August 1, 2023

The Honorable Ron Wyden
United States Senate
Washington, D.C. 20510

Dear Senator Wyden:

Thank you for your letter of June 2, 2023, regarding shortages of Adderall (which is an amphetamine mixed salt) and other medications needed to treat attention-deficit/hyperactivity disorder (ADHD).

The Food and Drug Administration (FDA or the Agency) agrees that prescription stimulants are an important treatment option for conditions such as ADHD and recognizes the importance of access to these medications. We also understand that the lack of availability of certain amphetamine mixed salts products to treat ADHD is frustrating for patients and their families. Although the impact has been disruptive to both patients and their families, there are some unique aspects to the Adderall shortage that distinguish it from other drug shortages.

At the crux of the issue is the substantial increase in prescribing, while simultaneously, supply has not been able to keep up with demand. Although some of this increase is related to virtual prescribing, the percentage of adolescents and adults receiving prescription stimulant fills increased steadily from 2016–2021. The increase from 2020–2021, when the percentages of stimulant fills in certain age groups grew by more than 10 percent,[1] raises questions about the impact of virtual prescribing and the pandemic. It is well known that the COVID pandemic had wide-ranging negative impacts on mental health. Virtual prescribing, while an important addition to medical practice to enable greater access to appropriate treatment, could make it easier to prescribe without a full in-person assessment. In the long term, much more research needs to be done to determine more precisely who benefits from these drugs, and in whom the risks occur. Along with enhanced research, there is a critical need to develop and implement more effective clinical standards and guidelines for treating ADHD.

While we should not delay these long-term strategies, we know that we need to act this summer to ensure that patients with a valid need have access.

Adderall is a Schedule II controlled substance with high potential for abuse. Because of this, there are several checks along the process to reduce misuse, including Drug Enforcement Administration (DEA) allocation of quota and algorithms to help distributors identify suspicious orders. While total quota does not appear to be an issue, we have heard from manufacturers that the timing and metering of allocations has presented challenges in allowing sufficient lead time to maximize production. We have also been told that the Multistate Litigation and Settlements have had an impact on business decisions, leading firms to manufacture less product because of concerns that a similar situation could occur with stimulants as occurred with opioids. This same

[1] https://www.cdc.gov/mmwr/volumes/72/wr/mm7213a1.htm#F1_down

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dynamic has also resulted in additional orders being flagged as suspicious, leading to canceling or delaying the order.

To address continuing concerns of misuse, abuse, addiction, and overdose of prescription stimulants, in May 2023, FDA issued a drug safety communication and required label updates including to the boxed warning to update and standardize prescribing information, to clearly inform patients, caregivers, and healthcare professionals of risks associated with their medications.[2] FDA has awarded a grant to the National Academies of Sciences, Engineering, and Medicine to support a conference and scientific meeting on adult ADHD and considerations for diagnosis and treatment. We hope this workshop will help inform the development of clinical standards and guidelines and that further research will be stimulated to fill the considerable gaps in knowledge about practical approaches to assessment and decisions about which interventions to use in which patients.

DEA and FDA recently worked to develop and provide a joint presentation to industry and other stakeholders during the DEA Supply Chain Conference in May 2023.[3] The presentation focused on ADHD medications and included the roles of DEA and FDA in the quota process and recommended best practices for industry in regard to quota requests. We will continue our efforts to work closely together under our Memorandum of Understanding on shortage issues related to quotas.[4]

As with every drug shortage, we understand the significant impact that supply disruptions and shortages can have on patient care and are doing everything within our authority to help prevent and alleviate them. Toward that end, please see the responses to your specific questions below:

1. **Does the agency have the authority to disclose when a drug manufacturer refuses a request from the FDA to provide information on the cause(s) or extent of the shortage?**

   Section 506C of the Federal Food, Drug, and Cosmetic Act requires that manufacturers provide the reasons for discontinuations and manufacturing interruptions that are likely to lead to supply disruptions in their initial notifications regarding potential shortages. Once a shortage occurs, FDA is required to list the reason for the shortage on the FDA drug shortage database. Generally, companies are sharing information regarding the cause of the shortage and their activities to resolve. However, if a company refuses to provide information on the cause or extent of the shortage, we can disclose on the website that the company has not provided that information.

2. **Understanding that the two organizations share information, how does the FDA work to reconcile this situation when drug shortages appear on both lists and some drugs that are only present on ASHP's list?**

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[2] https://www.fda.gov/drugs/drug-safety-and-availability/fda-requires-updates-clarify-labeling-prescription-stimulants-used-treat-adhd-and-other-conditions

[3] https://www.deadiversion.usdoj.gov/mtgs/supply_chain/conf_2023/supply_chain.html#:~:text=The%20Drug%20Enforcement%20Administration%20(DEA,Galleria%20Houston%20in%20Houston%2C%20Texas.

