National Comprehensive Cancer Network®

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Katherine Reid
Director
Office of Strategic Industries & Economic Security
Bureau of Industry and Security
U.S Department of Commerce
1401 Constitution Avenue, NW
Room 3876
Washington, DC 20230

RE: Notice of Request for Public Comments on Section 232 National Security Investigation of Imports of Pharmaceuticals and Pharmaceutical Ingredients (XRIN 0694-XC120)

Dear Director Reid:

The National Comprehensive Cancer Network® (NCCN®) appreciates the opportunity to comment on the Department of Commerce's (Department) Bureau of Industry and Security (BIS), Office of Strategic Industries and Economic Security's *Section 232 National Security Investigation of Imports of Pharmaceuticals and Pharmaceutical Ingredients* as it relates to NCCN's mission of defining and advancing quality, effective, equitable, and accessible cancer care and prevention so all people can live better lives.

NCCN Background

As an alliance of 33 leading academic cancer centers in the United States (US) that treat hundreds of thousands of patients with cancer annually, NCCN® is a developer of authoritative information regarding cancer prevention, screening, diagnosis, treatment, survivorship care, palliative care, and supportive care that is widely used by clinical professionals and payers alike. The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) are a comprehensive set of guidelines detailing the sequential management decisions and interventions that currently apply to 97 percent of cancers affecting patients in the US.

NCCN Guidelines® and Library of Compendia products help ensure access to appropriate care, clinical decision-making, and assessment of quality improvement initiatives. The NCCN Drugs & Biologics Compendium (NCCN Compendium®) has been recognized by CMS and clinical professionals in the commercial payer setting since 2008 as an evidence-based reference for establishment of coverage policy and coverage decisions regarding off-label use of anticancer and cancer-related medications. NCCN was recognized by CMS in 2016 and renewed in 2021 as a qualified Provider Led Entity (PLE) for the Medicare Appropriate Use Criteria (AUC) Program for the development of AUC and the establishment of policy and decision-making for diagnostic imaging in patients with cancer.

NCCN imposes strict policies to shield the guidelines development processes from external influences. The "firewall" surrounding the NCCN Guidelines processes includes financial support policies; panel participation and communication policies; guidelines disclosure policies; and policies regarding relationships to NCCN's other business development activities. The guidelines development is supported exclusively by the Member Institutions' dues and does not accept any form of industry or other external financial support for the guidelines development program. The NCCN Guidelines are updated at least annually in an evidence-based process integrated with the expert judgment of multidisciplinary panels of expert physicians from NCCN Member Institutions. The NCCN Guidelines are transparent, continuously updated, available free of charge online for non-commercial use and are available through a multitude of health information technology (HIT) vendors.

Impact of Drug Shortages on Cancer Care

NCCN appreciates the Department's initiation of this investigation. NCCN supports efforts aimed at reducing dependency on pharmaceutical imports and encouraging the growth of domestic pharmaceutical production. However, NCCN urges that these initiatives and policies be implemented strategically and with great care to avoid unintended consequences that could harm certain populations, such as cancer patients in active treatment and survivorship.

For patients with cancer, access to timely and appropriate treatment is essential. Cancer treatment regimens are often complex, including but not limited to combinations of surgery, chemotherapy, radiation therapy, immunotherapy, clinical trials, and bone marrow transplants.[1] These treatments frequently require multiple medications, not only to target cancer cells but also to manage side effects such as pain, nausea, and low blood counts.[2] Adherence to medication plans is critical for optimal patient outcomes.[3]

Despite the critical need to maintain treatment adherence, cancer care has experienced significant strain and disruption in recent years due to shortages of essential cancer medications such as Carboplatin, Cisplatin, and Vinblastine, threatening patient outcomes, and the progress of cancer care research.[4] According to a 2023 survey by the American Cancer Society Cancer Action Network, approximately 1 in 10 cancer patients reported disruptions in their care due to drug shortages, with nearly half experiencing treatment delays and over two-thirds facing challenges in finding substitute medications.[5]

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[1] *Types of cancer treatment.* NCI. (n.d.). https://www.cancer.gov/about-cancer/treatment/types

[2] *Managing medications.* MD Anderson Cancer Center. (n.d.). https://www.mdanderson.org/patients-family/diagnosis-treatment/emotional-physical-effects/managing-medications.html#:~:text=Cancer%20treatment%20usually%20involves%20taking,to%2020%20pills%20a%20day.

