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Rx newsletter

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Market Trends

The impact of drug shortages within the U.S.

Drug shortages in the U.S. have become a pressing issue, impacting patient care, health care costs, and the overall health care system. According to the U.S. Pharmacopeia, the number of drug shortages has increased dramatically over the past decade, from 82 FDA-monitored drug shortages in December 2014 to 125 shortages in December 2023.[1] A primary concern is the increasing frequency and duration of shortages. A recent report from IQVIA (a provider of technology, analytics, and research services to the life sciences industry) noted that therapeutic areas impacted by drug shortages include pain/anesthesia, oncology, central nervous system, and infectious disease, as well as the recent shortages seen with GLP-1 medications used to treat diabetes and weight loss.[2] Of the 132 medications in shortage as of June 2023, 75% have been active shortages for more than one year and 58% have been ongoing for greater than two years.[2]

Impact on patient safety & clinical outcomes

When a patient does not have easy access to their medication, health care providers will often look to alternative drug therapies to treat their condition. This could lead to adverse drug reactions, interruptions in treatment, drug errors, as well as increases in hospitalization or utilization of other health care services. Antimicrobials and oncology medications are the medication classes most tied to poor patient outcomes.[3] For example, medication errors may occur due to clinicians being unfamiliar with the alternative therapies. One study found that in 54% of drug shortages, clinicians may be unfamiliar with the alternative product regarding its mechanism of action, adverse effects, or interactions.[4] Additionally, patients requiring chemotherapy or critical antibiotics may face interruptions in their treatment regimens, increasing the risk of disease progression or complications.

Impact on drug costs

From a cost perspective, plan sponsors may face significant financial implications. When shortages occur, health care providers may resort to using higher-cost alternatives or off-label medications, leading to increased claims and higher premiums for self-funded medical and pharmacy benefits. Additionally, employees may experience higher out-of-pocket costs if they are required to pay for more expensive alternatives or if their treatment plans are disrupted. One analysis observed between a 7.2% and 16.6% increase in drug prices for insured patients 12 months after a shortage occurs.[5] The financial impact of drug shortages can also extend beyond immediate costs. Delayed treatments may result in more severe health issues, leading to increased hospitalizations and long-term care needs, which can further inflate health care costs for plan sponsors.

Plan sponsors should assess the following key considerations:

- Stay informed about regulatory changes and ensure that your health plan and pharmacy providers comply with any new requirements related to drug availability.
- Collaborate with your pharmacy provider and MMA to develop protocols for addressing shortages, including communication strategies with both health care providers and patients.
- Connect with your pharmacy provider and MMA to understand the potential financial and clinical impact of moving patients to alternative therapies.

Sources:

1. "The U.S. drug shortage crisis, in 5 charts," Advisory Board Daily Briefing, accessed October 21, 2024, https://www.advisory.com/daily-briefing/2024/06/13/drug-shortages.
2. Aitken M, et al., "Drug Shortages in the U.S. 2023." IQVIA Institute for Human Data Science, accessed October 29, 2024, https://www.iqvia.com/-/media/iqvia/pdfs/institute-reports/drug-shortages-in-the-us-2023/drug-shortages-in-the-us-2023.pdf.
3. Minh Phuong J et al., "The impacts of medication shortages on patient outcomes: a scoping review," PLoS One, accessed October 21, 2024, https://pmc.ncbi.nlm.nih.gov/articles/PMC6499468/.
4. Fox ER, Tyler LS., "Managing drug shortages: seven years' experience at one health system," Am J Health Syst Pharm, accessed October 21, 2024, https://doi.org/10.1093/ajhp/60.3.245.
5. "Impact of Drug Shortages on Consumer Costs. U.S. Department of Health and Human Services," Office of the Assistant Secretary for Planning and Evaluation report to Congress, accessed October 21, 2024, https://aspe.hhs.gov/sites/default/files/documents/87781bc7f9a7fc3e6633199dc4507d3e/aspe-rtc-costs-drug-shortages.pdf#:~:text=Consumers%20may%20incur%20increased%20costs%20in%20the%20form,incur%20costs%20to%20manage%20or%20mitigate%20drug%20shortages.

