



A Patient's Guide to Understanding Biosimilars

FIRST EDITION



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PART I WELCOME

There's a lot of buzz in the news these days about biosimilars, the drugs similar to well-known brand biologics such as Remicade, Humira, and Enbrel, but with no meaningful clinical difference. Your doctor or nurses may have mentioned biosimilars to you as an option for treating your arthritis, psoriasis, or other inflammatory disease. Or you may have heard friends talk about these new medications. You may even already be taking a biosimilar.

Of course, you have plenty of questions about biosimilars. What are they? How are they the same as or different from the medication I'm taking now? Can switching to a biosimilar save me money? If so, how much? Should I switch to a biosimilar or stay with my current medicine? And most of all, are biosimilars safe, effective, and covered by my insurance?

This patient's guide to biosimilars will give you clear, simple answers to many of your questions about these new medications. We'll explain some common words and phrases about biosimilars. We hope this guide will help you have a comfortable, more informed conversation with your doctor about all of your treatment options.

Every person's health, concerns, and insurance coverage are unique. While this guide will give you a general overview of biosimilars, talk with your health care professionals including your nurses, physician assistants, doctors, health insurance company, medical benefits person at your work, and pharmacists to get all your questions answered. In addition to reading this patient guideline, look on creakyjoints.org for additional biosimilar information.

Before you read this guide:

Biosimilars are relatively new to the U.S. market. Many are not yet released, some are in litigation, and costs to patients are not yet predictable. As you read this, please keep in mind that although we update it regularly, there may be changes to the drugs or the marketplace that are not included here. If you see something that needs updating, please [click here](#) and tell us.



PART II PATIENT CHARTER

CreakyJoints is a patient-powered community of people with arthritis (and their families) that is part of the nonprofit the Global Healthy Living Foundation (GHLF). The CreakyJoints patient charter reflects our guiding principles, or the deeply held beliefs that drive our community's many efforts in arthritis education, support, advocacy, and research.

We believe:

- 1** The patient experience is at the heart of medicine; thus the patient must be at the center of all medical decision making.
- 2** The medical process should stay between the patient and their care provider.
- 3** The patient should have access to all treatments deemed appropriate by their care provider.
- 4** Access to care should not be limited by external forces, financial or otherwise.
- 5** Patients should be empowered and educated with the tools needed to make their voices heard.
- 6** Elected officials, insurance providers, drug manufacturers, and all those associated with the health care system shall make it their goal to ensure the patient is the focus of all decisions.
- 7** The medical team should strive not only to do no physical harm, but to do no emotional, mental, or financial harm to the patient.
- 8** Patients should be treated with dignity, transparency, and respect by everyone involved in the health care process.

▲ The information in these guidelines should never replace the information and advice from your treating physician. It is meant to inform the discussion that you have with health care professionals, as well as others who play a role in your care and well-being.

PART III UNDERSTANDING BIOSIMILARS

* — What's a biosimilar?

To understand biosimilars we first need to understand biologic drugs. When we think of drugs we often think of chemical compounds like aspirin, a pill that we can pick up from our local pharmacy or supermarket. Biologic drugs are a bit different. They are proteins made by living organisms, whereas traditional drugs are chemicals, referred to as small molecules. Biologic drugs are much larger in size than "small molecule drugs" like aspirin.



You'll learn more later in this document but, for now, just focus on the fact that the production of biologics is a complicated procedure.

Biosimilars are not new drugs, but rather they are copies of biologic drugs that have been used to treat many diseases and conditions, such as rheumatoid arthritis, psoriatic arthritis, psoriasis, Crohn's disease, ankylosing spondylitis, ulcerative colitis, and some types of cancer. Familiar biologic drugs include widely prescribed therapies like etanercept (Enbrel®), infliximab (Remicade®), adalimumab (Humira®), and others.

Each biosimilar is made using the same amino acid starting materials and the same precise, step-by-step processes as its **reference drug** — a well-tested, widely used biologic drug that's already been on the market for years. All biosimilars are **prescription drugs**. You cannot get them without your health care professional's prescription.

Because of how they are developed, biosimilars are not completely identical copies of their reference drugs. But they're made using the exact same starting materials and similar manufacturing processes as the original biologic. They are designed and developed to be highly similar to the original drug upon which they are based, and they will not be approved as a biosimilar if they are not.