[3] V, R., Chacko, A. M., Abdulla, N., Annamalai, M., & Kandi, V. (2024). Medication Adherence in Cancer Patients: A Comprehensive Review. *Cureus*, *16*(1), e52721. https://doi.org/10.7759/cureus.52721

[4] Santos, E. S., Oliver, T. K., Lacchetti, C., Geisel, R., Wilfong, L. S., Fader, A. N., & Eng, C. (2024). Drug shortages in oncology: Asco clinical guidance for alternative treatments. *JCO Oncology Practice*, *20*(1), 19–32. https://doi.org/10.1200/op.23.00545

[5] *Survivor views: Drug Shortages, Telehealth, & Biomarker Testing.* American Cancer Society Cancer Action Network. (2023, September). https://www.fightcancer.org/policy-resources/survivor-views-one-ten-impacted-recent-drug-shortages

Similarly, in 2024, NCCN's Best Practices Committee conducted a series of surveys involving the academic cancer centers in our alliance to better understand the impact of shortages on cancer care.[6,7] These surveys found that drug shortages pose significant threats to patient access to optimal care and have also impacted the operations of clinical trials, posing a risk to future innovations.[6,7] NCCN is thankful that the urgent crisis of the Carboplatin and Cisplatin shortages has finally subsided following numerous months of shortage. However, NCCN notes that our survey from June 2024 found ongoing drug shortage challenges across a wide array of generic drugs. Of the twenty-eight responding academic cancer centers, 89% reported at least one drug in shortage, with a majority reporting more than one drug in shortage.[6,7] NCCN also notes that this survey troublingly found that a majority of centers reported shortage related disruptions to clinical trials that increased administrative burden, decreased trial enrollment, and delayed openings of trials due to necessary drugs being in shortage.[6,7] Shortages of oncology drugs place strain on an already overburdened health system and can add significant stress to healthcare providers and patients with cancer during the treatment process.

Challenges of the Generic Oncology Drug Market

In the US, the majority of drug shortages occur among generic medications.[8] Approximately nine out of 10 prescriptions filled in the US are generic drugs, yet these drugs account for only 17.5% of prescription drug spending and less than 2% of overall healthcare spending.[9] Affordable generic medications are vital to expanding access to healthcare, especially for individuals who are uninsured or underinsured. In oncology, generics can serve as cost-effective alternatives to brand name drugs. In 2021, generics and biosimilars saved patients with cancer $17.9 billion.[10] This affordability allows healthcare providers to personalize treatment strategies more effectively, balancing patient needs, preferences, and financial circumstances. Despite their crucial role, many of these essential generic oncology drugs are at risk.

A significant driver of this vulnerability is the reliance on foreign pharmaceutical manufacturing. Approximately 80% of the active pharmaceutical ingredients (APIs) used in US generic drugs are produced outside of the country, often in regions where production costs are lower and regulatory oversight may differ from US standards.[11] Notably, research indicates that the US accounts for 22% of FDA-registered API manufacturing sites, while the remaining 78% FDA-

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[6] *NCCN findings on cancer drug shortages*. NCCN. (n.d.). https://www.nccn.org/business-policy/policy-and-advocacy-program/nccn-findings-on-cancer-drug-shortages

[7] *NCCN Best Practices Committee New Information and Survey Results from June 2024*. National Comprehensive Cancer Network. (2024, June). https://www.nccn.org/docs/default-source/oncology-policy-program/nccnbestpracticesdrugshortagesurvey.pdf?sfvrsn=b081351e_6

[8] Ventola CL. The drug shortage crisis in the United States: causes, impact, and management strategies. P T. 2011 Nov;36(11):740-57. PMID: 22346307; PMCID: PMC3278171.

