PREMIER TRANSFORMING HEALTHCARE TOGETHER®

July 7, 2023

The Honorable Cathy McMorris Rodgers
Chair
House Energy and Commerce Committee
2188 Rayburn House Office Building
Washington, DC 20515

The Honorable Mike Crapo
Ranking Member
Senate Finance Committee
239 Dirksen Senate Office Building
Washington, DC 20510

Submitted electronically via drugshortages@mail.house.gov

Re: Request for Information to Inform Policymaking on Drug Shortages

Dear Chair Rodgers and Ranking Member Crapo:

Premier Inc. appreciates the opportunity to submit comments to the request for information (RFI) issued on June 12, 2023, to inform policymaking on drug shortages. The RFI seeks to examine the drivers of life-threatening medication shortages, as well as to pursue potential policy solutions to bolster patient access and shore up our critical drug supply chains. Premier applauds your bicameral commitment to minimizing the downstream impact of drug shortages to healthcare providers and patient care. Premier further appreciates the thoughtful approach outlined under your leadership to seek stakeholder input as part of the process of developing consensus policy proposals.

Premier has been a leader in mitigating drug shortages for over twenty years and remains committed to eliminating them. Premier believes that a holistic, multi-stakeholder, and inter-agency approach is necessary to truly address drug shortages. While Premier applauds Congress for its bipartisan and bicameral efforts to date to alleviate drug shortages, drug shortages continue to persist and greater action is necessary to eliminate them, including legislative and regulatory action as well as Congressional oversight. ***Sustainable solutions to address drug shortages must decrease manufacturer barriers to entry, namely the time and cost to enter the marketplace, while maintaining the quality and safety of the product.***

Premier's responses to the RFI focus on understanding the root causes of drug shortages and long-term, sustainable solutions to address them.

I. BACKGROUND ON PREMIER INC. AND OUR LEADERSHIP IN ADDRESSING DRUG SHORTAGES

Premier is a leading healthcare improvement company, uniting an alliance of more than 4,400 U.S. hospitals and 250,000 continuum of care providers to transform healthcare. With integrated data and analytics, collaboratives, supply chain solutions, consulting and other services, Premier enables better care and outcomes at a lower cost. A 2006 Malcolm Baldrige National Quality Award recipient, Premier plays a critical role in the rapidly evolving healthcare industry, collaborating with providers to co-develop long-term innovations that reinvent and improve the way care is delivered to patients nationwide. A key component of Premier's alliance is our Integrated Pharmacy Program, which combines essential clinical and operational data with purchasing power to deliver reduced costs, improved quality, safety and resiliency, and increased knowledge-sharing among healthcare professionals.

A Malcolm Baldrige National Quality Award recipient, Premier plays a critical role in the rapidly evolving healthcare industry, collaborating with healthcare providers, manufacturers, distributors, government stakeholders and other entities to co-develop long-term innovations that reinvent and improve the way care is delivered to patients nationwide. Headquartered in Charlotte, North Carolina, Premier is passionate about transforming American healthcare.

Premier has been a leader in addressing drug shortages for more than twenty years and is committed to eliminating drug shortages from both a policy perspective via legislative and regulatory action as well as pursuing market-based solutions. Premier's multifaceted and ongoing initiatives to mitigate drug shortages include, but are not limited to:

- **Contracting Process** - A key component to Premier's success in mitigating drug shortages is the stringent contracting and vetting process manufacturers who wish to work with Premier must undergo. This includes sharing information regarding the location of their finished dose manufacturing and active pharmaceutical ingredient (API) sources. Premier also collects additional information regarding the source and quality of ancillary items leveraged in the manufacturing process such as glass vials and stoppers that can also play a role in downstream shortages. In addition, all manufacturers participating in Premier programs are vetted to enable more geographically diverse production capability, adequate safety stocks and surge capabilities to meet sudden spikes in demand. Finally, manufacturers are asked to share their redundancy and contingency plans to help mitigate risk and ensure ongoing supply of product.

  Premier maintains this level of detail currently for 5,200 unique National Drug Codes (NDCs). This information, as well as additional supplier attributes, is then utilized by Premier and its hospital-led sourcing committees to make contracting decisions that are in the best interest of high-quality patient care and supply chain resiliency. In many cases, Premier's hospital-led sourcing committees vote to contract with a higher cost supplier due a combination of factors supporting greater quality and resiliency.

- **PremierProRx®** – For the past ten years, Premier has invested in the PremierProRx program that offers longer-term contracts with participating manufacturers – creating a steady demand signal and guaranteed buyer base in exchange for increasing production of generics in shortage, maintaining safety stocks or diversifying sources of supply. Suppliers participating in the program are evaluated on resiliency metrics and pricing along with review of potential supply chain risks.

  Critical product features such as diversity in manufacturing and API sources, history of clean Food and Drug Administration (FDA) inspections, supplier reliability, competitiveness of the market and ability to meet market demand informs decisions around contracting that protects access to critical drugs. The program also helps to better manage inventory and support product identification at the wholesaler and enabling efficient product allocation and helping prevent grey market activities.

  The program currently includes 61 molecules spanning 215 NDCs that are on the FDA and/or American Society of Health System Pharmacists (ASHP) drug shortage list.

- **ProvideGx®** – To build upon Premier's track record of direct contracting for vital healthcare products and the PremierProRx program, Premier established a new subsidiary in 2019 to supply shortage drugs. Known as ProvideGx, the goal of the program is to permanently address the drug shortage problem, ensuring continuous access to life-saving products at an affordable price. ProvideGx also targets and supplies medications that lack market competition and are at risk for shortages and price spikes.

  ProvideGx provides a vehicle for Premier to invest in innovative new business models and partnerships to address drug shortages, including partnering with quality generic drug manufacturers that can supply shortage products, co-funding the development of affordable products that address specific market needs, securing contracts for APIs to help ensure continuous supply, as well as strategic sourcing agreements.

  Premier's ProvideGx program identifies secure, high-quality supply sources for drugs that are or may be at risk of being added to the national drug shortage list. Guided by health systems with more than 1,600 hospitals across the nation, Premier's ProvideGx program creates long-term committed buying contracts that provide participating manufacturers with the surety needed to

increase production or move into new markets. The ProvideGx program is open to all healthcare providers across the nation.

Since its inception, Premier's ProvideGx program has:

- Successfully resolved 14 drug shortages, resulting in their official delisting from the FDA shortage list.
- Ensured uninterrupted supply of many shortage drugs despite demand spikes of more than 150 percent during the pandemic.
- Continued to bring resiliency to the market by incenting the domestic manufacture of vital drugs through investments in VGYAAN and Exela Pharma Sciences, which combined are working to bring new, domestic sources of 20 different shortage drugs and counting to market.

The program currently includes 38 molecules spanning 87 NDCs that are on the FDA and/or ASHP drug shortage list.

- **Commitment Programs** – Premier has found that highly committed programs, such as ProvideGx, deliver consistent supply and help avoid pricing spikes. Commitment improves forecasting, allows the supplier to plan ahead for raw material purchasing (including APIs and components), reduces waste, and optimizes production schedules. When purchasers commit demand over an extended period of time and suppliers reciprocate with capacity and safety stock, market stability ensues.

  The Premier commitment model is open to all drug purchasers in the United States and does not limit participation to select groups of providers or dispensers. Additionally, the committed purchase model can lead to reduced instances of hoarding that further harm disrupted markets, as committed purchasers are ensured of availability of key drugs, leaving remaining limited supplies available to others.

  For example, data demonstrates the success of Premier's commitment programs:

  - Average fill rates of all drugs sold in Premier commitment programs through a dedicated distribution channel have maintained year-over-year fill rates of 90+ percent (97-98+ percent)
  - Average fill rates for the same committed program NDCs through national wholesaler channels = 85 percent
  - Average fill rates for equivalent competitive suppliers = 73.8 percent

  Data also demonstrates how the inability of 340B covered entities to participate in commitment programs adversely impacts them:

  - Average fill rates of all drugs in the PremierProRx private label program (including manufacturer-label NDC equivalent) for participating purchasers = 90 percent
  - Average fill rates for 340B covered entities who opt out of the private label / equivalent manufacturer-label = 80 percent

- **Data Mining** – In certain situations, Premier can utilize its robust data capabilities to predict future shortages and alert the FDA and ASHP, as well as proactively implement drug shortage mitigation strategies. Specifically, Premier's CognitiveRx tool leverages integrated artificial intelligence and machine learning to achieve a 76 percent early detection rate of impending drug shortages at least three weeks prior to the listing of the shortage on the FDA or ASHP drug shortage list.

