

**2024-2025 Vulnerable Medicines List for the United States:
A data-based approach to identify
risks and enable interventions to
increase reliability of supply**

Supply chain risks and drug shortages are persistent and pervasive in the United States

The risks in America's medicine supply are well documented. The number and duration of drug shortages in the United States (U.S.) have persisted for over a decade due to multifaceted and interrelated factors including low prices, geographic concentration of production location, manufacturing complexity, and manufacturing quality issues. Older generic drug products are particularly susceptible to shortage.¹ Drug shortages can have significant impacts on patients, potentially causing treatment delays or the use of less effective treatments, often with unfavorable outcomes.



Identifying medicines vulnerable to shortage can inform effective mitigation strategy

The establishment of a vulnerable medicines list (VML) – a list of medicines derived from an assessment of their essentiality, demand, and supply chain vulnerabilities – is a mitigation strategy recommended by USP and other stakeholders.² A vulnerable medicines list can be used to identify medicines at risk of shortage, allocate finite resources to improve medicine supply chain resiliency, inform future investments to manufacturers of vulnerable medicines, and preserve patient access to necessary medicines.³ USP conducted an analysis to identify 100 vulnerable medicines – 49 used to manage chronic conditions and 51 for acute care – to inform dialogue related to bolstering medicine supply chain resilience. This data-driven approach accounts for the level of use by the U.S. population, the vulnerability of the medicine to supply chain disruptions, and the availability of alternative therapies. The resulting list includes a wide range of therapeutic classes of medicines, as well as a variety of product types.

Our approach accounts for clinical importance and susceptibility to shortage

The methodology used to determine the VML involved two key steps: identification of essential medicines and assessment of supply chain vulnerabilities. This data-driven approach considers the essential role medicines play in U.S. patient care and healthcare systems, the level of use by the U.S. population, and the vulnerability of the medicine to supply chain disruptions. The analysis covers approximately 2,300 drugs separated into acute* and chronic* categories to account for differences in usage pattern data.

The first step determined which drugs are essential to the U.S. population and healthcare system. World Health Organization (WHO)⁴ and U.S. Food and Drug Administration (FDA)⁴ essential medicines lists were used to identify those drugs that are widely used by the U.S. population. To account for drugs that may not appear on either the WHO or FDA lists but are widely used in the U.S., a “reach” measure based on units was introduced to serve as a proxy for prescription data, indicating how extensively a drug is used by the U.S. population. A separate list was created for acute and chronic use drug products to account for differences in reach. A Factor Analysis of Mixed Data (FAMD) method generated a composite index representing the criticality and reach of each drug product.

In step two, vulnerability to supply chain disruptions was measured using the USP Medicine Supply Map's predicted shortage risk scores, which estimate the likelihood of drug shortages over a 12-month period.⁶ Drugs with a shortage risk score above 50% are considered highly vulnerable; those with a score below 50% were removed from analysis. Using the composite index generated in step one, drugs were ranked into a list of vulnerable medicines. An expert review process to account for available drug alternatives further reduced the list to approximately 50 drugs per category (49 for chronic and 51 for acute), yielding a final list of 100 vulnerable drugs as of October 2024. For further information regarding the methodology, see the appendix.



The USP vulnerable medicines list and analysis provide several insights

- Injectable drugs constitute the majority of the list, accounting for 71% of the total drugs.
- The five drugs identified as most vulnerable were all injectables (sodium chloride injection, dextrose injection, heparin sodium injection, propofol injectable emulsion, and lidocaine hydrochloride injection).
- Oral solid drugs, such as tablets and capsules, represent the second-largest group at 15%, while other dosage forms, including mucosal, inhalation, and oral liquids, comprise a smaller combined portion, with less than 15% of the total vulnerable drugs.
- The most prevalent therapeutic classes for vulnerable drugs include pain management, oncologics, hospital solutions, and antibacterial medications.

- Sixteen out of the 100 drugs on the list were not included on the WHO or FDA Essential Medicines Lists. However, they were included on the USP list due to their high reach and significant vulnerability to shortages.
- As of January 2025, 61% of the drugs on the list were not in shortage. Recognizing their high susceptibility to shortage can allow for proactive mitigation and prevention strategies to be enacted to reduce their vulnerability.