Pharmacy 101

Treatment of obesity: Beyond the GLP-1s

The GLP-1 medications have become deeply ingrained in our culture, thanks to extensive marketing efforts and a surge of social media posts, making many people aware of their potential for significant weight loss in those who are overweight. But often lost in the conversation is awareness of other oral anti-obesity medications (AOM) that have demonstrated moderate clinical success and are available at a much lower cost than their GLP-1 counterparts.

The most common weight loss medications outside of the GLP-1 category:

1. Orlistat: Works by reducing the amount of fat that is absorbed, leading to weight loss. Orlistat is available over-the-counter (Alli®) and in prescription strength (Xenical®).
2. Phentermine: A generic stimulant medication that suppresses appetite and increases feelings of fullness. It is typically used for short-term management of obesity.
3. Phentermine/Topiramate (Qsymia®): Combines phentermine, an appetite suppressant, with topiramate, an anticonvulsant medication.
4. Bupropion/Naltrexone (Contrave®): This combination medication includes bupropion, an antidepressant, and naltrexone, a medication used to treat opioid addiction.

Before GLP-1 medications were introduced, AOMs were prescribed less frequently due to their side effects and modest weight loss. The initial clinical studies showing over 15% weight loss with GLP-1s quickly shifted the focus away from other alternative options.[1]

Comparison of study results for GLP-1s & AOMs

Recent real-world evidence of persistence issues, side effects, and modest weight loss in GLP-1s suggests that alternative AOMs may be a more cost-effective treatment option or or as a first-line agent within a step-therapy protocol, which requires patients to try lower-cost medications before accessing more expensive treatments.

No head-to-head studies currently compare the efficacy of GLP-1s to Qsymia, but we can compare results of the individual studies. Researchers found that the use of semaglutide (Wegovy®) resulted in 14.9% weight loss at 68 weeks, with 69% of participants losing at least 10% of their starting weight.[2] In contrast, the CONQUER study for Qsymia® showed weight loss of 8-10% after 56 weeks, with 48% losing at least 10% of their starting weight.[3] While side effects differ (including dry mouth, insomnia, and dizziness), both medications have similar discontinuation rates

These studies suggest that anti-obesity medications (AOMs), particularly a less costly oral medication, may be a viable treatment option for certain patient populations, especially those with a lower BMI who do not need to lose significant weight.

Plan sponsors should assess the following key considerations:

- Engage with your pharmacy benefit managers to discuss the formulary options available for anti-obesity medications. PBMs can provide information on the cost, coverage, and utilization management strategies associated with different medications, including those used as first-line treatments.
- Transparent communication with employees is essential when considering alternative anti-obesity medications. Plan sponsors should ensure that employees have resources available to understand their anti-obesity treatment options, including coverage and cost.

Sources:

1. "Two-year effects of semaglutide in adults with overweight or obesity: the STEP 5 trial, Nat Med, accessed September 19, 2024, https://doi.org/10.1038/s41591-022-02026-4.
2. John PH, et al., "Once-Weekly Semaglutide in Adults with Overweight or Obesity," The New England Journal of Medicine, accessed September 19, 2024, https://www.nejm.org/doi/full/10.1056/NEJMoa2032183.
3. Gadde KM, et al., "Effects of low-dose, controlled-release, phentermine plus topiramate combination on weight and associated comorbidities in overweight and obese adults (CONQUER): a randomized, placebo-controlled, phase 3 trial," The Lancet, September 19, 2024, https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(11)60205-5/abstract.

Disease Spotlight

Notable new gene therapies in the treatment of hemophilia

Gene therapy has emerged as a promising approach for the treatment of hemophilia, a hereditary bleeding disorder caused by defects in the F8 or F9 gene. Traditional treatment methods for hemophilia involve frequent intravenous administration of factor concentrate, which can be burdensome, time-consuming, and can be quite expensive over time. Gene therapy offers the possibility of a one-time treatment that provides sustained factor expression, reducing the need for regular infusions and improving patients' quality of life.