  Premier also leverages its robust capabilities to share data, for example most recently with the oncology shortages, with agencies such as the FDA, Drug Enforcement Administration (DEA),

Centers for Medicare and Medicaid Services (CMS), and others including the White House to underscore the duration and severity of shortages. During the pandemic, Premier leveraged its data assets and provided a weekly list of 250+ critical medications to the FDA. Premier proactively identified drugs at risk of shortage and helped the FDA consider mitigation strategies to minimize impact to patient care.

- **Healthcare Provider Resources** – Premier maintains a drug shortage website for our healthcare providers that is updated in real-time and is intended to serve as a "one stop shop" for our members by collating shortage information from both the FDA and ASHP. The website provides information and educational materials about therapeutic alternatives, pertinent updates to clinical guidelines, and best practices for handling shortages. Premier also employs a dedicated team of pharmacists that serve as a resource for healthcare providers during drug shortages, including assisting with identifying alternative medication therapies. Finally, Premier publishes a weekly pharmacy newsletter that highlights real-time information about shortages.

- **Interim Solutions** - To help temporarily combat drug shortages while a longer-term strategy is being developed, Premier maintains a network of 503B outsourcing facilities to compound products using current good manufacturing practices (cGMP). Given Premier's commitment to quality and safety, Premier personally audits every 503B outsourcing facility it contracts with using an assessment tool that goes above and beyond FDA and state board of pharmacy requirements.

  In addition, Premier has created a health system-led 503B Advisory Group for insights on outsourcing needs and supplier challenges to support managing supply disruptions, including insource compounding guidance and available alternatives on the market. Premier also engages with the FDA and sits on the FDA Compounding Center of Excellence workgroup where it helps federal partners understand the impact of 503B regulatory decisions on drug shortages and patient care.

- **Manufacturer Relationships** – A tenet of Premier's strategy to end drug shortages is our positive and long-standing relationships with manufacturers. Premier is able to discuss shortages directly with manufacturers and understand the root causes behind the shortage as well as the manufacturer's remediation strategy. Manufacturers tend to be very transparent with Premier as a trusted partner and forthcoming about Title X reporting requirements, sometimes in advance of formally reporting to the FDA.

- **Allocation** – In shortage situations, Premier utilizes a dynamic allocation process via a dedicated distribution channel to help ensure access to an adequate supply of product based upon clinical need. The allocation process helps to prevent hoarding and enables a healthy supply chain for as long as possible while pursuing additional mitigation strategies.

- **Advocacy** - Premier has been, and will continue to be, an active voice in advocating for legislative and regulatory changes to help combat drug shortages. Recent examples of Premier's leadership in this area include:

  - Competitive Generic Therapy (CGT) Pathway – Premier was a major proponent of the CGT pathway and advocated for its inclusion in the Food and Drug Administration Reauthorization Act (FDARA)[1] legislation. Premier applauds the FDA for expeditiously implementing the pathway and approving the first product under the pathway in September of 2018.

  - FDASIA Title X – Premier was a major proponent of the drug shortage notification requirements and advocated for their inclusion in the Food and Drug Administration Safety

[1] Pub.L. 115-52

and Innovation Act (FDASIA)[2] legislation. Premier believes these provisions have been impactful in mitigating shortages.

- CARES Act – Premier served as the lead proponent of the Mitigating Emergency Drug Shortages (MEDS) Act which was incorporated and signed into law as part of the CARES Act in March 2020. Specifically, these provisions:

  - Created a priority pathway for the review of drug shortage applications;
  - Required a report examining national security risks as a result of drug shortages;
  - Strengthened FDASIA Title X reporting requirements to include full disclosure of the problems resulting in a shortage, information concerning the extent of a shortage, its expected durations, and other information the Secretary may require;
  - Extended FDASIA Title X reporting requirements to API manufacturers; and
  - Required manufacturers to maintain redundancy and contingency plans to ensure ongoing supply.

While Premier has made significant progress in reducing the impact of drug shortages to healthcare providers and patient care, more work remains and increased collaboration among supply chain stakeholders is necessary to eliminate shortages once and for all. ***Premier continues to grow and evolve our drug shortage strategy and is committed to innovating and collaborating across diverse stakeholders to prevent and resolve ongoing drug shortages.***

II. DRUG SHORTAGES THREATEN PATIENT SAFETY

Drug shortages continue to plague the healthcare system and have grown in both number and intensity in the past several years.[3] Drug shortages invariably impact patient care, adding time and expense as providers manage supplies and search for therapeutic alternatives that can be less effective and more costly, potentially delaying treatment. Drug shortages are also a major driver of skyrocketing costs – contributing to over half a billion dollars in increased healthcare expenditures annually. A study found that prices for drugs in shortage increased more than twice as quickly as they would in the absence of a shortage – adding $230 million a year to U.S. drug costs.[4] Another study found that the price of fluphenazine tablets in 2016 increased by over 2000% during a shortage.[5]

In addition to the increase in drug prices, drug shortages cause a multitude of downstream impacts to the healthcare system such as:

- Increased labor costs associated with managing drug shortages, estimated to be $216 million annually.[6]
- Increased potential for adverse events, and consequently increased costs to the healthcare system such as increased hospital days due to the unavailability of a critical medication. For example, a shortage of norepinephrine was significantly associated with increased mortality amongst patients

[2] Pub.L. 112–144
[3] FDA Annual Report to Congress for CY 2022. Available at: https://www.fda.gov/media/169302/download?utm_medium=email&utm_source=govdelivery
[4] Hernandez I, Sampathkumar S, Good CB, Kesselheim AS, Shrank WH. Changes in Drug Pricing After Drug Shortages in the United States. Ann Intern Med; 170:74–76. doi: 10.7326/M18-1137
[5] Fox E. R., Tyler L. S. (2017). Potential association between drug shortages and high-cost medications. Pharmacotherapy 37, 36– 42. 10.1002/phar.1861
[6] "Impact of drug shortages on U.S. health systems" (American Journal of Health-System Pharmacy, October 2011). https://www.ncbi.nlm.nih.gov/pubmed/21930639

with septic shock.[7] The FDA estimates that the norepinephrine shortage resulted in $13.7 billion of projected losses to the U.S. healthcare system.[8]

- Decreased procedures and diagnostic testing. For example, a recent shortage of contrast media resulted in approximately 10 percent of patients who needed advanced imaging, such as computerized tomography (CT) scans, unable to receive one.[9] Similarly, current shortages of oncology agents are resulting in healthcare providers having to make difficult decisions regarding rationing available supply and prioritizing which patients should receive treatment.

III. ROOT CAUSES OF DRUG SHORTAGES ARE MULTIFACTORIAL

Premier has worked extensively to identify the root causes of drug shortages and develop sustainable solutions to address them. ***Given that there is no single cause of drug shortages and often multiple contributing factors, there is also no single solution to address drug shortages.*** Congress, the FDA, and the private sector will need to implement multifaceted solutions targeting the various causes of drug shortages to truly eliminate drug shortages for the long-term.

Historically, drug shortages primarily impacted generic sterile injectable drugs utilized in inpatient settings such as anesthetics and opioids. However, in the past two years or so, drug shortages are beginning to expand beyond this market into outpatient products, such as recent amoxicillin and oncology shortages, and brand name products as well, such as recent glucagon-like peptide-1 receptor agonist shortages.

The following outlines several root causes of drug shortages that Premier has identified, including examples of each.

- **Entry of a Low-Cost Competitor** – In recent years, the entry of a low-cost competitor to the marketplace has resulted in a ripple effect that disrupts the supply chain and ultimately results in a drug shortage. In many of these examples, the low-cost competitor enters the market to undercut other manufacturers but does not have the capacity to supply the entire market. Once other manufacturers exit the market due to their inability to compete at the low price point, the market is left with a sole supplier who cannot meet market demands. The following exhibits demonstrate two common examples of how the entry of a low-cost competitor has resulted in a drug shortage.

