Health Service (IHS).

Finally, because the lists provide information that on their own do not increase the supply of drugs, implementation of this tool would occur in conjunction with other tools and data that inform drug supply decisions. In addition, since there could be unintended consequences of providing regular updates, the proposed approach would seek to understand how manufacturers, payers and patients are utilizing the list to inform decisions regarding selection criteria and timing of updates, as well as to further understand the implication of the list on stockpiling behavior, supply decisions, trade agreements, relationships with trading partners and the pricing of medical products.

## **Centers for Medicare & Medicaid Services**

### **Allow for Fair Pricing Mechanism with Manufacturers**

The Inflation Reduction Act (IRA), signed into law by President Biden on August 16, 2022, requires the Secretary to negotiate prices for certain high expenditure, single source Medicare Part B or Part D drugs, beginning in 2026. The Congressional Budget Office (CBO) estimated that negotiation of certain drug prices can result in savings to Medicare of \$98.5 billion over 10 years. [55] Evidence from Germany and

France, although they have a different healthcare system, suggests that direct negotiation with manufacturers can result in a decrease of drug prices and increase competition. [56, 57] In these cases, negotiation occurred as part of a process aligning drug prices with expected treatment benefits and allowed for rebates or gainsharing to occur when negotiated prices resulted in cost savings to the government.

On January 13, 2022, the Centers for Medicare & Medicaid Services (CMS) published its IRA Drug Price Negotiation Program Implementation Plan which described comment opportunities from various stakeholders including members of the public, people with Medicare and their families, beneficiary and consumer advocates, pharmaceutical manufacturers, health care providers, and other interested parties. [58]

### **Disincentivize Price Increases of Certain Alternative Drugs**

The IRA requires manufacturers to pay a rebate if they raise their prices for certain drugs faster than the rate of inflation. This rebate is paid to Medicare and will be calculated and invoiced by CMS. Starting October 1, 2022, the law establishes the annual Medicare Part D prescription drug inflation rebates for certain drugs and biologicals with prices increasing faster than the rate of inflation. Beginning January 1, 2023, the law establishes quarterly Medicare Part B prescription drug inflation rebates for single-source drugs and biologicals with prices increasing faster than the rate of inflation, and provides for lower Part B beneficiary cost sharing on these drugs and biologicals starting April 1, 2023. The price changes would be based on the average sale price for Part B drugs and the average manufacturer price for Part D drugs, where the rebate amount would be calculated based on the total number of rebatable units furnished in the applicable rebate period and the amount that exceeded the inflation-adjusted benchmark. The inflation adjustment is to be calculated as the change in the Consumer Price Index-Urban (CPI-U) between the benchmark and applicable rebate period. The IRA provides discretion for the Secretary to reduce or waive rebate amount for certain rebatable drugs experiencing a shortage or severe supply chain disruption, such as those on the FDA drug shortage list.

Data show that the top causes of shortages are driven by quality issues, which are a result of lack of incentives for manufacturers to invest in manufacturing quality improvements. [2] This study found that after a shortage occurs, the price of alternative drugs can increase by more than two times the price of the drug in shortage, and that the supply of drugs is substantially reduced when the shortage is associated with supply chain disruptions. This IRA provision could reduce the impact on patients and manufacturers of low margin drugs such as generics by disincentivizing price increases of alternative drugs or when a supply chain disruption causes input prices to increase. However, it has been noted that because shortages often occur for reasons, such as quality manufacturing practices, under the manufacturers' control and because manufacturers have better information on market conditions and their production capacity that certain manufacturers could be incentivized to intentionally create a shortage or maintain a drug in shortage to avoid their obligation to pay a rebate. [59]

On February 9, 2023, CMS published its initial guidance documents regarding the payment by manufacturers of inflation rebates for Part B and Part D drugs. [60, 61] These guidance documents describe CMS' current approach to reducing and waiving rebates for drug shortages and supply chain disruptions. CMS is also soliciting comment on the amount and duration for a reduction or waiver of the rebate amount, and applicable timelines for such reduction or waiver in this scenario, among other topics pertaining to criteria and process to waive or reduce rebates for shortage drugs or supply chain disruptions. CMS stated its intent to structure this policy such that "it provides a period of financial relief for manufacturers in certain circumstances but does not create incentives for misuse" of established reporting processes or "for manufacturers to intentionally maintain their drug in shortage for the purpose of avoiding an obligation to pay a rebate."

### **Cap Out of Pocket Costs**

The IRA includes a full redesign of the standard Part D benefit, lowering out-of-pocket costs for enrollees. Starting in 2024, people enrolled in Medicare Part D who have higher drug costs so that they reach the catastrophic phase of Medicare drug coverage will no longer have to pay cost-sharing toward their prescription drugs in the catastrophic phase. Beginning in 2025, people enrolled in Medicare Part D will benefit from a yearly cap (\$2,000 in 2025) on what they pay out-of-pocket for prescription drugs. They will also have the option to pay their prescription costs in monthly amounts spread over the year rather than all at once, beginning in 2025.

The out-of-pocket spending cap is indexed in future years to the rate of increase in per capita part D costs. The IRA also includes other drug provisions, including waiving the deductible and imposing a cost sharing cap on insulin in Medicare. Under a Medicare Part D prescription drug plan, if an insulin is a covered on the Part D plan formulary, the \$35 cap for a month's supply for each insulin product applies, as of January 1, 2023. This includes any new insulin products that become available during the plan year. An insulin product might also be considered covered in other instances. In addition, under Medicare Part B, if insulin is delivered through a traditional pump that is covered under the durable medical equipment benefit, the cost-sharing amount for a person with Medicare is capped at \$35 for a month's supply of insulin beginning July 1, 2023.

This IRA provision could reduce the economic impact of drug shortages on patients with Medicare. A study that examined the implementation of caps on out-of-pocket payments for specialty drugs (drugs used to treat complex or life-threatening conditions) in three states showed that caps reduced out-of-pocket costs by 32 percent, without a notable increase in health plan spending. [62] This same study also found that the largest reduction was observed in users with the highest level of specialty-drug spending which suggests that policies may be more effective at protecting against very high out-of-pocket costs incurred over a short period of time. Another study suggests that how caps are defined can have different impacts on reducing out-of-pocket costs and the number of individuals benefiting from the cap. [63] Further research is needed to determine the overall impact of the IRA on out-of-pocket caps on patients, including spending of drugs in shortage or therapeutic alternatives.

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