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# Rx newsletter

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# Market trends

## What health care trends will be prominent in 2024 and beyond?

### Longer-living population:

With advancements in medical technology and improved health care services, people are living longer. Health care providers will strengthen their focus on preventative care including wellness, exercise, and diet to reduce costs associated with chronic disease such as obesity, diabetes, cardiovascular disease, and cancer. The advancement in technologies such as wearable devices to remotely monitor patients and for providers to deliver their care has been referred to as "telemedicine 2.0" as it goes beyond simple remote monitoring.[1]

### Transformative technologies:

The emergence of transformative technologies is revolutionizing the health care industry in 2024. These technologies have applications across the entire health care spectrum, from diagnosis and treatment to patient care and management. Examples of such technologies include artificial intelligence, telemedicine, and wearable devices. The most dramatic advancement may be around genomics and precision medicine, where AI can diagnose and treat diseases by analyzing patient DNA.[1] These innovations have the potential to improve patient outcomes, enhance efficiency, and reduce health care costs.

### Growth of the Specialty Pharmacy Market:

Specialty pharmacy has seen tremendous growth in the past decade, becoming a significant contributor to prescription revenue. Currently, it accounts for 40% of total revenue, and this figure is projected to increase to 50% by 2027.[2] The expansion of vertical relationships among insurers, pharmacy benefit managers, and providers will also include specialty pharmacies as a self-contained profit center. These vertically integrated pharmacies have successfully contracted with major health systems to provide specialty medications to 340b eligible hospitals.

The combination of restrictions placed on location and size of pharmacies that can provide covered services, coupled with the desire to maintain a large and growing revenue stream in-house, is expected to lead to increasing investments in hospital-owned specialty pharmacies.[2] This will also lead to expected growth in physician office and ambulatory infusion centers serviced by these hospital-owned pharmacies.

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# Pharmacy 101

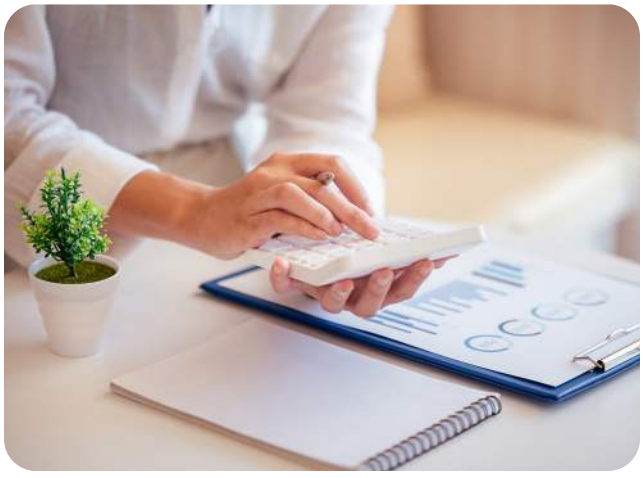
## Biosimilars impact to PBM's formulary & rebate language

### Biosimilars are shifting the Humira drug market by providing lower costs to patients and clients.

The first interchangeable biosimilar was approved in October 2021. Since then, a total of 10 FDA-approved biosimilars have been introduced. The most recent approval, in February 2024, was for a high concentration Humira biosimilar.[1] Pharmacy benefit managers have been actively updating their formularies and rebate contract language to accommodate the increasing number of FDA approvals for biosimilars.

### PBM's Evolving Formulary

The three major pharmacy benefit managers (PBMs) have been closely monitoring the increasing number of approvals for Humira biosimilars. They have been working to ensure that their formularies accurately reflect the coverage options for these new medications. There are a few potential approaches they can take in this regard: excluding Humira from their formularies altogether, modifying their formularies to classify Humira as a non-preferred medication, or incorporating the interchangeable biosimilars into their formularies.



CVS, for example, will completely exclude AbbVie's Humira from all of their formulary options starting April 1, 2024. By excluding Humira, patients will be recommended to take the biosimilars instead. On the other hand, Optum will continue to offer Humira on their formulary while also adding two low wholesale acquisition cost biosimilars. This gives clients the option to access biosimilars while still having coverage for Humira if they prefer. Similarly, ESI will adopt low wholesale acquisition cost (WAC) biosimilars to their National Preferred Formulary.[2]

### Rebate Contract Language Updates

Many PBM's will start to evaluate rebate contract language as they shift to utilizing interchangeable biosimilars versus Humira.

Typically, manufacturers provide rebates as a percentage of the wholesale cost. Therefore, if there is a lower-cost alternative available, the rebate amount would be lower as well. The cost of the biologics is less than that of the brand drug in which the PBM may propose a credit to account for this difference.