[7] Vail, Emily, Gershengorn, Hayley, Hua, May, Walkey, Allan, Rubenfeld, Gordon & Wunsch, Hannah. (2017). Association Between US Norepinephrine Shortage and Mortality Among Patients With Septic Shock. JAMA. 317.DOI: 10.1001/jama.2017.2841

[8] 6 FDA Public Hearing Identifying the Root Causes of Drug Shortages and Finding Enduring Solutions. Available at: https://healthpolicy.duke.edu/events/drug-shortage-task-force

[9] https://premierinc.com/newsroom/blog/anatomy-of-a-shortage-a-lack-of-contrast-media-supplies-compromised-care-for-up-to-10-percent-of-patients-in-key-clinical-categories

Exhibit A: Entry of a low-cost competitor results in others exiting the market.

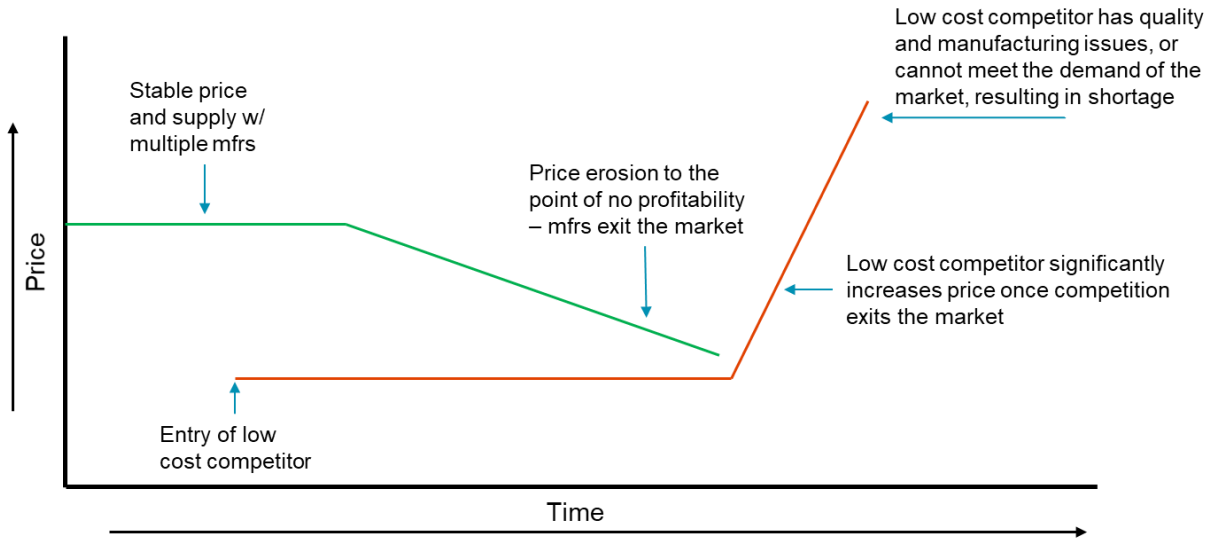
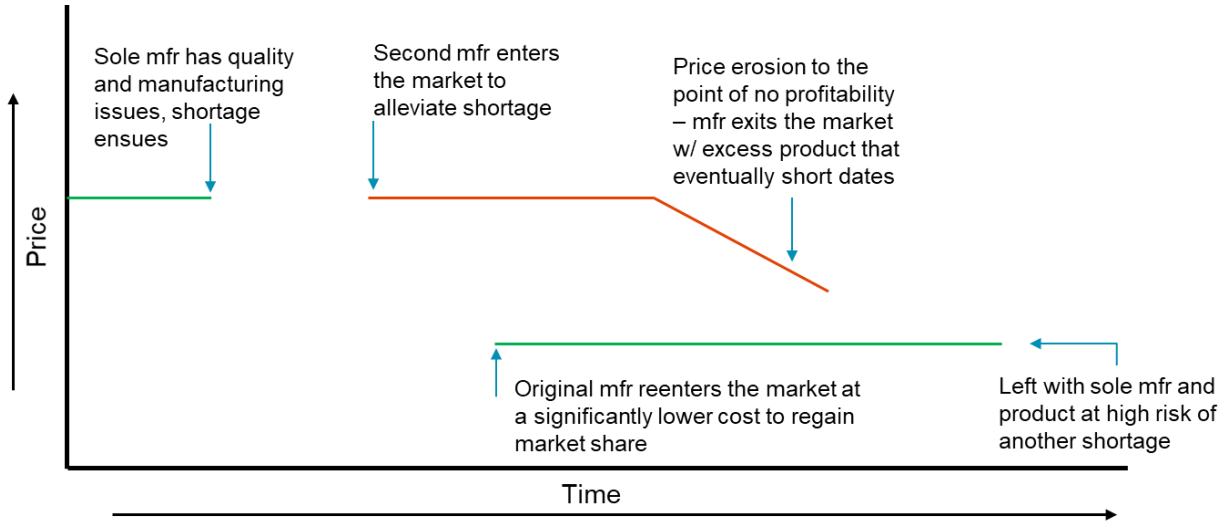


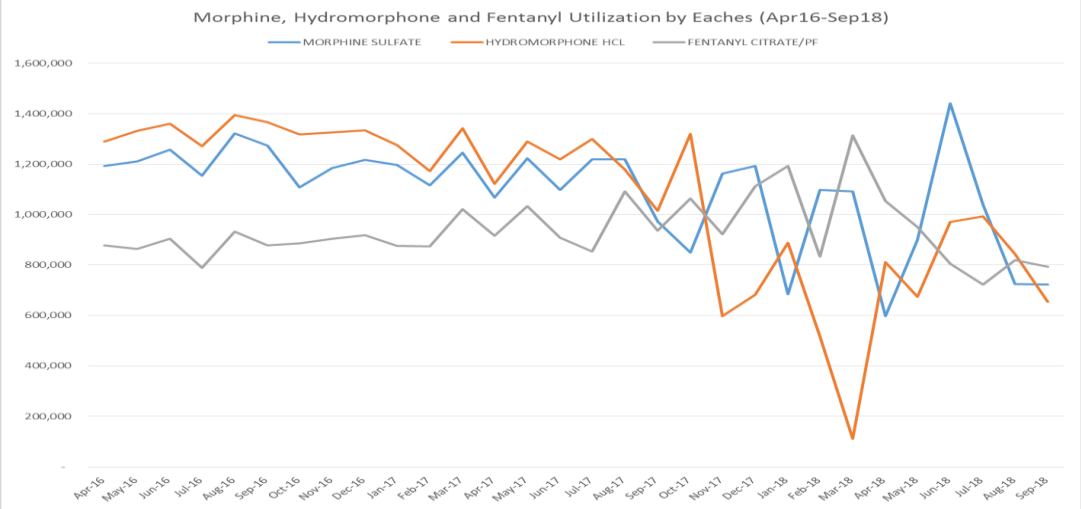
Exhibit B - Reentry of a low-cost competitor results in others exiting the market and hesitant to help mitigate future shortages.



- **Quality and Manufacturing Issues** - In a market with few manufacturers, when one manufacturer encounters quality or manufacturing issues and exits the market for an extended period, downstream pressure is placed on the remaining manufacturers to ramp up supply and fill the market void. In certain scenarios, external factors prevent other manufacturers from increasing production such as capacity restrictions and DEA quota allocations, resulting in drug shortages.

  As depicted in the following exhibit, a nationwide acute shortage of several injectable opioids that are critical for patient care occurred at the end of 2017 due to a single manufacturer encountering quality and manufacturing issues at several of their plants. The issue was further compounded by a lack of immediate coordination between the FDA and DEA to release additional quota to manufacturers who were able and willing to ramp up production to help mitigate the impact of the shortage.

Exhibit C - The ongoing shortage of injectable narcotics has been a major patient safety concern for health systems.



In a more recent example, downstream issues stemming from the FDA's inspection of Intas Pharmaceuticals' manufacturing plant in Gujarat, India, in December 2022, have resulted in a very concerning shortage of critical oncology therapies, namely, cisplatin and carboplatin, followed by methotrexate. Accord Healthcare, a wholly owned subsidiary of Intas Pharmaceuticals, maintained >40% market share for these three oncology therapies. Due to voluntary manufacturing cessation by Accord, the remaining manufacturers are facing a challenge to keep up with demand. In the past several weeks, many health systems have raised alarm of dwindling stock and anxiety over inability to continue to treat their patients with proven therapies.

In Appendix A, Premier shares additional data and insights regarding the impact of Intas Pharmaceuticals' quality manufacturing issues on the available supply of these critical oncology products. Premier shared this data, insights, and call to action with the FDA and White House in May 2023.

- **API or Raw Materials Shortages** - Over 80 percent of APIs and raw materials required for drug manufacturing are produced overseas.[10] The heavy reliance on foreign manufacturing of APIs and raw materials results in downstream drug shortages when a foreign manufacturer fails to meet cGMP or exits the market. In addition, the extent and duration of API or raw material shortages is unknown and results in downstream impact on hoarding and the gray market. Furthermore, the Chinese Blue Sky Initiative is resulting in API and raw material manufacturers being required to either halt production or shut down resulting in concerns that this may further exacerbate shortages, and may result in increased shortages for oral solid dosage forms. Finally, new tariffs are also putting pressure on foreign manufacturers of raw materials and may lead to entities exiting the market resulting in downstream drug shortages.

  For example, the recent valsartan recall was due to an impurity with the API and almost all manufacturers relied on a single API manufacturer, resulting in a major shortage. In addition, the recent injectable opioid shortages were exacerbated by an inability of the manufacturer to acquire the raw materials necessary for the injector.

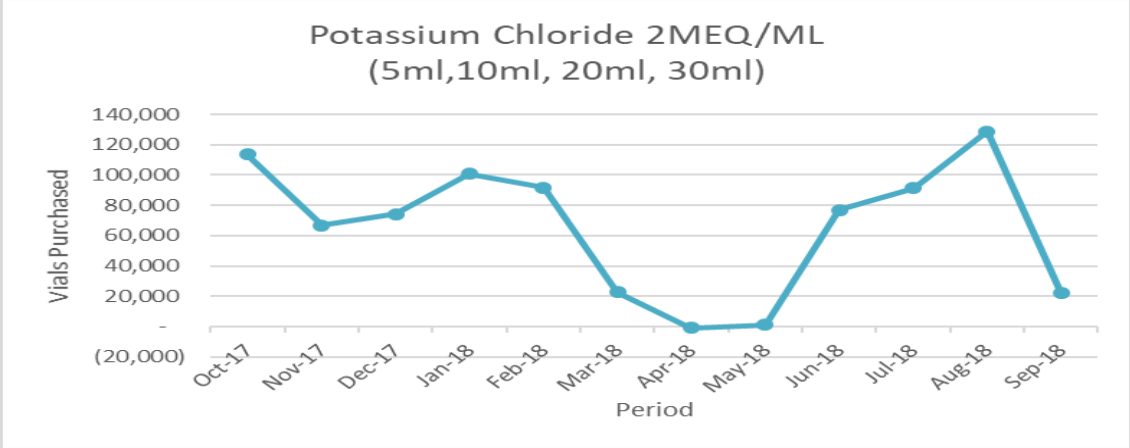
- **Changes in API Requirements** - Updates to United States Pharmacopeia (USP) monographs will often result in changes to API requirements. The changes to API requirements are typically

[10] Source: http://www.consumerreports.org/cro/news/2014/04/are-generic-drugs-made-in-india-safe/index.htm

effective immediately, resulting in shortages as manufacturers must suspend manufacturing using the old API and await new API, which can take several months, to resume manufacturing.

For example, as depicted in the following exhibit, changes to the USP monograph for potassium chloride resulted in an immediate shortage that lasted approximately six months until the new API was available and manufacturers could resume production of FDF.

Exhibit D - Changes to API requirements for potassium chloride resulted in a shortage.



- **Prioritization of Drugs to Manufacture –** Oftentimes, manufacturers are forced to prioritize which medications they will manufacture. Sometimes this prioritization is based upon factors such as high-revenue versus low-revenue medications, and in other situations the prioritization is based on what is in the best interest of public health. It is important to note that in the generic drug industry the machinery is validated to manufacture multiple products - there is not a one-machine-to-one-product ratio. In other words, when a manufacturer is asked to increase production to help alleviate a drug shortage, it may inadvertently result in downstream shortages of other drugs. For example, in 2021 several medications went into shortage as manufacturers prioritized the manufacturing of COVID-19 vaccine.[11] More recently, oncology drug shortages have been exacerbated as both carboplatin and cisplatin are produced on the same manufacturing line – trying to increase production of one medication inadvertently resulted in the other medication going into shortage as well.

- **Supply Versus Demand Mismatch –** In some scenarios, drug shortages occur due to unexpected spikes in demand. For example, earlier this year several medications used to treat cold and flu went into shortage as the nation grappled with the "tripledemic" (COVID-19, flu and RSV) and supply was unable to keep up with demand.[12] In another example, shortages of glucagon-like peptide-1 receptors have been due to higher than anticipated demand.

- **Government Reimbursement Models –** Under the current reimbursement model for inpatient services, healthcare providers are paid a fixed rate for services. With higher labor costs and ongoing inflation, providers must absorb added costs out of already-strained existing budgets and are sometimes forced to make difficult decisions daily on how to maximize limited government reimbursement that does not cover the cost of providing care. In other words, every penny counts and providers are often choosing lower cost alternatives to stretch valuable dollars. In these

11 https://premierinc.com/newsroom/blog/the-unintended-consequences-of-covid-19-vaccine-manufacturing-drug-shortages

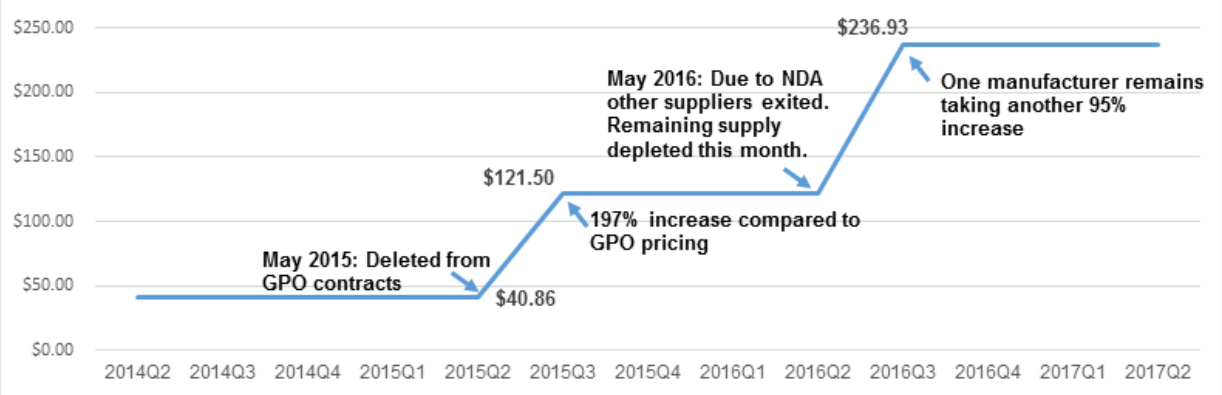
12 https://premierinc.com/newsroom/blog/premier-data-shows-key-factors-that-contribute-to-drug-shortages

scenarios, the lack of appropriate government reimbursement contributes to a race-to-the-bottom environment where providers are searching for the lowest cost option and supplier.

- **DESI Drugs** - Drug Efficacy Study Implementation (DESI) drugs are often at-risk for shortages as legacy manufacturers are required to exit the marketplace abruptly and typically only one or two manufacturers reenter the marketplace under the new requirements. During a DESI drug shortage, it is difficult for new manufacturers to enter the marketplace given the need to prove efficacy, an expensive and timely process for manufacturers, often resulting in significant price increases to offset the cost of market entry.

  For example, as depicted in the following exhibit, potassium chloride experienced a significant price increase due to the DESI drug pathway. In addition, it created a sole source situation that placed the drug at great risk for shortage.

Exhibit E – Potassium chloride experienced price spikes as a result of the DESI drug pathway



- **Gray Market** - During drug shortages, shortage drugs are often sold at exorbitant prices by unauthorized vendors. In recent years, several PremierProRx products have been found in the gray market with significant price increases:

  - Ondansetron – 1642 percent price increase
  - Naropin – 291 percent price increase
  - Rocuronium – 691 percent price increase

  Beyond pricing impacts, the gray market creates patient safety concerns as the products may not have been stored properly and therefore the integrity of the product cannot be confirmed.

- **Hoarding** - During drug shortages, hoarding often occurs as providers have limited information about the duration and severity of the shortage and are concerned about having adequate supply of product for patient care. This further exacerbates shortages as product is not available in the supply chain for other entities and often results in product being returned as unused or expired in lieu of being used for patient care.

IV. SOLUTIONS TO ADDRESS DRUG SHORTAGES MUST BE ATTAINABLE, PRACTICAL, AND SUSTAINABLE

While bipartisan and bicameral Congressional actions over the past 15 years have been monumental to continuing the fight against drug shortages, the pandemic highlighted additional vulnerabilities in the pharmaceutical supply chain that warrant a revisit of drug shortages legislation to strengthen the nation's ability to proactively address and resolve potential shortages. These include:

- ***Holding the FDA accountable for expeditiously implementing drug shortage provisions from the CARES Act in alignment with Congressional intent.***
    - In March 2020, Congress provided the FDA with several new statutory authorities to mitigate drug shortages. Specifically, these provisions:

        - Created a priority pathway for the review of drug shortage applications;
        - Required a report examining national security risks as a result of drug shortages;
        - Strengthened FDASIA Title X reporting requirements to include full disclosure of the problems resulting in a shortage, information concerning the extent of a shortage, its expected durations, and other information the Secretary may require;
        - Extended FDASIA Title X reporting requirements to API manufacturers; and
        - Required manufacturers to maintain redundancy and contingency plans to ensure ongoing supply.

      Unfortunately, it has been more than three years since the passage of these provisions and FDA has yet to fully implement any of them. For example, FDA published draft guidance on risk management plans in June 2022 and updated FDASIA Title X reporting requirements in April 2023, but has yet to finalize them. Furthermore, in the FDA's recent report to Congress for FY 2022, the FDA notes the CARES provisions but does not speak to an implementation timeline or how the new authorities helped mitigate shortages.[13]

      In addition, Premier has significant concerns that FDA is moving forward with implementing its new statutory authority in a manner that does not align with Congressional intent.[14] [15] For example, in passing the CARES Act, Congress intended to create upstream visibility into potential disruptions in the pharmaceutical supply chain and hold API manufacturers accountable for reporting discontinuances and interruptions to help mitigate potential downstream shortages as early as possible. In draft guidance, the FDA proposes passing this burden to finished-dose manufacturers who may not have proper visibility into API production, supply, or market share to determine early warning signals of a potential shortage is counter to the intent of the legislative language which is to hold manufacturers of API accountable for supply chain sustainability. Therefore, Premier urged FDA to reevaluate its interpretation of the CARES Act provisions and extend notification requirements regarding discontinuances and interruptions in the manufacturing of API to the manufacturer of the API itself.

      Given the delays with the FDA implementing statutory authorities from 3+ years ago, Premier recognizes it is difficult to provide FDA with additional statutory authority absent understanding how prior laws are impacting drug shortages. Therefore, Premier urges Congress to hold oversight hearings with FDA, including representatives from the Office of Drug Shortages, to understand the reason for the delay in the FDA implementing its

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[13] FDA Annual Report to Congress for CY 2022. Available at: https://www.fda.gov/media/169302/download?utm_medium=email&utm_source=govdelivery

[14] https://premierinc.com/downloads/Premier-Comments_FDA-Guidance-on-Risk-Management-Plans-to-Mitigate-Drug-Shortages.pdf

[15] https://premierinc.com/downloads/Premier-Comments_FDA-Guidance-on-Notifications-for-Supply-Disruptions-to-Mitigate-Drug-Shortages.pdf

CARES Act statutory authorities. Further, the oversight hearings should examine whether FDA's interpretation of its statutory authority is consistent with Congressional intent.

- ***Requiring manufacturers, including API manufacturers, to report the volume of product that is manufactured in each FDA-registered facility.***
    - The FDA currently collects information regarding the number of registered manufacturers in each country, but a blind spot is the actual volume of product that is produced by each facility. For example, FDA data shows that 18 percent of registered API manufacturers are located in India whereas Premier data shows that upwards of 30 percent of the world's API is manufactured in India. On the contrary, FDA data shows that 28 percent of registered API manufacturers are located in the United States whereas Premier data shows that approximately 15-20 percent of the world's API is manufactured domestically. Furthermore, it is estimated that upwards of 80 percent of the world's raw materials, also known as key starting materials, for pharmaceuticals are manufactured in China. The inability of the FDA to pinpoint the volume of product that is derived in each country results in a lack of transparency in the pharmaceutical supply chain regarding source of raw materials, API and FDF – making it difficult to assess the downstream risks to supply disruptions. This lack of transparency creates challenges to assess the true risk to the pharmaceutical supply chain due to manufacturing delays, export bans, global pandemics, etc.

      Two recent examples help exemplify the need for this added authority:

        - During Hurricane Maria, the U.S. faced a national shortage of intravenous fluids as a downstream impact of damage to drug manufacturing facilities located in Puerto Rico. Until the natural disaster struck, the FDA was not aware that approximately 90 percent of the U.S. supply of intravenous fluids was manufactured in Puerto Rico.
        - During COVID-19 lock downs in China, contrast media went into shortage as a downstream impact of manufacturing shutdowns at a Shanghai-based production center responsible for nearly 80 percent of product for one of the two primary suppliers serving U.S providers.[16]

      Had the FDA known this information, the nation could have been better prepared for potential shortages and proactively implemented risk management and mitigation strategies to diversify and reduce the overreliance on singular manufacturing locations.

- ***Modernizing the FDA's data infrastructure to collect shortage signals from the private sector.***
    - Oftentimes, the warning signals of an impending shortage can be seen weeks to months in advance due to discrepancies in demand vs. supply data. For example, during the COVID-19 pandemic, Premier shared weekly demand signals with the FDA for approximately 250 critical medications to help the FDA understand what medications were at risk for shortage due to increased demand. Premier's 360-degree view into the demand vs. supply signals from a broad swath of our membership across multiple suppliers provided an accurate and predictive model for determining which drug products were at risk of disruption. While individual suppliers could report increases in demand to the FDA, as requested in the President's FY 2024 budget, in practice – individual demand signals are not telling of a potential disruption and create unnecessary and undue reporting burden on the supplier. Instead, it is critical to work with larger data sets and predictive modeling with artificial intelligence to truly understand medications at risk for disruption. Therefore, to better help the FDA predict shortages before they occur, Premier recommends that Congress provide FDA with funding to modernize its data infrastructure and work with

[16] https://www.reuters.com/business/healthcare-pharmaceuticals/ge-unit-boosts-medical-dye-output-china-covid-lockdown-cuts-supplies-2022-05-10

existing private sector data sets to collect and analyze market demand signals. Furthermore, to expedite the availability of predictive data, Congress should encourage the FDA to adapt existing technology infrastructure and predictive algorithms from the private sector vs. attempting to build and train their own.

- ***Leveling the playing field for all FDA inspections.***[17]
    - The FDA has been pursuing a framework for a pharmaceutical manufacturing site rating system, the Quality Management Maturity (QMM) program, which aims to improve operations and curb drug shortages. Greater focus on supplier quality incentives and rewards, including payment for reliably meeting providers' supply requirements, is key to incenting manufacturers to participate in healthy and sustainable pharmaceutical markets. However, a rating system like the QMM may generate unintended downstream consequences that exacerbate drug shortages and create new operational challenges for U.S. healthcare providers.

      Rather than creating a net-new ranking system, Premier believes the quality standard should focus on FDA approval and inspection, with all FDA-registered global manufacturers inspected equitably and consistently via unannounced inspections at the same time intervals.

      Currently, the FDA assesses whether a facility is in a state of control through periodic inspections that provide an evaluation of manufacturing operations, including their system for quality management. However, not all facilities are treated the same as domestic manufacturers, which are inspected regularly via unannounced inspections vs. many foreign facilities, which are inspected less regularly via announced inspections. This dichotomy in inspection authority creates an undue burden for domestic manufacturers and can create an incentive for manufacturers to build their facilities overseas. It is welcome news that the Fiscal Year (FY) 2023 Omnibus Appropriations Bill contains a provision requiring the FDA to establish a pilot program for unannounced foreign inspections, but the quality standard should focus on FDA approval and inspection, with all FDA-registered global manufacturers inspected equitably and consistently via unannounced inspections at the same time intervals. Both domestic and overseas manufacturers of FDFs and APIs should be held to the same standard. To level the playing field, the FDA will require the appropriate resources in highly trained and experienced inspectors and may also need additional statutory authority. Once a level playing field is adopted as policy, the FDA should provide Congress with a five-year plan, inclusive of metrics and annual targets to achieve the desired parity.

- ***Expanding drug shortage authorities to vaccines.***
    - While the FDA has statutory authority to mitigate drug shortages, vaccines are currently excluded from those authorities. Therefore, if COVID-19, Mpox or other vaccines needed to address and treat a public health emergency were to go into shortage in the future, FDA would have limited visibility and authority to mitigate the shortage. As one example, recent shortages of Bacille Calmette-Guérin (BCG) vaccine, which is used to treat bladder cancer, resulted in limited opportunities to mitigate the shortage and impact to patient care because the medication was classified as a vaccine and not a drug.[18] Therefore, Premier recommends that Congress expand FDA's statutory authority to address shortages to include vaccines.

[17] https://www.hcinnovationgroup.com/policy-value-based-care/blog/53027224/industry-perspective-the-unintended-consequences-of-a-drug-quality-rating-system

[18] https://premierinc.com/newsroom/blog/bcg-for-bladder-cancer-treatment-how-providers-can-navigate-shortages-of-a-critical-drug

- ***Expanding the FDA drug shortage list to include regional shortages as well as shortages based on strength and dosage form.***
    - The FDA drug shortage list currently does not account for regional shortages or shortages based on excipient, strength or dosage form. These limitations created difficulties during the COVID-19 pandemic as drug shortages were rampant in hot spots while the majority of the nation did not experience the same. This resulted in an inability of providers and manufacturers to move product to areas of greatest need and leverage other statutory and regulatory flexibilities that would have otherwise been applicable in a shortage situation, such as 503B compounding as an interim solution.

- ***Revisiting GDUFA facility fees and their potential impact on drug shortages.***
    - In the Generic Drug User Fee Act (GDUFA) II, Congress created a facility fee for generic manufacturers that is tied to the number of abbreviated new drug applications (ANDAs) the manufacturer holds. For small to medium manufacturers, the facility fee can be daunting, and in some cases, serve as a deterrent for a manufacturer to enter the market for a product in shortage. For example, if entering the market for a drug in shortage and adding a new ANDA pushes the manufacturer into a higher facility fee tier, the manufacturer will often not pursue the opportunity. Therefore, Premier urges Congress to revisit the GDUFA facility fee and better understand its potential impact on drug shortages. Premier also urges Congress to consider whether drugs in shortage – and/or those on the FDA List of Essential Medications – should be exempted from GDUFA facility fees.

- ***Funding robust research to quantify the clinical and economic impact of drug shortages.***
    - There is little research documenting the clinical and economic impact that drug shortages have on patient outcomes and healthcare expenditures. One of the only studies to date that looked at the total cost of care and patient impact of drug shortages utilized the Premier Healthcare Database (PHD) and found that the 2011 shortage of norepinephrine was significantly associated with increased mortality among patients with septic shock.[19] Understanding the clinical and economic impact of drug shortages is integral to understanding the true impact of shortages and also deciphering what appropriate incentives or offsets should be implemented to help eliminate shortages. Therefore, funding should be allocated to study the clinical and economic impact of drug shortages on patient outcomes and healthcare expenditures. Research should be multi-faceted and encompass retrospective, prospective, quantitative, and qualitative studies.

- ***Testing reimbursement models that create stability for drugs prone to shortages.***
    - Current reimbursement models create misaligned incentives for providers to favor low-cost medications versus quality and/or stable supply. Premier urges Congress to work with the Centers for Medicare and Medicaid Innovation (CMMI) to test demonstration models that strive to create reimbursement models for low-margin, high-value medications that are prone to shortages to create sustainability and minimize the impact to patient care. Some options for consideration include differential reimbursement for medications prone to shortage, similar to a recent CMS payment policy that provides a differential reimbursement for domestically manufactured N95 masks. Alternatively, CMS may consider a new technology add-on payment (NTAP) like policy for medications prone to shortage – however, any such system must be automated, easy to use, and not create undue burden to file for reimbursement.

[19] Vail, Emily, Gershengorn, Hayley, Hua, May, Walkey, Allan, Rubenfeld, Gordon & Wunsch, Hannah. (2017). Association Between US Norepinephrine Shortage and Mortality Among Patients With Septic Shock. JAMA. 317.DOI: 10.1001/jama.2017.2841

- ***Requiring the DEA to establish APQs in terms of pharmaceutical dosage form for all CII controlled substances.***
    - In 2018, Congress passed the SUPPORT Act[20] giving the DEA new discretionary authority to establish aggregate production quotas (APQs) in terms of pharmaceutical dosage form. However, Premier is disappointed that DEA continues to use its current process of establishing APQs in terms in kilograms and has stated that implementation of dosage form APQs will be rare occurrences. By not implementing this statutory authority, the DEA is ignoring Congressional intent and jeopardizing the availability of essential medications needed to care for patients in the acute setting.

      Hospitals, health systems and other providers continue to grapple with acute nationwide shortages of several injectable opioid medications including morphine, hydromorphone and fentanyl.[21] These medications are critical to control pain during surgeries, interventional procedures, traumas, burns and other procedures where treatment with alternative pain therapies may not be clinically appropriate. Absent adequate supply of injectable opioids, patient care is threatened by cancelling or delaying surgical procedures and increasing the risk of medication errors.

      Injectable opioids are administered under the supervision of healthcare professionals in healthcare settings that have stringent policies and procedures in place to prevent diversion. Specifically, injectable opioids are distributed, stored and administered in tightly controlled environments, and are overseen by no fewer than five government agencies to ensure their appropriate handling and use (i.e., the DEA, State Bureau of Narcotic Enforcement, State Department of Health, Joint Commission and State Board of Pharmacy). Injectable opioids have historically not been the drugs of concern in the opioid epidemic, and data demonstrates that utilization has been consistent for many years and did not experience the spike in utilization that solid oral dosage opioids have in the past few years. Furthermore, FDA cGMP requirements for sterile injectable medications are very different than solid oral dosage medications, thereby making it more difficult to mitigate shortages for injectable medications due to sterility and quality assurance testing involved with manufacturing sterile products.

      Given the essential role of injectable opioids in providing clinically appropriate care to patients, especially COVID-19 patients, and ongoing drug shortages, Premier urges Congress to leverage its oversight authority to question why the DEA does not utilize its discretionary authority to establish APQs in terms of pharmaceutical dosage form for all CII controlled substances. The forthcoming reauthorization of the SUPPORT Act would be an appropriate time for Congress to consider whether the authority to establish APQs in terms of pharmaceutical dosage form should be made mandatory versus discretionary.

- ***Requiring entities who receive government grants for domestic manufacturing of drugs, vaccines, and API to manufacture drug shortage products when needed.***
    - Throughout the pandemic, the U.S. government provided billions of dollars of grants to support the domestic manufacturing of drugs, vaccines, and API through programs such as the Defense Production Act Title III and ASPR Industrial Base Expansion Program.[22] However, to Premier's knowledge, the grants do not require the recipients to manufacture items in shortage.

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[20] Substance Use-Disorder Prevention that Promotes Opioid Recovery and Treatment for Patients and Communities Act (SUPPORT Act), Public Law 115-271.
[21] According to the FDA drug shortage database, injectable fentanyl has been in shortage since May 2017 and hydromorphone injection has been in shortage since October 2017. https://www.accessdata.fda.gov/scripts/drugshortages/default.cfm (Accessed 11.17.2022)
[22] https://aspr.hhs.gov/mcm/ibx/portfolio/Pages/default.aspx

Oftentimes, the FDA speaks to its inability to require manufacturers to make anything, and therefore, its inability to require manufacturers to produce products in shortage. However, the same lack of authority does not exist for other federal agencies such as FEMA or ASPR. Therefore, Premier recommends that Congress work with these federal agencies to understand two primary questions:

1. Moving forward, can federal grants or funding for domestic manufacturing be tied to a requirement that as a condition of accepting the funds the government can mandate the recipient to manufacturer drugs in shortage to help alleviate the impact to patient care?
2. Can existing federal grants or funding for domestic manufacturing be amended to include a requirement that as a condition of accepting the funds the government can mandate the recipient to manufacturer drugs in shortage to help alleviate the impact to patient care?

Premier also urges Congress to leverage its oversight authority to understand how federal dollars distributed to support the domestic manufacturing of drugs, vaccines, and API have impacted drug shortages. Furthermore, Congress should require federal agencies, such as FEMA and APSR, to disclose the progress grant recipients have made in standing up their domestic manufacturing facilities in accordance with their contractual requirements.

- ***Streamlining the ability of 340B covered entities to purchase drug shortage items.***
  - During a drug shortage, HRSA permits covered entities to purchase drugs at a non-340B ceiling price, such as products from a GPO contract, private label, or wholesaler contract. However, HRSA requires a very lengthy form and documentation prior to the covered entity being permitted to make the purchase.[23] Given the complexity of the documentation and compliance requirements, many covered entities report to Premier that they often forego this "allowance" thereby limiting their options to address drug shortages for the patients they serve.

    During the COVID-19 public health emergency, HRSA had implemented an interim allowance that permitted covered entities to obtain drugs in shortage if they had a written policy and procedure in place outlining documentation and compliance requirements. This interim allowance was instrumental in allowing covered entities to easily obtain drug shortage items during the pandemic and minimized impacts to patient care. However, with the end of the public health emergency on May 11, this interim allowance expired and HRSA reverted to the former onerous documentation and compliance requirements.

    Given the benefit of the interim allowance, Premier urges Congress to work with HRSA to make permanent the ability of covered entities to obtain drugs in shortages if they have a written policy and procedure in place outlining documentation and compliance requirements. Premier believes that HRSA has the authority to implement this policy as permanent without Congressional action.

- ***Requiring a report to Congress with recommendations on consumer notification of shortages.***
  - There is currently no proactive mechanism to alert consumers, physicians, pharmacists, and others of a drug shortage. While the FDA posts this information on their website and entities can register for updates, it requires action and awareness on the part of the entity to receive this information. With more and more drug shortages impacting outpatient products, Premier believes it is important for FDA to study how its communications regarding drug shortages can be improved. Therefore, Premier urges Congress to require

[23] https://www.hrsa.gov/opa/updates/2015-december

the FDA to produce a report with recommendations on how improve notification of drug shortages to consumers, physicians, pharmacists, and others.

In summary, Premier urges Congress to provide FDA greater authority to further mitigate drug shortages. In addition, Congress should play a greater oversight role to ensure FDA is expeditiously implementing its statutory authority in alignment with Congressional intent. Potential Congressional action to address drug shortages must look beyond the FDA to additional federal agencies such as the DEA, ASPR, and HRSA to name a few – addressing drug shortages requires a whole-of-government approach coupled with public-private sector collaboration. And finally, Congress has historically always tackled drug shortage legislation in a bipartisan and bicameral manner and additional action at this juncture should be no different.

V. CONCLUSION

In closing, Premier appreciates the opportunity to submit comments on the RFI to inform policymaking for drug shortages. Premier looks forward to continuing to work with Congress to help prevent and resolve these shortages today and for the future.

If you have any questions regarding our comments or need more information, please feel free to contact me at soumi_saha@premierinc.com or 732-266-5472.

Sincerely,

Soumi Saha, PharmD, JD
Senior Vice President of Government Affairs
Premier Inc.

Appendix A – This information was provided to the FDA and White House in May 2023.

Oncology Drug Shortages
May 2023

Asks:

- Interim allowances for Accord to resume manufacturing under stringent supervisory conditions
- Facilitate alternate manufacturers ramp capabilities
- Explore temporary importation potential from approved manufacturers who produce these medications overseas
- Meet with Premier pharmacy team to discuss alternatives

Some informative links:

- https://www.pharmacypracticenews.com/Online-First/Article/04-23/Drug-Shortages-Reach-10-Year-High/70131
- https://www.fiercepharma.com/manufacturing/burn-after-reading-fda-blasts-intas-cascade-failures-after-investigators-find-heaps

Background:

Downstream issues stemming from the FDA's inspection of Intas Pharmaceuticals' manufacturing plant in Gujarat, India, in December 2022, have resulted in a very concerning shortage of critical oncology therapies, namely, cisplatin and carboplatin, followed by methotrexate. Accord Healthcare, a wholly owned subsidiary of Intas Pharmaceuticals, maintained >40% market share for the above therapies. Due to voluntary manufacturing cessation by Accord, the remaining manufacturers are facing a challenge to keep up with demand. In the past several weeks, many health systems have connected with Premier raising alarm of dwindling stock and anxiety over inability to continue to treat their patients with proven therapies.

As Premier, we have been monitoring the supply chain for several months. Premier receives member hospital purchase data on a daily basis from the wholesaler channel as our members place orders and receive shipments. The data provided in this document reflects orders and receipts from January 2022 through February 2023. The charts demonstrate Total Units Ordered and Total Units Received. Those data points are displayed in the charts in monthly buckets. The Fill Rate Percentage is calculated from these two data points and displayed in the chart monthly.

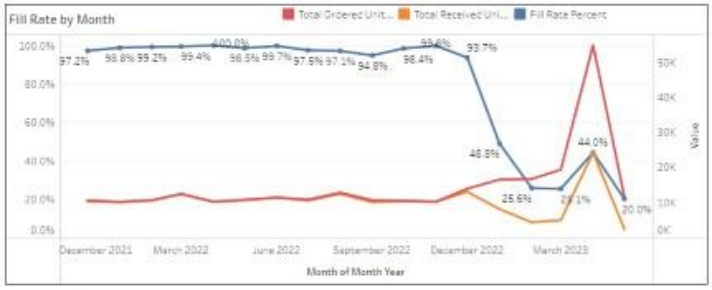
What are we providing?

Please find a summary of information by Drug Name and Form which provides our Fill Rate Data along with a synopsis of our market insights. Each Drug/Form has various strengths and package sizes which are grouped together for the graph. When available, insight is provided on location of Finished Good and API (Active Pharmaceutical Ingredient) manufacturer. Premier obtains this data under confidentiality.

Below is a Data Key to guide the review of the Fill Rate charts. Based on our experience, once a product reaches Fill Rates below 80%, we start to receive complaints regarding inability to receive product and concerns over a potential shortage. As you review the charts below, each of these products is experiencing Fill Rates significantly lower than 80%.

	FILL RATE DATA KEY
RED BAR	TOTAL UNITS FACILITIES ORDERED
YELLOW BAR	TOTAL UNITS FACILITIES RECEIVED
BLUE BAR	FILL RATE PERCENTAGE

Cisplatin 50mg/50mL



- Premier has a multi source award for this product (Accord, Hikma & Teva)
- Accord supplied approximately 43% of volume to Premier members for this presentation.
- The fill rate has significantly been reduced by as much as 60% due to the Accord disruption.
- Premier is relying Teva and Hikma for supply who has been unable to fill the gap to date and some members have been unable to obtain any product when needed.

Product Detail Monthly Units

ProductDesc	Supplier	NDC	12/2021	01/2022	02/2022	03/2022	04/2022	05/2022	06/2022	07/2022	08/2022	09/2022	10/2022	11/2022	12/2022	01/2023	02/2023	03/2023	04/2023	05/2023	Grand Tot.
CISPLATIN - VIAL 1 MG/ML, 50x1,No	Blueprint Labor	69001028527	95	141	110	121	73	65	18	81	73	53	53	40	63	305	554	1			1,884
	Fresenius Kabi	63323012061	131	179	162	196	221	236	216	155	114	90	17	120	279	912	627	-18	1,954	58	5,607
	Hikma	00143950401	51	36	40	27	61	92	165	181	342	227	181	127	217	649	338	15	424	240	3,336
	Teva	00703874711	234	170	158	278	283	217	158	208	218	289	304	308	431	1,139	2,240	1,805	762	274	9,454
CISPLATIN - VIAL 1 MG/ML, 50x1,NO	ATHENEX PHARMAC	70860020650										0				0	0	0	0	0	0
CISPLATIN - VIAL 1 MG/ML, 50x10,No	Accord	16729010011	955	932	992	1,152	923	935	1,061	962	1,156	928	959	902	1,123	446	4	257	1,999	170	15,916
CISPLATIN - VIAL 50 MG, 1x1,No	Wg Critical Car	44567053001	10						4			1	1		6	79	133	344	0	0	578

Cisplatin 100mg/100mL

- Premier has a multi source award for this product (Accord, Hikma & Teva)
- Accord supplied approximately 65% of volume to Premier members for this presentation.
- The fill rate has significantly been reduced by as much as 94% due to the Accord disruption.
- Premier is relying Teva and Hikma for supply who has been unable to fill the gap to date and some members have been unable to obtain any product when needed.

Product Detail Monthly Units

ProductDesc	Supplier	NDC	12/2021	01/2022	02/2022	03/2022	04/2022	05/2022	06/2022	07/2022	08/2022	09/2022	10/2022	11/2022	12/2022	01/2023	02/2023	03/2023	04/2023	05/2023	Grand Tot.
CISPLATIN - VIAL 1 MG/ML, 100x1,No	Blueprint Labor	69001028332	41	55	59	65	53	70	37	23	43	55	16	34	120	778	1,143	204	5		2,766
	Fresenius Kabi	63323010965	387	402	388	421	620	453	283	205	77	10	17	150	666	810	904	2,374	38	80	8,010
	Hikma	00143950501	117	129	55	76	130	159	183	204	218	310	404	202	138	694	146	437	1,806	205	5,601
	Teva	00703874611	577	594	625	650	592	625	668	537	625	670	592	745	290	392	951	1,529	469	324	10,998
CISPLATIN - VIAL 1 MG/ML, 100x1,NO	ATHENEX PHARMAC	70860020651	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
CISPLATIN - VIAL 1 MG/ML, 100x10,No	Accord	16729010033	3,505	3,198	3,466	4,270	3,814	3,620	4,212	3,657	4,094	3,913	3,839	4,530	4,255	765	0	10	0	0	51,149

Carboplatin 45mL

- Teva is the current supplier for Premier.
- Carboplatin is produced on the same lines as Cisplatin.
- Fill rates have declined since the Accord disruption on both Carboplatin and Cisplatin mainly due to the need to compete for line capacity.
- The decrease in output in the overall market has a compounding effect on Premier supply as manufacturers attempt to fill the gap for the entire market.

Product Detail Monthly Units

ProductDesc	Supplier	NDC	12/2021	01/2022	02/2022	03/2022	04/2022	05/2022	06/2022	07/2022	08/2022	09/2022	10/2022	11/2022	12/2022	01/2023	02/2023	03/2023	04/2023	05/2023	Grand Tot.
CARBOPLATIN - VIAL 10 MG/ML, 45x1,NO	APP/PRESENIUS K	63323017245																	0	0	0
	MYLAN INSTITUTI	67457048548																	0		0
CARBOPLATIN - VIAL 10 MG/ML, 45x1,No	AUROMEDICS PHAR	55150015501	59	165	85	150	142	187	246	153	161	77	279	332	281	422	606	135	542	0	4,051
	Pfizer	61703033650	929	1,104	1,008	985	1,281	972	1,281	1,038	1,258	1,281	898	998	990	1,168	1,147	1,426	3,409	246	20,778
	Teva	00703424501	1,716	1,607	1,477	1,947	1,540	1,905	1,803	1,521	1,733	1,599	1,479	1,378	1,561	2,012	1,769	2,088	767	4	27,744
		00703424681	392	402	420	450	478	405	458	406	467	408	299	348	417	530	390	559	1,565	220	8,612
	TEVA/NOVAPLUS	00703424691								1											1
CARBOPLATIN - VIAL 10 MG/ML, 45x10,No	Accord	16729029534	722	623	468	708	729	453	586	462	599	734	771	732	710	900	118	56	1	0	8,803
		69468000534	64	83	13	17	14	50	4		1							17			243

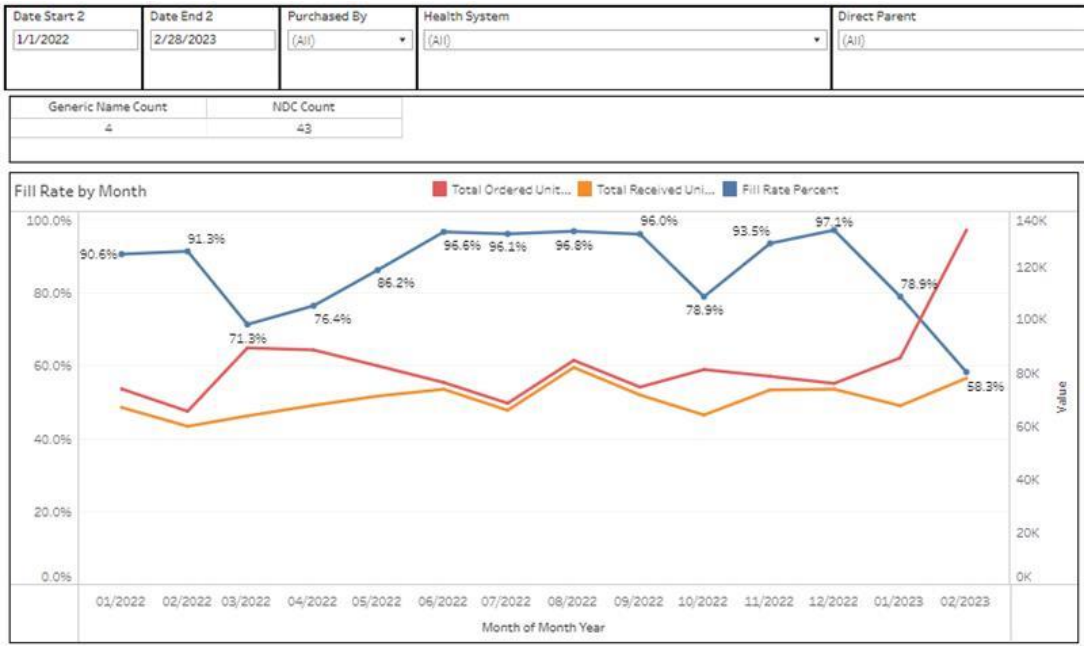
Carboplatin 5mL

- Teva is the current supplier for Premier.
- Carboplatin is produced on the same lines as Cisplatin.
- Fill rates have declined since the Accord disruption on both Carboplatin and Cisplatin mainly due to the need to compete for line capacity.
- The decrease in output in the overall market has a compounding effect on Premier supply as manufacturers attempt to fill the gap for the entire market.

Product Detail Monthly Units

ProductDesc	Supplier	NDC	12/2021	01/2022	02/2022	03/2022	04/2022	05/2022	06/2022	07/2022	08/2022	09/2022	10/2022	11/2022	12/2022	01/2023	02/2023	03/2023	04/2023	05/2023	Grand Tot.
CARBOPLATIN - VIAL 10 MG/ML, 5x1,No	HOSPIRA/NOVAPLU	61703038018																11			11
	Pfizer	61703033618	223	233	204	202	107	93	17	6	83	94	114	107	113	151	123	274	291	0	2,416
	Teva	00703424401	678	651	665	667	799	672	663	669	675	621	593	514	540	959	1,275	1,675	4,098	875	17,238
		00703424481	88	76	62	107	84	68	117	84	62	72	68	51	72	58	56	68	651	887	2,731
CARBOPLATIN - VIAL 10 MG/ML, 5x10,No	Accord	16729029531	348	288	463	587	478	517	640	532	812	788	658	725	819	479	152	44	47	0	8,375
		69468000531	6	13																	19

METHOTREXATE – VIALS - VARIOUS STRENGTHS AND PACKAGE SIZES



Data demonstrates that product Fill Rates (blue line) have been challenging since January 2023. There are four alternate suppliers who manufacture various sku's which comprise the product family. Each of these four suppliers are ramping up product production but continue to struggle to make up the supply gap and product is on backorder or allocation. Intermittent shipments from the four suppliers are occurring, yet it is not enough at one time to meet 100% of the market demand.

Finished good is manufactured in Australia and Europe. API coming from Europe, Australia, US and Asia.

Drug Shortages Currently In Focus

Drug	Summary	Distribution/Comments
Carboplatin	• Accord voluntarily export hold. • Teva 60mL (highest volume presentation) and 45mL (second highest volume presentation) of the 4 presentations in Premier ProRx. • These delays all stem from line time issues. • PPRx Teva short dated stock has also been exhausted	Wholesale channel • Teva 45mL late May • Teva 60mL June • Accord - Unknown
Cisplatin	• Accord – voluntary export hold • Hikma and Teva 50 & 100 mL on contract, both on allocation • FK on contract 200 mL • WG Critical not on contract	FFF Rapid Commit • (Hikma 100mL) 4/3, 4/12, 4/26 • (Hikma 50mL) 4/26 • (Accord 100mL) 5/8 Wholesale channel • Next Accord release- unknown • Next Hikma release due by late May • Next Teva release due by early June
Methotrexate	• Pfizer initially launched the PremierProRx label. • Initial build was based on historical demand, 800% sold vs the forecast • Teva has inventory of short dated PremierProRx label as they were the previous supplier. Product has been made available through the 3 major wholesalers. • Accord – voluntary export hold	Wholesale channel • Pfizer label releasing weekly, on allocation • Next Pfizer ProRx release in July