[4] https://www.fda.gov/about-fda/domestic-mous/mou-225-15-11

FDA and the American Society of Health-System Pharmacists (ASHP) both have language posted on our respective websites about the differences in our websites and why the lists are not identical. As posted on the FDA website,[5] FDA focuses on national shortages and lists drugs on its website once it has confirmed that overall market demand is not being met by the manufacturers of the product. FDA does not consider a product to be in shortage if one or more manufacturers are able to fully supply market demand for the product. In contrast, ASHP provides information about which manufacturers have the drug available and which ones do not even if total national demand is being met.

3. **How does the agency, with the use of market data, factor in availability to more affordable generics and access to rural areas in its work to anticipate and mitigate shortages, particularly given potential limitations on information?**

FDA has very limited visibility into regional and local access issues, but FDA does have access to data on the national level and can assess whether supply is meeting national demand. Information FDA considers includes voluntarily provided information from the manufacturers on their supplies and production, inventory levels, and backorder status, and current and historical national sales data. We focus our efforts on restoring supply to meet full national demand. When manufacturers are able to fill all current and projected orders, build up inventory, and restore safety stocks, FDA resolves the designation of shortage. If a rural hospital or pharmacy reports difficulty accessing supply, we can connect them with the manufacturers that have product available to access the supply directly from the manufacturer.

4. **Does the agency have plans or a position on identifying medical products that do not fall into that category but whose shortage would present serious public health concern?**

When a potential shortage is reported, part of FDA's initial process, as outlined in our Manual of Policies and Procedures for Drug Shortage Management,[6] is to assess the medical necessity of the drug. A medically necessary drug is any drug product used to diagnose, treat or prevent a serious disease or medical condition for which there is no other drug that is judged by FDA's Center for Drug Evaluation and Research (CDER) medical staff to be an appropriate substitute, or there is an inadequate supply of an acceptable alternative. We focus our drug shortage mitigation and prevention efforts on medically necessary drugs because these drugs present the greatest public health concern. We do not use the essential medicine list to guide our shortage activities, we look at each medication under the criteria above.

5. **Please provide an update on the FDA's finalization of the guidance and any plans for further rulemaking in this area.**

[5] https://www.fda.gov/drugs/drug-shortages/frequently-asked-questions-about-drug-shortages
[6] https://www.fda.gov/media/72447/download

As you may know, the draft guidance was issued in April 2023 and the comment period closed in June 2023. We are in the process of considering the public comments received on the draft guidance.

6. **Should Congress require manufacturers to provide any of the recommended additional information or give the FDA authority to require certain of the information be provided as relevant to the situation?**

The President's fiscal year 2024 budget includes several critical legislative proposals[7] intended to promote FDA's response efforts that we believe would greatly enhance the work we do to address potential drug shortages. We would welcome the opportunity to work with you and your colleagues on these proposals.

Please know that we have deep empathy for the patients and families impacted by these shortages and many of our employees have family members who have been affected themselves. We also note that the most difficulty is being experienced by those who are disadvantaged by social and economic circumstances and especially those living in rural areas. When a patient needs this medication, that person should have access regardless of who they are or where they live.

At the same time, because of the catastrophic overdose crisis in this country, we need to work together and act responsibly to strike that delicate balance to ensure that only those who need these drugs can access them. This is a multifactorial challenge, and we recognize that FDA and DEA play very important roles. We also understand the importance of clear communication with the public. Toward that, we intend to release a joint statement to the public. We are actively working on this statement. In the meantime, we will continue to work with DEA and around the clock to mitigate this drug shortage. We will also keep the public informed with regular updates on FDA's shortage website.[8]

Thank you again for your interest in this important issue. We understand you may be interested, as Chairman of the Senate Finance Committee, in holding further discussions on solutions to this multidimensional problem. We stand ready to support those conversations and look forward to working with you.

Sincerely,

Robert M. Califf, M.D.
Commissioner of Food and Drugs

cc: The Honorable Anne Milgram, Administrator, Drug Enforcement Administration

[7] https://www.fda.gov/media/166049/download#:~:text=FDA%20proposes%20to%20create%20a,medical%20countermeasure%20development%20to%20address.
[8] https://www.fda.gov/drugs/drug-safety-and-availability/drug-shortages