Additional research can help to improve vulnerability measurement

This list is intended to complement other resources to identify potential drugs at risk of shortage in the U.S. While comprehensive and data-driven, this list is a snapshot and reflection of the medicines susceptible to supply chain vulnerabilities at the time of analysis and is subject to change over time. Reliance on extended units data as a proxy for prescription data may not capture the full scope of drug utilization. Additionally, the USP Medicine Supply Map's predicted shortage risk scores may not fully account for unlikely events such as natural disasters or geopolitical tensions that can abruptly and acutely affect supply chains. Furthermore, a measure for available medicine alternatives does not exist; future analysis should consider refinement to account for the availability of therapeutic alternatives for each of the approximately 2,300 drugs under consideration.

About USP

The U.S. Pharmacopeia (USP) is an independent, scientific health organization focused on building trust in the supply of safe, quality medicines, dietary supplements, and foods, through setting public quality standards in its various compendia.

Vulnerable chronic condition management medicines

Drug (in alphabetical order)	Dosage Form	Therapeutic Class	Essential Medicine Listed on FDA/ WHO list	Shortage FDA list Jan 2025
amphetamine aspartate, amphetamine sulfate, dextroamphetamine saccharate and dextroamphetamine sulfate tablets	oral solid	attention-deficit/hyperactivity disorder (ADHD)		✓
arformoterol inhalation solution	inhalation	respiratory agent		
budesonide inhalation suspension	mucosal	respiratory agent		
bumetanide injection	injectable	antihypertensive		✓
desmopressin acetate injection	injectable	hormone	✓	
desmopressin nasal spray solution	mucosal	hormone	✓	✓
diazepam injection	injectable	central nervous system (CNS) agent	✓	
diazepam oral solution	oral liquid	CNS agent	✓	
diltiazem hydrochloride injection	injectable	antihypertensive	✓	
diphenhydramine hydrochloride injection	injectable	allergy	✓	
dobutamine in dextrose injection	injectable	cardiovascular	✓	✓
dopamine hydrochloride injection	injectable	cardiovascular	✓	✓
duloxetine delayed-release capsules	oral solid	mental health		
epinephrine injection	injectable	cardiovascular	✓	
flumazenil injection	injectable	CNS agent	✓	
furosemide injection	injectable	antihypertensive	✓	✓
glucagon for injection	injectable	antidiabetic	✓	
haloperidol injection	injectable	mental health	✓	
insulin human injection	injectable	antidiabetic	✓	
ipratropium bromide and albuterol sulfate inhalation solution	inhalation	respiratory agent		
isoniazid injection	injectable	antitubercular	✓	
isoniazid tablets	oral solid	antitubercular	✓	
labetalol hydrochloride injection	injectable	antihypertensive	✓	
levetiracetam injection	injectable	nervous system agent	✓	
levothyroxine sodium injection	injectable	thyroid/anti-thyroid agent	✓	
lisdexamfetamine dimesylate capsules	oral solid	ADHD		✓
lorazepam injection	injectable	CNS agent	✓	✓
lorazepam tablets	oral solid	CNS agent		
magnesium sulfate injection	injectable	nervous system agent	✓	
methotrexate injection	injectable	oncologic	✓	✓
methylphenidate hydrochloride tablets / extended-release tablets	oral solid	ADHD		✓
mometasone furoate inhalation powder	inhalation	respiratory agent		
naltrexone hydrochloride tablets	oral solid	CNS agent	✓	✓
norepinephrine bitartrate injection	injectable	cardiovascular	✓	
olanzapine for extended-release injectable suspension	injectable	mental health	✓	
phenytoin sodium injection	injectable	nervous system agent	✓	
promethazine hydrochloride injection	injectable	allergy	✓	✓
propranolol hydrochloride injection	injectable	antihypertensive	✓	✓
rifampin capsules	oral solid	antitubercular		✓
rifampin for injection	injectable	antitubercular	✓	✓
semaglutide injection	injectable	antidiabetic		✓
sodium chloride irrigation	mucosal	hospital solution		✓
sterile water for irrigation	mucosal	hospital solution		✓
timolol maleate ophthalmic solution	mucosal	antiglaucoma agent	✓	
tirofiban injection	injectable	antithrombotic		
tropicamide ophthalmic solution	mucosal	ophthalmologic	✓	
valganciclovir tablets	oral solid	antiviral	✓	
vasopressin injection	injectable	hormone	✓	
zoledronic acid injection	injectable	osteoporosis	✓	