That's why they're called biosimilars: They're made of biological materials (bio-) and are highly similar to an approved, widely tested, and prescribed biologic. A biosimilar is compared to its already approved reference product through an extensive array of analytical tests and clinical studies. Once it has been shown to be highly similar to the reference product, it is carefully reviewed and approved by the U.S. Food and Drug Administration (FDA) before being released for use by patients.

If it helps, think of biosimilars as generic biologics. Although this is technically not true, since a generic small molecule drug has the exact same chemical structure as the original drug, thinking of biosimilars this way helps some people understand them better.

If you're prescribed a biosimilar or your doctor talks to you about switching to one from your biologic, keep this in mind:

- ▶ The biosimilar **works exactly the same way** as the reference biologic.

- ▶ The biosimilar will have the **exact same interactions with other drugs, potential side effects, and risks or safety precautions** as the reference biologic.
- ▶ The biosimilar is **taken the exact same way as the reference biologic**. If you self-inject your biologic with a prefilled pen, you'll self-inject the biosimilar with a prefilled pen. If you get your biologic at an infusion center, you'll do the same for the biosimilar.
- ▶ The **dose and dosing schedule** for your biosimilar will be exactly the same as for the reference biologic.
- ▶ A specialty pharmacy likely will fulfill your biosimilar. Your doctor will write the prescription, and you'll either get the supply of your biosimilar shipped to you from the pharmacy or you'll go to your local infusion center for your regular treatments.

* — **Are biosimilars the same as generics?**

We'll talk about that a little later in this guide, but they're not generics or exact copies. That's because these drugs are made by living cells. But biosimilars are required to be, and their makers must have conducted tests that proved them to be, highly similar to the original, reference biologic – to have no "clinically meaningful differences" from your biologic, according to the law.

Each biologic drug is manufactured by a complex process that includes many precise steps. Even though the same exact process is followed every time that biologic drug is made, because these are made by living cells, there may be slight changes from batch to batch. These variations are normal and acceptable, according to the FDA. Every lot meets the same high standards to be pure, safe, and effective.

The development and production of biosimilars must follow strict regulations in the Biologics Price Competition and Innovation Act. That's a U.S. law that set up the system for developing and approving new biosimilars. Biosimilars are manufactured by the same process as the biologic drugs upon which they are based. They are highly similar to their reference drugs, so they have the same effect on you: They treat your disease safely and effectively.

* — **Then how are biosimilars different? Why do we care?**

Because a biosimilar is based on an already approved drug, like generics, the testing and approval process for a biosimilar is condensed compared to that through which the original drug had to go. That's because biosimilars don't have to start from scratch with just a theory about how it may or may not work to treat a disease. They can reproduce a drug that's already been approved and widely tested. Biosimilars do not have to go through the years of early, "trial-and-error" testing as did the original biologic drug.

When a manufacturer wants to create a biosimilar, they must do tests to show that the biosimilar has the exact same protein structure and works the same way as does its reference drug. Biosimilar manufacturers perform high-tech tests to prove that the new product has the same

sequence of amino acid building blocks and is just as pure as the original drug, and that its active ingredients work the same way. If there are any differences between the two drugs' inactive ingredients, the biosimilar's manufacturer has to prove that these very slight differences don't affect how safe or effective it is.

There may be very slight differences between different batches or lots of a biologic drug. Likewise, there may be slight differences between a biosimilar and its original biologic drug. However, these small differences have been demonstrated to have no significant effect on how it works. Biosimilars approved by the FDA have to prove that they're as safe, pure, and effective as their reference products.

The idea behind the creation of biosimilars is that, if a biologic drug that went through years of expensive, detailed development and testing, works well, and is safe to use, a copy that used similar manufacturing processes could have a shorter, more economical development process because it would not have to prove again that it works in all of the diseases for which its reference drug is approved. Biosimilars, therefore, should cost less to you because they cost less to their manufacturer to develop and test. But this depends on your insurance company and whether it will pass on savings to you.

*** — So...are biosimilars cheaper for you to use yet still will provide the same effect as your current biologic?**

The savings to patients do not appear to be as large, or exist at all, as many proponents of biosimilars initially suggested. There may be savings to the health care systems like Medicare and Medicaid, or to insurance companies, but these savings have not yet been passed on directly to patients in the form of lower copays, deductibles, or premiums. (When traditional drugs become generic, the savings are passed on to consumers.)

Although a biosimilar is less expensive to develop than a new biologic drug, the savings, so far, have not been passed on to you. Presently, your health insurance company chalks up the savings to additional profit. Medicare and Medicaid use the savings to continue to allocate 98 cents of every dollar to patient care — the highest ratio in the U.S., and one of the highest in the world.

If you use an injectable biologic like Enbrel or Humira or their biosimilars (not an IV infused drug), "rebates" or discounts on bulk orders are received by your insurance company or its pharmacy benefits manager (companies that manage your drug coverage). If the manufacturer offers a discount on your drug, your insurance company might take the price break yet charge you full price. Right now, the FDA and Congress are looking into how some insurance companies and pharmacy benefits managers are operating to see if they're stifling competition — in other words, operating in a way that gets in the way of free market competition that would otherwise bring costs for these drugs down.

If you use an infused drug (an IV) like Remicade® or Orencia®, you either go to a hospital or to your doctor's smaller infusion clinic to get the drug. The doctor or hospital buys the drug and marks up its price before submitting a bill to the health benefits department of your health insurance

company. It is expensive to keep a stock of these drugs, so many small infusion centers only offer one brand. If your insurance company covers a different brand, you might have to go to another infusion center or hospital to get the drug that's covered. If you are receiving Remicade®, you may not be able to switch to a biosimilar because your infusion center may not stock it. Whether you and your doctor decide to switch to a biosimilar or start on one as your first biologic treatment, you may have to travel to have it infused. Although biosimilars of adalimumab and etanercept have been approved in the U.S., because of patent lawsuits infliximab biosimilars are currently available only for autoimmune diseases like arthritis, psoriasis, and inflammatory bowel disease like Crohn's disease.

Biosimilars are not like generics when it comes to patient savings. When a pill has a generic alternative, you often can save a substantial amount of money by switching from the brand name to the generic. This is not usually the case with biosimilars. Health insurance companies prefer not to share these savings with patients.

CreakyJoints is working with state and federal legislators, insurance companies, doctors, hospitals, employers, and pharmaceutical companies to help find a way for patients to share in these savings. If you want to help too, go to 50statenetwork.org and learn more about this important issue. Many pharmaceutical companies, doctors, and legislators in Congress and at the state level agree with us when it comes to arguing on behalf of the patient on this important matter.

PART IV BEING PRESCRIBED A BIOSIMILAR

* — Why might my doctor prescribe a biosimilar for me?

Your doctor may prescribe an infused biosimilar because it costs less, providing savings to a system like Medicare and Medicaid (which is paid for by our taxes) but not necessarily directly to you. Your insurance company or employer may require that you take a biosimilar. CreakyJoints believes that any drug switch should occur after you and your doctor discuss the potential benefits and after you examine how the switch will affect your costs and, in the case of infusions, the location of the treatment.

* — How are these drugs named or labeled?

One thing that's really important about a biosimilar is its label or name. When a biosimilar is developed, it's given a name that tells you (and your doctor and pharmacist) what its reference drug is – the original biologic that it copies in a highly similar way – followed by a four-letter suffix, or tag at the end, that tells you which version of that drug you're taking. Like reference products that also have a four-letter suffix, each biosimilar also has a brand name that you'll see in their advertising or on their packaging.

That's because there are or may be multiple biosimilars for the same reference drug. So each one will identify its brand name and, by the four-letter tag, which exact biosimilar you're taking.



For example, there are two biosimilars of the biologic drug infliximab (Remicade®): Inflectra® (infliximab-dyyb) and Renflexis® (infliximab-abda). You may not really care about that suffix, but your doctor and pharmacist can use that information to identify which biosimilar you are using. While they're highly similar, and all must meet the same high standards to ensure that they're safe and effective, your doctor may still prefer one over the other based on data from studies that are published about that exact biosimilar and the experience with other patients.

* — You may soon start to hear about an even newer category of biosimilars: interchangeables. What's that?

An interchangeable is a biosimilar that, according to the strict rules and definitions of the Biologics Price Competition and Innovation Act (BPCIA), must have undergone additional testing – beyond that required to demonstrate biosimilarity – to show that it can be substituted for their reference product by your pharmacy without having to involve the health care professional who prescribed it.

CreakyJoints' Principles About Biosimilar Substitution:

- Substitution without the direct authorization of the prescribing health care provider may occur only when the FDA has designated a biosimilar as interchangeable.
- The prescribing physician can prevent substitution by writing "no substitution" on the prescription.
- The prescribing physician and patient must be notified of any substitution.
- The pharmacist and the physician must keep records of any substitution.
- The patient must participate in biosimilar savings.
- Biosimilar manufacturers must offer relevant patient support programs.
- Biosimilar manufacturers must commit to a stable and safe supply chain to avoid product interruptions and ensure safety.

notification must occur within a short time after the substitution has been made. The FDA has not published its final guidance on interchangeability — the parameters for the process. But, if interchangeable biosimilars come onto the market in the years to come, there may be some debate about who decides what drug you actually receive when you fill a prescription.

The possible benefit of interchangeables is that they might cost less to you. The only difference between a biosimilar and an interchangeable biosimilar is the additional testing the manufacturer must do. Practically speaking, health insurance companies already implement non-medical switching among biologic agents and other drugs and may do so for biosimilars, without any biosimilar approved as being "interchangeable" by the FDA. This occurs when your insurance company says it will only cover a specific drug, and that drug has not been prescribed for you. In this case, you either must be switched to a covered drug or pay the much higher price to stay on a drug which no longer is covered. There is a lot of disagreement about what exactly non-medical

Interchangeability is a different designation from biosimilarity and does not equate to the product being more safe or effective or of higher quality. The designation allows for the automatic substitution at the pharmacy level. It is anticipated that many infused biosimilars will not be interchangeable because there won't be two available at the infusion site.

According to the BPCIA laws, any drug maker that develops a biosimilar and wants to apply for it to be labeled as being interchangeable must offer additional data to show that, if a patient is switched back and forth at least three times between the biosimilar and its reference drug, there will be no differences — no risk of any changes in safety or effectiveness.

So all interchangeables would be biosimilars, but they have to provide additional data about repeated switching to get that extra designation. However, no biosimilar has yet been designated as being interchangeable.

One possible concern about interchangeables is that your doctor or other prescribers (such as your physician assistant or nurse practitioner if you see these health care professionals from time to time) might not be told if your pharmacist fills your prescription with the interchangeable instead of the reference biologic. However, state laws about interchangeability specify that such

switching is, but to stay out of the weeds on this, we define non-medical switching as you being switched to a new drug for non-medical reasons.

If an insurance company gets a better price on biosimilar A vs. brand name B, non-medical switching may occur. Often when you hear people disparage biosimilars it is because of the unknown issues around frequent switching, including the possibility that the drug will stop working. Although nobody knows for sure about the long-term effects of switching, there aren't enough different biosimilars on the market for this to be an issue. In addition, insurance companies, so far, have said they have no interest in switching patients back and forth between biosimilars or brand name biologics. However, since biosimilars are highly similar to their reference drugs and biosimilars of the same reference drug should be highly similar to each other, it is unlikely that the consequences of such switching should be any different from those of using different batches and lots of a reference biologic drug over time.

Our recommendation is simple: switching should only occur when a drug stops working. However, you and your health care professional should discuss whether you need to switch to a different class of biologics or just a different drug in the same class. Currently approved biosimilars for autoimmune arthritis, psoriasis, and Crohn's are all in the same class.

* — **Are biosimilars safe to use?**

Yes, biosimilars are absolutely safe. Every drug that's been approved for your use by the FDA must meet very high standards of safety. This includes all biosimilars and biologics. They are prescription drugs, so in the U.S., the FDA regulates how they are manufactured and delivered to you.

While biosimilars follow a shorter track to FDA approval, their makers still must test them thoroughly to show that they're highly similar in structure and function to their reference products, that they're safe, and that they work to treat diseases as they should. These tests often include:

- ▶ Many analytical studies that show that your biosimilar is highly similar to its reference biologic and has no clinically meaningful differences from the original drug. Any differences would be of the inactive ingredients, like buffers.
- ▶ Studies in animals to show that the biosimilar is safe.
- ▶ Clinical studies in patients that show that the biosimilar is equivalently effective as the reference drug, pure, and safe to use to treat your condition, but biosimilars are not required to be studied in all indications for which they will be approved for use. This is called extrapolation. If a biosimilar is approved for one indication of its brand name biologic — say rheumatoid arthritis — then all the indications of the brand name — psoriatic arthritis and ankylosing spondylitis, for example — are approved for the biosimilar.

* — **What's the history of biosimilars? Why do we need them?**

Biosimilars are the result of the widespread need for more affordable medications and an

initiative by Congress to develop more affordable biologics to treat serious diseases like rheumatoid arthritis, psoriasis, or cancer, among many others.

Why? Because biologics are expensive to make. They're expensive to buy. A single dose can cost \$10,000 and up (and way up). Your insurance policy likely covers most of that cost, but there's still a big impact on our overall health care costs because these very effective drugs are very expensive.

The Biologics Price Competition and Innovation Act of 2009 was a U.S. law passed by Congress to set up a "fast-track" development and approval process for biosimilars. It was part of a larger set of laws called the Patient Protection and Affordable Care Act (ACA), which was passed in 2010. Once the BPCIA became law, the FDA set up a step-by-step process for drug makers to follow to develop a biosimilar.

Instead of starting from square one to develop a whole new "molecule," or biologic formula, the biosimilar manufacturer uses the original biologic's molecular structure. They can also follow the similar production processes to create a "lot" or batch of the drug. This cuts out years in the typical development process for a new drug.

They conduct tests to prove that the biosimilar is highly similar to the reference drug and has no clinically meaningful differences. (It may have some changes to its inactive ingredients, but these must be proven to have no difference to you or in how safe or effective the biosimilar is.) They must do tests to show it's safe, potent, and pure.

However, for a biosimilar, equivalent effectiveness and comparable safety need be demonstrated in a clinical trial in only one disease, rather than in each disease for which approval is sought, since the effectiveness of the reference product has already been proven in each of these indications. That means if the original biologic is approved for more than one disease — such as rheumatoid arthritis and ankylosing spondylitis — the biosimilar may be approved for those indications too. That's because the reference drug has already been tested and approved for treatment of those diseases.

So biosimilars were created to help relieve some of the rising costs of treating serious diseases. Because many analytical and human tests have shown that a certain biosimilar is highly similar to its reference product, safe and equivalently effective for you, the FDA's policy was that there was no need for a new biosimilar to duplicate clinical trials in patients with every disease. By doing so, development of a biosimilar could save time and money.

* — Are biosimilars the same as generic drugs?

Biosimilars are not the same as regular generic drugs. Generic drugs are exact copies of much simpler "small-molecule" drugs like aspirin, ibuprofen, omeprazole (Prilosec®, which reduces stomach acid and prevents heartburn), antibiotics, or loratadine (Claritin®, the antihistamine used to treat hay fever), and many, many others. Today, 87 percent of prescription drugs are generic but they only account for 26 percent of total drug costs in the U.S., according to the Association for Accessible Medicine, a generic medicine trade association.

Most drugs that your pharmacist fills at your local drugstore are usually small-molecule drugs. All the over-the-counter drugs on the shelves of your pharmacy, supermarket, or discount store are small molecules. Their active ingredients are chemicals with relatively simple structures.

These chemical structures can be replicated relatively easily to create “generic” versions. There is no difference in the chemical structure of the active ingredient in the name-brand version of your heartburn drug (say, Prilosec®) and that in the generic or store-brand version right next to it on the shelf. The generic brand may have some differences in its inactive ingredients, like fillers. The generic brand may cost less, in part, because it’s not marketed like a brand-name drug. It has simpler packaging. But it’s exactly the same drug. Generic drugs are available after the patent on the brand drug has expired.

Biologic drugs are proteins, cells, tissues, antibodies, and vaccines. Because these are made by living organisms, there may be very slight variations between batches or lots. All batches and lots of both reference biologic drugs and biosimilars are tested to demonstrate that every batch and lot meets prespecified quality standards to assure that it is pure, potent, and safe.

Unlike generic small molecule drugs, most biosimilars are not absolutely exact copies of their reference products. However, the concept of biosimilars is very much like that of generic drugs. By reducing the cost of developing and testing a drug, it should cost less to you. Both biosimilars and generic drugs are intended to be more affordable versions of name-brand drugs — and proven to be just as safe and effective. Like small molecule generic drugs, biosimilars may become available when patent protection for the name-brand biologic expires.

PART V BIOSIMILAR COSTS

* — Do biosimilars cost less? Will they save me money?

Biosimilars cost less than their reference biologic. However, patients in the U.S. have not seen direct dollar savings yet. Health insurance companies say the lower price, while not passed on to patients, helps to keep the price of premiums low, but CreakyJoints has not seen evidence of this. We've never seen a health insurance premium go down unless the coverage is reduced, too.

We have heard that some Medicare patients have seen reductions in their copay as a result of the lower cost of biosimilars to the Medicare system, but we have not been able to verify this. If you are reading this and have switched from a biologic to a biosimilar and your copay has been reduced, please let us know by emailing Regis Wagner, Patient Advocate, Community Outreach Manager at rwanagern@ghlf.org.

Both biologics and biosimilars are expensive to manufacture and test. The average daily dose of a biologic drug costs 20 times more than the average daily dose of a small-molecule drug. It's estimated that a manufacturer may spend anywhere from \$100 to \$300 million to develop a biosimilar drug. That's much less than it takes to develop a biologic, which may cost between \$800 million and \$1 billion. Biologic drugs are made by living cells, produced in state-of-the art facilities, and follow a complex process to ensure their purity, safety, and effectiveness. The same process applies to biosimilars.

Still, the manufacturing, testing, and marketing costs for a biosimilar should be lower than those for a new biologic drug. Biosimilar manufacturers can use data from clinical trials for the original biologic drug to support approval for indications in which the biosimilar was not studied.

Manufacturers of biosimilars have given these drugs lower prices than their reference products. For example, infliximab-dyyb (Inflectra®) was introduced at a price that was 19 percent lower than infliximab's (Remicade®) list price. However, those lower list prices have not resulted in lower out-of-pocket costs for you because insurance companies and pharmacy benefit managers have not passed these savings on to you. The price of a drug to you, the patient, is your deductible and copay, not the retail price of a drug. Both expensive biologic drugs and biosimilars can easily burn through your deductible. After that, you pay the copay for a biosimilar as you would if you were on a reference biologic drug.

The retail or "list" price of a biosimilar is usually less than a biologic, but how much varies, and you don't really care what the list price is unless you are one of the very few people without insurance coverage who buys drugs at list.

There are no injectable biosimilars for rheumatologic diseases available in the U.S. yet (some are approved for oncology), but when they are, your insurance company or pharmacy benefits manager (third-parties that manage drug coverage for insurers or large health plans) may not be eager to switch patients to a new biosimilar, because the manufacturers of biosimilars are

not selling to them at deep discounts. According to one report, insurance companies (called payers) want to see biosimilars discounted as much as 40 to 60 percent to offset the already-deep discounts and rebates they get from biologics makers. This may all be very confusing to you, because how drugs are priced and what you pay in the end is an unclear process.

* — **Biosimilars are still very new.**

The FDA and other government agencies are addressing the problem of rising drug costs and trying to find out if drug manufacturers, private insurance companies, and pharmacy benefits managers are setting up any barriers to competition among these drugs that would keep prices to consumers high, or at least higher than they might be.

The RAND Corporation, a nonprofit that analyzes many programs and industries, published a report in 2017 that predicted that, overall, biosimilars would cut direct spending for biologics by \$54 billion by 2026. The way the system is set up now, none of these savings go directly to patients. Lower costs for manufacturing, testing, and marketing biosimilars could translate into savings for the American health care system, which is good for Medicare and Medicaid because taxpayers pay for these programs. As of 2018, manufacturers of injectable biosimilars can now participate in Medicare Part D's Coverage Gap Discount Program. However, none are yet on the market to treat inflammatory diseases because of lawsuits over patent-related issues. Eventually, the availability of injectable biosimilars to treat inflammatory diseases should boost competition among makers of these drugs (biologics were already included in this program), but this does still not affect the amount of out-of-pocket costs that patients covered by Medicare Part D must pay.

In Europe, where biosimilars have been on the market since 2006, biosimilars typically cost between 10 percent and 30 percent less than their reference biologics. In Norway, the cost of biosimilar infliximab has been nearly 70 percent lower than that of the reference product, Remicade. In Europe, Japan, South Korea, and other regions where biosimilars are on the market, biosimilars are gaining a larger portion of the overall market share. More people are starting to use the biosimilar in place of the reference biologic. In Europe, there are more than 700 million patient days of experience with biosimilars that illustrates their safety and efficacy in a real-world setting.

* — **What about you?**

As a patient, you deserve relief from rising drug costs. According to the lobbying group America's Health Insurance Plans (AHIP), as more biosimilars are approved and enter the market, competition will increase and prices should come down. However, savings to you may not be as much as you'd like. The FDA is looking into how the cost savings for biosimilars (or other drugs) are passed from their manufacturer to you, the consumer. There may be savings from corporate rebates or discounts that are not passed on to you. Hopefully, this will change so that you will pay less.

* — **What's out there? What's in the pipeline?**

Right now there are six biosimilars approved for use in the U.S. for patients with inflammatory

diseases, but only two of these are available in part because lawsuits among manufacturers are delaying the marketing of the others. For example, the injectable biosimilar adalimumab, adalimumab-atto (Amjevita®), was approved by the FDA in 2016 but, as the result of a lawsuit settlement agreement, won't be available to patients in the U.S. until 2023.

* —— FDA-Approved Biosimilars for Rheumatic Diseases:

Biosimilar	Approved to treat the following conditions
Infliximab-dyyb (Inflectra®) — a biosimilar to Remicade® Infliximab-abda (Renflexis®) — a biosimilar to Remicade®	Moderately to severely active Crohn's disease Moderately to severely active pediatric Crohn's disease Moderately to severely active ulcerative colitis Moderately to severely active pediatric ulcerative colitis Moderately to severely active rheumatoid arthritis Active psoriatic arthritis Active ankylosing spondylitis Chronic severe plaque psoriasis
Etanercept-szzs (Erelzi®) — a biosimilar to Enbrel® (unannounced launch date)	Moderate to severe rheumatoid arthritis Moderate to severe plaque psoriasis Psoriatic arthritis Ankylosing spondylitis Moderate to severe polyarticular juvenile idiopathic arthritis
Adalimumab-atto (Amjevita®) — a biosimilar to Humira® (available 2023) Adalimumab-adaz (Hyrimoz®) — a biosimilar to Humira® (available 2023) Adalimumab-abdm (Cyltezo®) — a biosimilar to Humira® (unannounced launch date)	Moderate to severe rheumatoid arthritis Moderate to severe chronic plaque psoriasis Psoriatic arthritis Ankylosing spondylitis Moderate to severe Crohn's disease Moderate to severe pediatric Crohn's disease Moderate to severe ulcerative colitis Moderate to severe polyarticular juvenile idiopathic arthritis Intermediate, posterior, and panuveitis non-infectious uveitis Moderate to severe hidradenitis suppurativa

More biosimilars are in the drug approval pipeline. That means testing is being conducted or analyzed and these drugs may be approved soon.

There are two biosimilars for rituximab (Rituxan®) that have been accepted for FDA review, a key step in the approval process.

There's also a biosimilar to etanercept that's approved in Canada and South Korea as Brenzys® and in Australia and the European Union as Benepali®, but it has not yet been approved in the U.S. The biosimilar Cyltezo has been approved and is in litigation in the U.S. It is a biosimilar for Humira.

* — **Are there patient support programs for biosimilars that can help reduce out-of-pocket costs?**

Yes, there are patient assistance programs for biosimilars offered by their manufacturers. These programs can offer you coupons or discounts to bring your out-of-pocket costs for your drug way down.

How do you find these programs? Go to creakyjoints.org/support/arthritis-copay-cards-assistance

Not everyone qualifies for copay assistance or discount programs. It will depend on your insurance coverage and other factors. But these programs do help many people afford the drugs they or their family members need.

PART VI CONCERNS AND ADVOCACY

* — Are there any concerns about biosimilars or interchangeables?

Right now, the FDA's stringent regulations for the manufacturing and approval of biosimilars shouldn't cause any concerns for you or your doctor. If your doctor prescribes a biosimilar for your treatment, you can be fully confident that the drug is safe and effective. The FDA states that biosimilars are safe and effective to use whether you've already been using the reference biologic or you are getting a biosimilar as your first treatment.

Of course, any biologic drug — including biosimilars — typically varies slightly from lot to lot. The FDA requires that these variations fall within prespecified proven acceptable quality ranges and that they not result in any clinically meaningful differences.

There are a few important concerns about biosimilars — mainly, their price to patients and who will control how these drugs are prescribed in the future. The list prices for biosimilars are lower than those of their reference drugs, but may not be as low as expected. And so far, patients are not seeing any savings.

In addition, your doctors may be concerned that your insurance company, pharmacy benefit manager, or health benefits group will pressure them to switch you to a biosimilar when you're doing well on a given biologic to save the insurance company some money. However, this "non-medical switching" has occurred even before biosimilars became available, requiring use of one anti-TNF drug instead of another because of a financial benefit to the payer. It is unlikely that switching between a biosimilar and its reference drug or among biosimilars of the same reference drug would result in clinically significant adverse effects.



Many doctors may not like the idea that your pharmacist could one day switch your drug without notifying the doctor, which would be legal if a biosimilar were to be approved as being "interchangeable." However, no biosimilar has yet been approved as being interchangeable. If interchangeable biosimilars become available, CreakyJoints and other patient groups have worked hard to make sure that laws have been enacted in virtually every state to regulate this process strictly. These laws include requiring notification of both the patient and prescribing health care provider of any change, as well as keeping strict records of any substitution that has been made.

These concerns are valid. But in addition, you want to be able to have more than one option to safely, effectively treat your disease — and to do so at an affordable price for you. Biosimilars

create more competition for biologic medications. They should lower costs for consumers and insurers, including Medicare and managed health plans. This increased competition, if it can continue and thrive, should drive drug costs down.

What's the future for biosimilars? There will likely be even more biosimilars coming onto the market in the next few years. Some that are already approved, but tied up in lawsuits, should become available to patients as well.

So if you're using a biologic now, and you're curious about whether a biosimilar may be a good option for you, here are some tips:

- ▶ Talk to your doctor. Find out if there is a biosimilar that is available, and if your doctor thinks it may be right for you.
- ▶ Find out if your insurance plan covers the biosimilar. If it doesn't, ask them to notify you when coverage for a biosimilar becomes available.
- ▶ Ask your doctor and your pharmacist to explain how the biosimilar will work as part of your treatment plan. Ask any questions you have about its safety, effectiveness, and cost.

Biosimilars offer patients additional options for treatment of chronic diseases and may also save money for health systems such as Medicare, the Veterans Administration, and Medicaid. There are still challenges to be worked out: how more biosimilars can reach the market, how these drugs are distributed, and how you can participate in the savings.

* — Your voice matters!

Speak up. Start by going to 50statenetwork.org, a part of CreakyJoints that allows you to speak out to your community, your local, state, and federal elected officials, and many government agencies.

Biosimilars were created as a way to bring down medication costs and drive competition in the market. Biosimilars are safe, effective and accessible. Biosimilars meet the same stringent standards as other prescription drugs. Ask your doctor about biosimilars to find out if one is available and right for you.

REVIEWERS



Eddie Applegate

Mr. Applegate was diagnosed with psoriatic arthritis in 2003. He is originally from Alabama but has lived in the suburbs of Atlanta for the last few years. He works as a sales support trainer. When he's at home, Mr. Applegate enjoys reading, crosswords, going to the movies, and watching his favorite sports teams (the Atlanta Braves and the Alabama Crimson Tide). Mr. Applegate is a member of the Global Healthy Living Foundation's 50-State Network, is a Patient Governor for GHLF's ArthritisPower® research registry, and is an active patient advocate on social media, including on the CreakyJoints Twitter and Facebook pages.



Jonathan Kay, MD

Jonathan Kay, MD, is a professor of medicine and holds the Timothy S. and Elaine L. Peterson Chair in Rheumatology at the University of Massachusetts Medical School in Worcester, where he directs clinical research in the division of rheumatology. His clinical appointment is as a physician at UMass Memorial Medical Center, also in Worcester. He received his medical degree from the University of California School of Medicine in San Francisco, California. He then completed an internship and residency at the Hospital of the University of Pennsylvania in Philadelphia and fellowships in rheumatology and immunology at the Brigham and Women's Hospital and Harvard Medical School in Boston, Massachusetts.

Dr. