MARSH & McLENNAN AGENCY

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Rx Newsletter

In This Issue

Market Trends

Biosimilar vs biologics: what are they and is cost savings coming?

Biologics generally come from living organisms, which can include animal cells and microorganisms, such as yeast and bacteria.

That makes biologics different from conventional medications, which are commonly made from chemicals. Due to the complex nature of living organisms, biologics cannot be made by following a chemical "recipe," as is the case when creating a generic version of a conventional medication.

What is a biosimilar?

According to the FDA, biosimilars are medications made from natural living ingredients. They are highly similar but not exact copies of the original biological drug. Biosimilars are made from the same types of living sources as original biologics and before they are approved, the FDA makes sure that biosimilars are just as safe and effective as the original biologic.

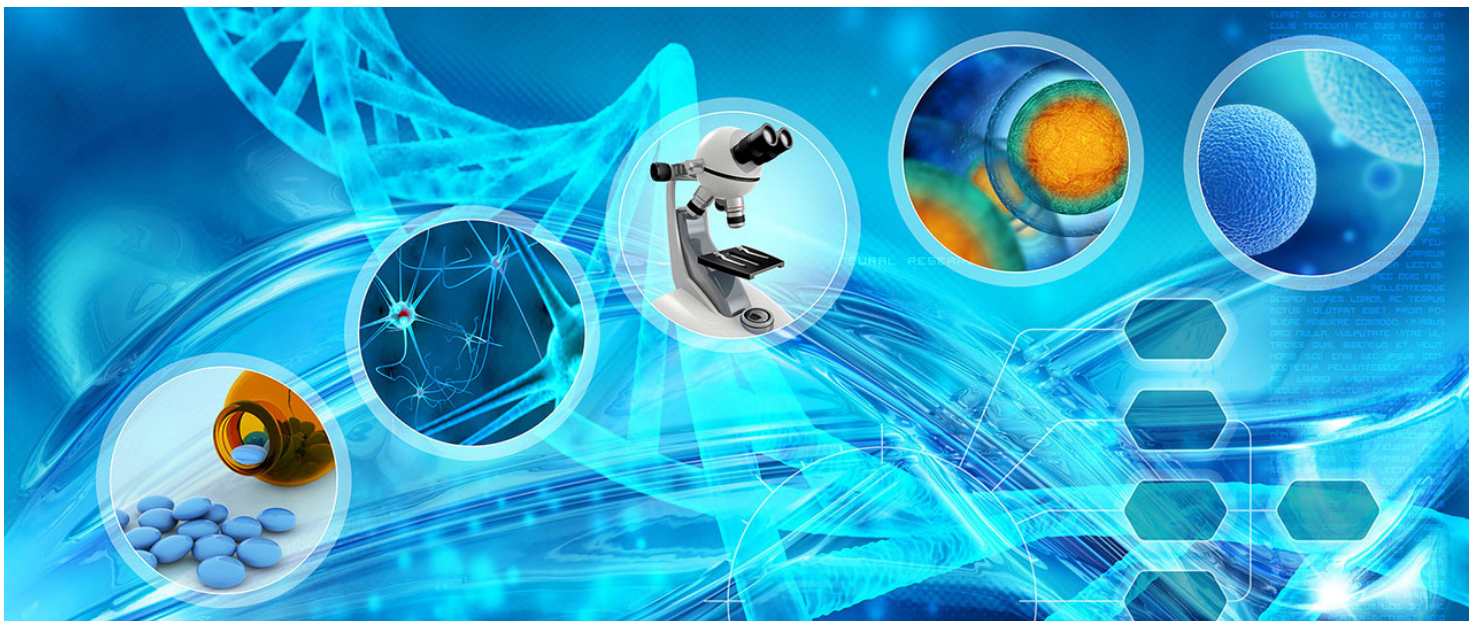
- Biosimilars and biologics both:
  - are made with the same types of natural sources,
  - are administered the same way,
  - provide the same treatment benefits,
  - have the same potential side effects,
  - have the same strength and dosage.

Once a drug has been shown to be biosimilar to a reference medication (aka the original biologic), it can be approved for all the same conditions as that reference medication even if it hasn't been specifically tested for each and every condition.

The biosimilar impact

The hope is that biosimilars will bring less expensive copies of many biologic drugs to the market, thereby increasing affordability and expanding access to many different types of therapies around the world. While producing a generic drug is fairly easy, the production of a biosimilar requires highly specialized knowledge and expertise, and capital investment. While generic pharmaceutical production facilities can be used to produce multiple lines of small molecule generic drugs, biosimilars are mostly injected or infused, meaning their production facilities are highly specialized and are not easily transferrable to the production of other drugs. This means companies producing biosimilars face higher upfront fixed costs in development, establishment of facilities, and higher marginal costs in production.

Even with these uphill production challenges, biosimilar sales continue to grow, topping out around $15 billion in 2020. According to McKinsey's biosimilars market model, the market is set to continue its double-digit growth, doubling in size to more than $30 billion by 2025, and over $60 billion by the end of the decade. So far, the United States biosimilar market operates mostly through the buy-and-bill channel administered by physicians' offices and is limited in retail. However, by 2023 it is expected there will be six to eight biosimilars for adalimumab (e.g. Humira) launched in the United States, operating through the retail pharmacy channel and expected to be worth$18 billion by 2025.



Pharmacy 101

Many different types of pharmacies make up a PBM network

Most Pharmacy Benefit Managers (PBMs) contract with a network of pharmacies in addition to their own their home delivery and specialty pharmacies.

There are exceptions since some PBMs contract with other PBMs to use all or portions of their negotiated networks. This is a way for a new or small PBM to have a broad network without the need of additional staff.

Different types of pharmacies comprise a network

A **retail pharmacy** is a local pharmacy that is either stand alone or inside a grocery or retail store. Retail pharmacies can be independent or part of larger retail chain. Patients typically drop off prescriptions or have their providers call in their medication and they pick them up in the store or have them delivered to their homes.

A **mail order pharmacy** is a pharmacy where patients mail their prescription into the pharmacy. They can be more convenient since the patient doesn't have to pick up the medication. The prescription is mailed directly to the patient once approved and paid. The most common types of prescriptions at a mail order pharmacy are maintenance medications like those for high blood pressure or diabetes. Below are some pros and cons to using a mail order pharmacy.

- Pros of mail order
  - Due to size, mail order facilities can purchase large volumes of prescription drugs directly from the manufacturer or wholesaler. They are then able to pass on additional savings to clients.
  - Mail order plan designs are normally more convenient for the patient and more cost effective as typical copays are normally 2 (two) to 2.5 (two and a half) times the retail copay.
  - Mail order pharmacies are often broken into specialized departments, so each role within the pharmacy has a specialized team, unlike the retail setting, where technicians share most roles with the pharmacist. This design divides roles such as data entry, fulfilment, clinical reviews, and shipping into multiple departments, removing some of the stress from the fulfillment team.
  - Mail order pharmacies can focus on filling prescriptions, while retail pharmacies have other tasks like giving immunizations or assisting with over the counter (OTC) medications.
- Cons of mail order
  - Mail order pharmacies are typically used for maintenance medications and are not able to fill acute (short-term) prescriptions.
  - Items like antibiotics or pain medications are typically filled at a retail pharmacy since the member does not plan on using these types of medication for a prolonged period.
  - Despite mail order being able to purchase in larger quantities, they are not always the cheapest option for all medications. Patients normally have a large retail network to pick from, which allows them to shop around to find the lowest cost for each prescription. This is not an option with mail order. The patient normally has a single mail order option based on their employer's pharmacy contract.

A **compound pharmacy** is a pharmacy that specializes in compounding medications. Compound medications are normally created to fill a gap in the market for patients whose medication needs are not commercially available. This can be something as simple as the dose not being available in a certain form or the form of the medication not being appropriate for the patient who needs it. It is up to the PBM to regulate compound safety and efficacy since compound prescriptions are not regulated by the FDA.

A **hospital pharmacy** is a pharmacy inside of the hospital. Most Hospital pharmacies only dispense to patients who are inpatient at the hospital or are being released from their services. Hospital pharmacies tend to stock a large range of medications, including specialty and infused medications. Due to the treatments being provided at the hospital, a Hospital pharmacy is more likely to have the ability to process sterile compounds than a retail pharmacy. Eye drops, injections, and inhalations are all examples of compounds that would need a sterile environment.

A **specialty pharmacy** is either a stand-alone or PBM owned pharmacy. Not only do most specialty drugs require special handling, but they are often quite expensive. Specialty pharmacies are designed to manage and support the use of specialty drugs treating complex diseases.

Disease Spotlight

Migraines

A migraine is more than just a headache. Migraines are the third most prevalent illness in the world with more than 4 million adults experiencing daily chronic migraine pain.

According to the Migraine Research Foundation, migraines are a common neurological disease that affect almost 40 million Americans. A migraine causes severe throbbing pain, usually on one side of the head. Other symptoms include nausea, vomiting, dizziness, sensitivity to light, noise, and smells, and worsening pain with physical activity. A migraine attack can last anywhere from four hours to several days. Migraines often follow a four-phase pattern: prodrome, aura, headache, and postdrome.

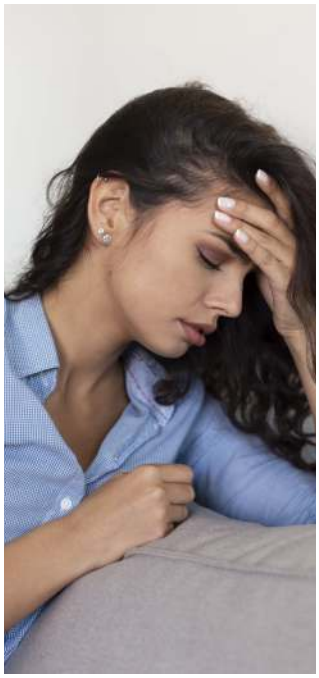
- Prodrome: the first phase of a migraine attack. This phase can be a warning sign that an attack is coming.
- Aura: the second phase of a migraine attack. About 1 in 4 people experience aura. This phase refers to a change in the senses, most commonly sight. Speech and movement may also be affected.
- Headache: the third phase of a migraine attack. This phase is characterized by pulsing or throbbing pain in the head.
- Postdrome: the final phase of a migraine attack. Many migraine sufferers report feeling drained, exhausted, and even hungover during this phase.

Treatment Landscape

Treatments for migraines are classified into three categories: acute (used as a migraine is occurring), preventative (used to help prevent future attacks), and complementary (non-drug therapy mostly used for prevention such as lifestyle changes). Acute migraine medications include analgesics such as ibuprofen, acetaminophen, and opiates. Triptans and ergot alkaloids are also used as acute treatment specifically for migraine attacks.

Current preventative medications include Botox and CGRP-targeted therapies. CGRP stands for calcitonin gene-related peptide. Having high levels of CGRP in the blood may cause and/or contribute to both episodic and chronic migraines. CGRP-targeted therapies work by blocking the sites in and around the brain where the CGRP must attach to in order to work. In 2018, the FDA approved three new CGRP targeted therapies: Aimovig, Ajovy, and Emgality. All three drugs are self-administered subcutaneous injections. CGRP therapies continue to evolve to include oral products for both acute and preventative treatment. Ubrelvy, Nurtec ODT, Reyvow, and Qulipta are all oral CGRP treatments for migraines. Approved in 2021, Trudhesa is another acute migraine treatment that can be administered nasally. According to an October, 21, 2021 CVS Health briefing, upcoming notable drugs for migraines include:

- **Zavegepant** – an intranasal CGRP antagonist developed by Biohaven to be approved in the fourth quarter of 2022.
- **Qtrypta** – a topical patch for acute migraines developed by Zosano Pharma to be approved in the second quarter of 2022.
- **Rizaport** – an oral film for acute migraines developed by InterlGenX to be approved in the second quarter of 2022.
- **AXS-07** – a combination of a NSAID and a triptan for acute migraines developed by Axsome Therapeutics to be approved in the second quarter of 2022.



Economic and social impact of migraines

Migraine sufferers, like many chronic illness sufferers, have increased health care costs and decreased productivity when compared to those who do not experience migraines. According to the Migraine Research Foundation, health care and lost productivity costs associated with migraine are estimated to be as high as $36 billion annually in the U.S. For a family with a migraine sufferer, health care costs are 70% higher than a non-migraine affected family. 1.2 million emergency room visits are for acute migraine attacks. Each year due to migraines, 157 million work days are lost in the U.S. Migraines can be debilitating and are the sixth most disabling illness in the world. Migraine sufferers ninety percent of the time cannot participate in work, school, or social activities during a migraine attack.

Cost management strategies for high cost therapies

With new drug therapies expected to be approved in 2022, competition among existing migraine treatments in the market will increase. A competitive market often helps drive down costs. There are a variety of utilization management techniques available for migraine medications. Utilization management is a set of managed care techniques that assess the appropriate use of health care services, procedures, and facilities under a health benefits plan. These techniques in turn help payers manage the cost of health care benefits. Utilization management techniques can be implemented before, during, and after clinical intervention. Some utilization management techniques used to manage the cost of migraine treatments are prior authorization, quantity limits, and step therapy.

Clinical Spotlight

FDA approved digital therapy – there's an app for that!

There are already multiple digital therapies approved by the FDA, and several Pharmacy Benefit Managers (PBMs) have established digital health formularies. What are digital therapies and should your plan cover them?

Digital therapies defined

Digital therapeutics (DTx), are defined by the Digital Therapeutics Alliance as "evidence-based therapeutic interventions driven by high-quality software programs to prevent, manage, or treat a medical disorder or disease." Due to the expected growth and evolution in this space, The Food and Drug Administration (FDA) has established a Digital Health Center of Excellence with the goal to: "Empower stakeholders to advance health care by fostering responsible and high-quality digital health innovation." There are over two dozen FDA-approved digital therapy applications that have also obtained a National Drug Code (NDC). NDCs enable these therapies to be included on drug formularies and be eligible for reimbursement through prescription drug programs.

Consumers have become accustomed to using mobile apps for everything from getting directions to managing household finances. So, why not use apps to manage one's health? There are already multiple apps on the market that address common health concerns such as stress, sleep habits, diet and exercise, medication adherence, and more. These types of apps are often incorporated in a wellness program and are also available to be purchased outside of an employee benefits plan. Some digital therapies require a prescription and target chronic, behavioral-modifiable conditions including Type II diabetes, substance abuse disorder, autism spectrum disorder, and major depressive disorder[1].

Product	Use
reSET	Substance use disorder
reSET -O	Opioid use disorder
Somryst	Insomnia
EndeavorRx	ADD/ADHD
Sleepio	Sleep disorder
Whil	Stress/sleep disorder
Hinge	Musculoskeletal disorder

Generally, digital therapies have the ability to collect data from the end-user and transmit it to a physician, health care provider such as a nurse or health coach, or even to family members or caregivers that are designated by the end-user. The technology uses the data to measure results and provide feedback to the end-user, health care providers, and other caregivers.

As this type of therapy becomes more prevalent, plan sponsors should consider whether to cover them as part of the prescription drug program.

Regulatory oversight

Digital therapies obtain FDA approval through the premarket notification 510(k) pathway (typically for medical devices) if it's demonstrated that the device is at least as safe and effective, and is substantially equivalent to a legally marketed device. This FDA regulatory pathway was established in 1976 and likely will need to be reviewed and modernized to keep pace with the dynamic nature of digital therapies. Digital therapy falls under the medical device classification due to the intended use of the product, but the technology may also fall under the purview of the Federal Trade Commission, Federal Communications Commission, National Institute of Standards and Technology, and Office of the National Coordinator for Health Information Technology[1].

Is Medicare onboard?

The Centers for Medicaid and Medicaid Services (CMS) has not yet issued clear guidance on whether or not digital therapies qualify for reimbursement. Given the adoption of existing therapies and the robust pipeline for those in development, it seems likely that CMS will establish its own set of rules.

Additional consideration for PBMs, group health plans and the end-user

As with any emerging technology, cybersecurity risk is a top concern. These apps and devices are collecting personal health information and transmitting it over the internet. Ensuring that the information is protected and is being transmitted securely is crucial.

Additionally, the U.S. healthcare system is broadly criticized for being complex and difficult to navigate. In order for digital therapies to be taken seriously by the medical community it is important that they improve communication between the end-user and the medical professional; not hinder it.

Digital therapies are considered viable alternatives to other treatment options and are demonstrating meaningful results. As long as the outcomes continue to be positive and cost-effective, and PBMs add them to their formularies, plan sponsors will need to decide whether or not to include them as covered services on their plans. With over two dozen therapies currently approved and countless others in the pipeline being developed, it's clear that these therapies are here to stay.

Source:

1. Patel, N.A.& Butte, A.J. "Characteristics and challenges of the clinical pipeline of digital therapeutics," npj Digital Medicine, December 11, 2020. https://doi.org/10.1038/s41746-020-00370-8.

Pipeline
Pending drug approvals

Drug name	Manufacturer	Indication/use	Expected FDA decision date
adalimumab (biosimilar to Abbvie's Humira)	Coherus	RA; AS; PSO; PsA; JIA; CD; UC	December 2021
buprenorphine ER	Braeburn	opioid use disorder (moderate to severe)	12/15/2021
efgartigimod	Argenx	generalized myasthenia gravis	12/17/2021
levoketoconazole	Strongbridge	Cushing's syndrome	12/31/2021
tezepelumab	Amgen/AstraZeneca	severe asthma	1/10/2022
pegfilgrastim (biosimilar to Amgen's Neulasta)	Amneal	neutropenia/leukopenia	1/13/2022
budesonide (long-acting)	Calliditas	IgA nephropathy (Berger's disease)	1/15/2022
mavacamten	Bristol-Myers Squibb	obstructive hypertrophic cardiomyopathy (oHCM)	1/28/2022
faricimab	Genentech	wet AMD and DME	1/31/2022
mitapivat	Agios	pyruvate kinase deficiency	2/17/2022
tebentafusp	Immunocore	uveal melanoma (metastatic)	2/23/2022
bardoxolone methyl	Reata	Alport syndrome-related chronic kidney disease (CKD)	2/25/2022
lenacapavir	Gilead	HIV-1	2/28/2022
donepezil	Corium	Alzheimer's disease (mild to severe)	3/11/2022
ganaxolone	Marinus	CDKL5 deficiency disorder-related seizures	3/18/2022
ublituximab	TG Therapeutics	chronic lymphocytic leukemia (CLL)/Small cell lymphocytic lymphoma (SLL)	3/25/2022

Brands losing patent

While these drugs are nearing the end of their patent term, the release of generics may be delayed due to litigation or exclusivities.

Brand name	Generic name	Indication/use	Date generic available
Licart	diclofenac epolamine	topical treatment of acute pain	Dec 2021
Dulera	formoterol fumarate/ mometasone furoate	asthma therapy	Dec 2021
Vazalore	aspirin	aspirin therapy	Dec 2021
Femtrace	estradiol acetate	vasomotor symptoms	Dec 2021
Spiriva respimat	Tiotropium bromide	bronchospasm associated with COPD	Feb 2022
Crixivan	indinavir	HIV	Feb 2022
Cholbam	cholic acid	adjunctive treatment of peroxisomal disorders (PDs)	Mar 2022
Vimpat	lacosamide	osteoarthritis, rheumatoid arthritis and ankylosing spondylitis	Mar 2022
Jatenzo	testosterone undecanoate	hypogonadism	Mar 2022

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