Drug (in alphabetical order)	Dosage Form	Therapeutic Class	Essential Medicine Listed on FDA/ WHO list	Shortage FDA list Jan 2025
acetylcysteine solution	mucosal	cough and cold	✓	
adenosine injection	injectable	cardiovascular	✓	
amiodarone hydrochloride injection	injectable	cardiovascular	✓	
amoxicillin for oral suspension / tablets	oral liquid	antibacterial	✓	✓
capecitabine tablets	oral solid	oncologic	✓	
carboplatin injection	injectable	oncologic	✓	✓
cisplatin injection	injectable	oncologic	✓	
clindamycin injection	injectable	antibacterial	✓	✓
dexamethasone sodium phosphate injection	injectable	corticosteroid	✓	✓
dexmedetomidine injection	injectable	pain management	✓	✓
dextrose injection	injectable	hospital solution	✓	✓
doxorubicin hydrochloride injection	injectable	oncologic	✓	
enoxaparin sodium injection	injectable	anticoagulant	✓	
erythromycin ophthalmic ointment	mucosal	ophthalmologic	✓	
etomidate injection	injectable	pain management	✓	✓
etoposide injection	injectable	oncologic	✓	
fentanyl citrate injection	injectable	pain management	✓	✓
fluconazole injection	injectable	antifungal	✓	
fluorouracil injection	injectable	oncologic	✓	
gentamicin injection	injectable	antibacterial	✓	
heparin sodium injection	injectable	antithrombotic	✓	✓
hydromorphone hydrochloride injection	injectable	pain management	✓	✓
ketamine hydrochloride injection	injectable	pain management	✓	✓
lenalidomide capsules	oral solid	oncologic	✓	
leucovorin calcium injection	injectable	anti-nauseant		✓
levofloxacin injection	injectable	antibacterial	✓	
lidocaine hydrochloride injection	injectable	pain management	✓	✓
mannitol injection	injectable	hospital solution	✓	
mercaptopurine tablets	oral solid	oncologic	✓	
methotrexate tablets	oral solid	oncologic	✓	
methylprednisolone sodium succinate for injection	injectable	corticosteroid	✓	✓
metronidazole injection	injectable	antibacterial	✓	✓
midazolam injection	injectable	pain management	✓	✓
morphine injection	injectable	pain management	✓	✓
octreotide injection	injectable	hypothalamic hormone	✓	
ofloxacin ophthalmic solution	mucosal	ophthalmologic	✓	
ondansetron injection	injectable	anti-nauseant	✓	
oxycodone hydrochloride tablets	oral solid	pain management	✓	
oxytocin injection	injectable	labor inducer	✓	
paclitaxel injection	injectable	oncologic	✓	
piperacillin and tazobactam injection	injectable	antibacterial	✓	
prednisone tablets	oral solid	corticosteroid		
propofol injectable emulsion	injectable	pain management	✓	
protamine sulfate injection	injectable	coagulant	✓	
rocuronium bromide injection	injectable	pain management	✓	✓
sodium bicarbonate injection	injectable	hospital solution	✓	✓
sodium chloride injection	injectable	hospital solution	✓	✓
sodium phosphates injection	injectable	hospital solution	✓	
sterile water for injection	injectable	hospital solution	✓	✓
succinylcholine chloride injection	injectable	pain management	✓	
vancomycin injection	injectable	antibacterial	✓	

Appendix – Detailed Methodology

This analysis determined and prioritized essential medicines in the U.S. based on their importance to individual patients, overall population, and a functioning healthcare system, as well as their vulnerability to supply chain disruptions. The analysis covers approximately 2,300 drugs and was conducted in two main steps:



Step 1: Identifying Essential Medicines

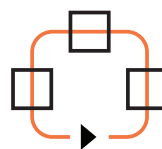
Before identifying essential medicines and assessing their supply chain vulnerabilities, this analysis separated drugs into acute and chronic categories to account for differences in usage patterns. Acute drugs, such as antibiotics, are used for short periods, while chronic drugs, like insulin, are used continuously over long periods. Comparing these drug categories without distinction could lead to skewed results, as chronic drugs would appear to have more widespread use even though acute drugs may affect larger patient populations in short-term scenarios.