Recent research has focused on developing gene therapies that can provide long-term relief from hemophilia symptoms by introducing functional copies of the defective genes. This has the potential to revolutionize the delivery of care for patients with hemophilia. In June 2023, the U.S. Food and Drug Administration (FDA) approved Roctavian™ (Valoctocogene roxaparvovec), an adeno-associated virus (AAV) vector-based gene therapy, for the treatment of severe hemophilia A in adults. This approval is a significant milestone in the field of gene therapy for hemophilia, offering a new treatment option for patients. Clinical trials have shown promising results, with the average annualized bleed rate (ABR) decreasing from 5.4 to 2.6 during the 3-year follow-up period.[1]

The cost-effectiveness of gene therapy for hemophilia is a topic of ongoing research and discussion. One study compared the cost-effectiveness of gene therapy with standard prophylactic treatment using factor VIII replacement therapy for hemophilia A. Over a 10-year period, gene therapy cost $1 million and resulted in 8.33 quality-adjusted life years (QALYs), while prophylactic treatment cost $1.7 million and resulted in 6.62 QALYs.[2]

There are currently two gene-based therapies in phase 3 clinical trials competing to be the second therapy for hemophilia A alongside Roctavian™. Dirloctogene (Spark Therapeutics) and Giroctocogene (Pfizer and Sangamo Therapeutics) both use viral vectors (adeno-associated virus) to deliver the therapeutic gene once injected into the patient. These therapies are expected to receive FDA approval in 2025.[3]

Plan sponsors should assess the following key considerations:

- Plan Sponsors need to assess the financial impact on their self-funded medical and pharmacy benefits. This includes evaluating how such a high-cost treatment will affect overall claims and premiums.
- Plans should assess their current Stop Loss coverage and any lasering that may be in place. Many health plans offer cost management options that can be evaluated as an option.
- Gene and cellular therapies may lead to long-term savings by reducing the need for ongoing factor replacement therapies, which can be costly over a patient's lifetime. Assess any cost-benefit analyses to determine the potential for reduced health care expenditures in the long

Sources:

1. "Roctavian Clinical Study Results", ROCTAVIAN, accessed September 24, 2024, https://www.roctavian.com/en-us/roctavian-results/.
2. Machin N, et al., "Gene therapy in hemophilia A: a cost-effectiveness analysis," Blood Advances, accessed September 24, 2024, https://ashpublications.org/bloodadvances/article/2/14/1792/16245/Gene-therapy-in-hemophilia-A-a-cost-effectiveness.
3. "Drug and biologic pipeline update Q3 2024," CarelonRx," accessed September 24, 2024, https://www.carelonrx.com/content/dam/digital/carelon/crx-assets/documents/Q3_2024_Drug_and_Biologic_Pipeline_NL.pdf.

Clinical Spotlight

Intravenous immune globulin (IVIG)

Intravenous immune globulin (IVIG) is a therapy that involves the administration of human antibodies derived from blood donors through subcutaneous or intravenous injection. Known as a "plasma derivative," it is derived from the liquid portion of blood plasma without cells. IVIG is used to treat various immunodeficiencies and conditions, including autoimmune, infectious, and inflammatory disorders.

History of IVIG therapy

The history of IVIG therapy dates to the 1950s when it was first used to treat patients with primary immunodeficiency disorders. IVIG works by providing a boost to the immune system, helping to normalize a compromised immune system and improve the body's ability to fight off infections and diseases.

Today's immunoglobulin product market

As of now, there are 16 different immunoglobulin products available on the market, which have six FDA-approved indications.[1] Eight have a subcutaneous formulation and the others are administered intravenously. The indications for IVIG therapy are diverse and include primary immunodeficiency (PID), idiopathic thrombocytopenic purpura (ITP), chronic lymphocytic leukemia, multifocal motor neuropathy, chronic inflammatory demyelinating polyneuropathy (CIDP), and Kawasaki disease. Additionally, immunoglobulin has been used in the treatment of more than 100 other disease states but are considered off-label due to their lack of clinical trial data.[1]

Although each available product is similar, there are clinical factors that need to be considered when switching products. Each product contains immunoglobulin G but may also contain other immunoglobulins, such as immunoglobulin A and immunoglobulin M, along with other ingredients that can create tolerability issues when switching between products. The different formulations also can result in changes in product concentration and infusion rates, as well as tolerability.[2]

In terms of cost, IVIG therapy can be quite expensive. The cost varies depending on factors such as the dosage, frequency of administration, and the specific brand of IVIG used. In 2023, IVIG ranked as #16 in the top U.S. healthcare expenditures at $6.3 billion, up 2.5% from the previous year.[3]