[9] *The U.S. Generic & Biosimilar Medicines Savings Report*. Association for Accessible Medicines. (n.d.). https://accessiblemeds.org/wp-content/uploads/2024/11/AAM-2023-Generic-Biosimilar-Medicines-Savings-Report-web.pdf

[10] *The U.S. Generic & Biosimilar Medicines Savings Report - Cancer*. Association for Accessible Medicines. (n.d.-b). https://accessiblemeds.org/wp-content/uploads/2024/11/AAM-2023-Generic-Biosimilar-Medicines-Savings-Report-web.pdf

[11] *A Bold Goal: Reshoring 25% of Small Molecule API to the U.S. in 5 Years*. API Innovation Center. (n.d.). https://www.aapa.org/wp-content/uploads/2024/01/EHRs_and_PAs_White_Paper_1-2024.pdf

registered API manufacturing sites are overseas.[12] The lack of manufacturing options leaves supply chain vulnerable to disruptions, even from relatively minor issues.

After the COVID-19 pandemic revealed critical weaknesses, efforts were made to improve domestic pharmaceutical manufacturing. However, progress has been slow. From 2019-2025, the number of FDA-registered API facilities in the US rose only slightly from 510 to 521. In contrast, China more than doubled its facilities in the same timeframe, jumping from 230 to 467.[11] These figures continue to underscore the dominance of foreign manufacturing and the significant challenges in expanding pharmaceutical production within the US to improve supply stability.

Historically, the US has both relied more heavily on generic medications and paid lower prices for them compared to other high-income nations.[13] However, the challenging market conditions in the U.S. have led to the exit of numerous generics manufacturers out of business, compromised quality standards, and resulted in drug shortages that increase overall healthcare system costs.[12] Generic drugs operate in a completely separate market from brand name drugs and are often priced so low that sustainable and high-quality manufacturing processes are challenging to maintain.

Recommendations for Improvement

Given the challenges outlined above, NCCN supports strengthening the U.S pharmaceutical supply chain to ensure its resilience, stability, and accessibility. However, to ensure these efforts do not inadvertently cause significant drug shortages or harm cancer patients and survivors, NCCN recommends a balanced and strategic approach.

Specifically, NCCN recommends:

- Exemptions from import restrictions or potential tariffs for essential oncology medications recommended for use in NCCN Guidelines.
    - Such exemptions are critical for ensuring continued access to life-saving treatments without interruption.
- Establishment of economic incentives such as tax credits and manufacturing grants to encourage domestic production of high-quality generic drugs.
    - These measures would help overcome some of the financial barriers that discourage investment in generic drug production.
- Development of coordinated systems that allow for early identification and communication of potential supply disruptions, which can lead to faster and more effective responses to emerging shortages.
    - Successfully addressing these complex challenges will require coordinated collaboration among federal agencies, manufacturers, and health care providers.

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[12] *Tariffs and geopolitics: API supply chain resilience in 2025*. LGM Pharma. (2025, March 6). https://lgmpharma.com/blog/tariffs-api-supply-chain-resilience-in-2025/#:~:text=As%20of%20February%202025%2C%20China,API%20manufacturing%20has%20only%20strengthened.

[13] Wouters OJ, Kanavos PG, McKEE M. Comparing Generic Drug Markets in Europe and the United States: Prices, Volumes, and Spending. Milbank Q. 2017 Sep;95(3):554-601. doi: 10.1111/1468-0009.12279. PMID: 28895227; PMCID: PMC5594322.

NCCN appreciates the opportunity to provide input and applauds the Department for initiating this important investigation. We hope the findings will help advance the US marketplace for generic drugs. NCCN is happy to serve as a resource and looks forward to working together to advance access to high-quality cancer care and treatment of all people.

Sincerely,

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