To illustrate this further, let's consider a hypothetical scenario. Suppose we have a specialty rebate guarantee of $3,000 based on a $10,000 drug. If the price of the drug decreases to $5,000, the expected rebate would be $1,500, which falls short of meeting the rebate guarantee outlined in the contract. This poses a risk for the PBM, as they may not be able to fulfill the rebate guarantee. To mitigate this risk, the PBM has developed a methodology to provide a rebate credit. This credit will be calculated alongside the regular rebates, ensuring that the rebate guarantee is not impacted by the dispensing of these less costly drugs. Ultimately, the net cost to the plan should remain the same.

While the client pays less for the biologic upfront, there may be a potential reduction in the rebate amount compared to the brand drug. On the other hand, with Humira, the client pays more for the drug but receives a higher rebate. The goal is to maintain a balanced approach that considers both the upfront cost and the rebate amount.

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1. "FDA Oks First Interchangeable, High Concentration Humira Biosimilar," Medscape Medical News, accessed April 10, 2024, https://www.medscape.com/viewarticle/fda-oks-first-interchangeable-high-concentration-humira-2024a10003rd?form=fpf
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# Disease Spotlight

## Metabolic dysfunction-associated steatohepatitis (MASH)

Metabolic dysfunction-associated steatohepatitis (MASH), formerly referred to as NASH), is a progressive form of metabolic dysfunction-associated steatotic liver disease (MASLD) characterized by inflammation and liver cell damage. MASH occurs when excess fat accumulates in the liver, leading to inflammation and injury. The exact cause is not fully understood, but it is believed to be a multifactorial disease with a combination of genetic, metabolic, and environmental factors playing a role.[1]

The prevalence of MASH is increasing worldwide, largely due to the rising rates of obesity and metabolic disorders. It is estimated that up to 25% of the adults in the U.S. may have MASLD, and approximately 20% of these individuals have progressed to MASH.[1] MASH is more common in individuals with certain risk factors, such as obesity, type 2 diabetes, high cholesterol, and high blood pressure, as well as Hispanic or Asian ethnicity, age over 40, and postmenopause.[1]

Symptoms of MASH can be nonspecific and may include fatigue, abdominal discomfort, and mild jaundice. However, many individuals are asymptomatic and may only be diagnosed through routine liver function tests or imaging studies. Diagnosis requires a liver biopsy to assess the degree of inflammation, liver cell damage, and fibrosis.

The management of MASH involves lifestyle modifications, including weight loss, regular exercise, and a healthy diet. Studies have shown that a weight loss of 10% or more has been shown to improve liver histology, reduce disease progression and in some cases reverse liver fibrosis.[2] In addition, controlling underlying metabolic conditions, such as diabetes and high cholesterol, is important in managing this condition.

In severe cases, up to 20% of patients will progress to cirrhosis over a 15-year time period and liver transplantation may be necessary.[3] However, prevention and early intervention are key in managing

and preventing disease progression. Regular monitoring of liver function, lifestyle modifications, and close collaboration with healthcare providers are essential in the management of MASH.

Until recently, there were no therapeutic pharmaceutical treatments to manage MASH. On March 16, 2024, the FDA approved the first medication treatment for this condition, Resmetirom (Madrigal Pharmaceuticals). It is approved as an oral formulation for use in conjunction with diet and exercise for adults with noncirrhotic MASH with moderate to advanced liver fibrosis (stages F2-F3 fibrosis). Clinical trials have shown a 50-60% reduction in liver fat associated with a 64% MASH resolution.[4] The company said it expects resmetirom to be available through a limited specialty pharmacy network in the United States in April.

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# Clinical Spotlight

## Pharmacy compounding & compounded GLP-1 products

The history of retail pharmacy compounding of prescriptions dates to the early 20th century. In the 1930s, approximately 75% of prescriptions required some form of in-pharmacy compounding. However, this practice has significantly declined over the years. By the 1950s, only 25% of prescriptions required compounding, and by 1970, only 1% of prescriptions needed compounding in retail pharmacies.[1]

Pharmacy compounding refers to the practice of preparing customized medications to meet specific patient needs when a commercially available product or formulation is unavailable. While compounding plays a crucial role in pharmacy, it is subject to various laws and regulations that ensure patient safety and quality control.

In the United States, compounding is primarily regulated by the Food and Drug Administration (FDA) and individual state boards of pharmacy. The FDA oversees compounding under the Drug Quality and Security Act (DQSA), which distinguishes between traditional compounding, exempt from certain FDA requirements, and non-traditional compounding, which requires compliance with more stringent regulations.

For example, the Pennsylvania State Board of Pharmacy regulates traditional compounding practices in pharmacies within the state. It defines compounding as the preparation, mixing, assembling, packaging, or labeling of a drug or device based on a prescription order or a practitioner's authorization in accordance with section 503a of the Food, Drug, and Cosmetic Act.

It specifically prohibits the preparation of drugs that are essentially copies of a commercially available product.[2] This statement is impactful if pharmacies begin to compound prescriptions when a commercially available product is available. The FDA does maintain a list of bulk drug substances that may be used in compounding if it determines there is a clinical need, or the drug appears on the FDA's drug shortage list.[3]

With the explosion of the use of GLP-1 medications for weight loss, patients have looked for ways to obtain these medications when they are not covered by their plan or when supply is not keeping up with demand. This has led to entities marketing compounded version of the weight loss GLP-1's to patients using social media and web marketing tactics. Since GLP-1 medications are available as commercially manufactured products; compounding GLP-1 medications can pose legal risks due to potential violations of patent laws and FDA regulations. In June of 2023, Novo Nordisk, the manufacturer of Ozempic® and Wegovy®, filed multiple lawsuits against spas and clinics in four states alleging that they infringed on its trademarks, falsely advertised their products, and created unfair competition by marketing and selling unapproved compounded versions of their products.[4]

Additionally, there are safety and efficacy concerns associated with compounded injectable GLP-1 products, as they do not undergo the same level of testing and quality control as the commercially available versions. The FDA has received reports of compounders using salt forms of semaglutide that are different from the active ingredients used in the approved drugs. Furthermore, the FDA has received adverse event reports following the use of these compounded products by patients.[5]

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# Pipeline

## Pending drug approvals

| Drug name | Manufacturer | Indication/use | Expected FDA decision date |
|---|---|---|---|
| Dupixent (dupilumab) | Regeneron/Sanofi | Chronic obstructive pulmonary disease | 6/27/2024 |
| aflibercept (biosimilar to Regeneron's Eylea) | Celltrion | DME; Diabetic retinopathy; Macular edema following RVO; Wet AMD | 6/28/2024 |
| aflibercept (biosimilar to Regeneron's Eylea) | Coherus | DME; Diabetic retinopathy; Macular edema following RVO; Wet AMD | 6/28/2024 |
| Iptacopan | Novartis | Paroxysmal nocturnal hemoglobinuria (PNH) | |
| Deuruxolitinib | Sun Pharmaceuticals | Alopecia areata | July 2024 |
| Crovalimab | Genentech | Paroxysmal nocturnal hemoglobinuria (PNH) | 7/27/2024 |
| Danicopan | AstraZeneca | Paroxysmal nocturnal hemoglobinuria (PNH) | 7/27/2024 |
| sotatercept | Merck/Bristol-Myers Squibb | PAH | 8/01/2024 |
| Nemolizumab | Galderma | Prurigo nodularis (PN) | 8/12/2024 |
| Seladelpar | Gilead/CymaBay Therapeutics | Primary biliary cholangitis | 8/14/2024 |
| Linvoseltamab | Regeneron Pharmaceuticals | Multiple myeloma | 8/22/2024 |
| mavorixafor | X4 | Warts, hypogammaglobulinemia, infections, and myelokathexis (WHIM) syndrome | 9/05/2024 |
| Tovorafenib | Day One Bio | Glioma (relapsed/ progressive, low-grade, monotherapy) | 9/11/2024 |
| Ocrevus SC (ocrelizumab/ hyaluronidase) | Genentech | Multiple sclerosis | 9/13/2024 |
| Tradipitant | Vanda Pharmaceuticals | Gastroparesis | 9/18/2024 |
| Xanomeline/trospium | Bristol Myers Squibb | Schizophrenia | 9/26/2024 |

## Brands Losing Patent

| Brand name | Generic name | Indication/use | Date generic available |
|---|---|---|---|
| Complera | Emtricitabine, Rilpivirine, Tenofovir | HIV | January 2024 |
| Gralise | Gabapentin | Neuropathic pain | January 2024 |
| Omidria | Ketorolac 0.3%/ Phenylephrine 1% | Used during eye surgery & to lower eye pain after eye surgery | January 2024 |
| Exparel | bupivacaine | Post-operative pain management | March 2024 |
| Farxiga | dapagliflozin | Diabetes, heart disease, kidney disease | April 2024 |
| Ionsys | fentanyl hydrochloride | Pain management | April 2024 |
| Contrave | bupropion hydrochloride; naltrexone hydrochloride | Weight management | April 2024 |
| Entresto | sacubitril and valsartan | Chronic heart failure | May 2024 |
| Xarelto | rivaroxaban | Prevent blood clots | August 2024 |
| Vandazole | Metronidazole | Bacterial vaginosis | September 2024 |

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

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