Essential medicines, as defined by the World Health Organization (WHO),⁴ are those that satisfy the priority healthcare needs of the population. These drugs are selected based on disease prevalence, public health relevance, efficacy, safety, and cost-effectiveness, and are intended to be available in functioning health systems at all times. The U.S. Food and Drug Administration (FDA)⁵ defines Essential Medicines as medical countermeasures (e.g., for responding to future pandemics, epidemics, and chemical, biological, and radiological/ nuclear threats) and drugs for patients in U.S. acute care medical facilities specializing in the short-term treatment of severe injuries, illnesses, and urgent conditions.

Not all essential drugs listed by the WHO are directly relevant to the U.S. healthcare system; some drugs may not be as essential due to varying public health needs or availability of alternative treatments. Furthermore, the scope of the FDA Essential Medicines list is limited to medical countermeasures and drugs used in acute-care settings; it does not consider drugs used to treat chronic long-term diseases. To refine the analysis and better assess which drugs are most essential in the U.S., criteria were extended to include a reach measure which evaluates the extent to which a drug is used across the population. This reach

measure helps account for drugs that are widely used, and therefore essential to public health in the U.S., even if they are not included in the WHO or FDA essential medicines lists. Reach is based on IQVIA's extended units (tabs/capsules/mL), which serve as a proxy for prescription data, indicating how extensively a drug is used by the population.

To synthesize the criticality (categorical) and reach (continuous) variables into a meaningful measure that not only reflects the importance of the medicine to the patient, population, and healthcare system but also serves the purpose of ranking the medicines with respect to essentiality, a Factor Analysis of Mixed Data (FAMD) method was applied. FAMD is a dimensionality reduction technique designed to handle datasets that contain both categorical and continuous variables. FAMD generated a composite index – essentiality – that captures the most important information regarding the criticality and reach of each drug.*



Step 2: Assessing Supply Chain Weaknesses

After identifying the most essential medicines for the U.S., a second step evaluated the shortage risk for each medicine. Vulnerability to supply chain disruptions is measured using the USP Medicine Supply Map's predicted shortage risk scores, which estimate the likelihood of drug shortages over a 12-month period. Factors such as manufacturing complexity, concentration of production location, price, quality, shortage history, and others are used in the algorithm to calculate the Medicine Supply Map risk score.⁶ Drugs with a shortage risk score above 50% are considered highly vulnerable. Using the USP Medicine Supply Map's predicted shortage risk scores, drugs with a score below 50% were filtered out, focusing on those medicines that are most at risk of supply shortages in the coming year.

The remaining medicines (those with the largest composite index) were flagged as vulnerable medicines. Clinical experts from a USP Expert Committee did a final review to prioritize drugs with no available therapeutic alternatives since these data are not readily available to factor into the data analysis. This review further shortened the lists.

Footnotes

- † Acute drugs, such as antibiotics, are used for short periods.
- ‡ Chronic drugs, like insulin, are used continuously over long periods.
- * A naïve-distance approach was also attempted. A comparison of the lists generated reveals that the acute lists differ by only 2-3 drugs (depending on the year considered), while the chronic lists are identical.

References

1. United States Pharmacopeia. [USP Annual Drug Shortage Report: Economic factors underpin 2023 shortages](#). 2024.
2. USP's approach borrows from the framework proposed in the article: "Wosinska, M., Mattingly, T., & Conti, R. [A Framework for Prioritizing Pharmaceutical Supply Chain Interventions](#). 2023." We extend our gratitude to the authors for their input.
3. United States Pharmacopeia. [USP Global Public Policy Position: Identifying and addressing vulnerabilities in the upstream medicines supply chain to build resilience and reduce drug shortages](#). 2023.
4. World Health Organization. [WHO Model Lists of Essential Medicines](#). 2023.
5. U.S. Food and Drug Administration. [Executive Order 13944 List of Essential Medicines, Medical Countermeasures, and Critical Inputs](#). 2022.
6. [Medicine Supply Map](#). The Medicine Supply Map uses over 100 different features of a drug to predict its likelihood of going into a shortage in the near future. Features include market and supply economics (e.g., market concentration, price), manufacturing complexity (e.g., API synthesis complexity), quality (e.g., regulatory agency inspections) and geographic concentration. Predictions are available for over 92 percent of FDA-approved generic prescription drugs. In 2023, the USP Medicine Supply Map identified a "severe risk of shortage" for 91% of generic sterile injectable shortages in 2023, including 58% of injectable drugs that newly went into shortage.