Current research and development efforts

The pharmaceutical industry is continuously working on research and development efforts to improve the effectiveness and safety of IVIG therapy. This includes exploring new formulations, delivery methods, and potential indications for its use. Targeted new indications include Myasthenia Gravis, Chronic Inflammatory Demyelinating Polyradiculoneuropathy, and Late-Onset Combined Immune Deficiency which uses phenotyping to target specific patients and could lead to insights into genetic diagnoses.[1]

Plan sponsors should assess the following key considerations:

- IVIG is indicated for several conditions. Plan Sponsors should ask their pharmacy teams to explain how they develop guidelines for appropriate use, ensuring that IVIG is prescribed only when clinically necessary and to prevent off-label use.
- With the large number of immunoglobulin products on the market, formulary management is an important way to maximize the value of these therapies. Plan Sponsors should work with their pharmacy provider and MMA to assure appropriate patient access to immunoglobulins.

Sources:

1. Siegel J., "Ig FAQ: What's the Future for Ig Therapies?," Specialty Pharmacy Continuum Ask the Expert, accessed September 23, 2024, https://www.specialtypharmacycontinuum.com/Ask-The-Expert/Article/09-21/Ig-FAQ-Whats-the-Future-for-Ig-Therapies/64749.
2. Siegel J., "Immune Globulins: Therapeutic, Pharmaceutical, Cost, and Administration Considerations," Specialty Pharmacy Continuum, accessed September 23, 2024, https://www.specialtypharmacycontinuum.com/download/PF241_WM.pdf.
3. Tichy EM, et al., "National trends in prescription drug expenditures and projections for 2024," American Journal of Health-System Pharmacy, accessed September 23, 2024, https://academic.oup.com/ajhp/article-abstract/81/14/583/7657643?redirectedFrom=fulltext&login=false.

Pipeline

Pending drug approvals

Drug name	Manufacturer	Indication/use	Expected FDA decision date
eladocagene exuparvovec (Upstaza™)	PTC Therapeutics	Aromatic L-amino acid decarboxylase (AADC) deficiency	11/13/2024
govorestat	Applied Therapeutics	Classic galactosemia	11/28/2024
acoramidis	Bridgebio / AstraZeneca	Transthyretin amyloid cardiomyopathy	11/29/2024
nemolizumab	Galderma	Atopic dermatitis	12/14/2024
revakinagene taroretcel	Neurotech	Macular telangiectasia type 2	12/17/2024
irinotecan liposome	CSPC	Pancreatic cancer	12/18/2024
olezarsen	Akcea	Familial chylomicronemia syndrome	12/19/2024
glepaglutide	Zealand	Short bowel syndrome	12/20/2024
nivolumab/hyaluronidase (Opdivo® SC)	Bristol-Myers Squibb	Bladder cancer; Melanoma; RCC; Solid tumors	12/27/2024
ensartinib	Xcovery	NSCLC	12/28/2024
crinecerfont	Neurocrine	Congenital adrenal hyperplasia	12/29/2024
vanzacaftor/tezacaftor/ deutivacaftor	Vertex	CF (ages > 6 years)	1/02/2025
zenocutuzumab	Merus	NSCLC (NRG1+); Pancreatic cancer (NRG1+)	1/06/2024
elamipretide	Stealth	Barth syndrome	1/29/2024

Brands Losing Patent

Drug name	Manufacturer	Indication/use	Date Generic Available
Nourianz	istradefylline	"wearing-off" episodes in adults with Parkinson's disease	November 2024
Macrilen	macimorelin acetate	Adult growth hormone deficiency	December 2024
Ryaltris	mometasone furoate; olopatadine hydrochloride	Seasonal allergic rhinitis	January 2025
Sancuso	granisetron	Prevention of nausea and vomiting	January 2025
Duaklir Pressair	aclidinium bromide; formoterol fumarate	COPD	February 2025
Tudorza Pressair	aclidinium bromide	COPD	February 2025
Izervay	avacincaptad pegol sodium	Geographic atrophy due to AMD	February 2025
Juxtapid	lomitapide mesylate	Lipid lowering treatment	March 2025
Targiniq	naloxone hydrochloride; oxycodone hydrochloride	Pain medication	March 2025

*Actual launch dates depend on FDA approvals and may change at any time

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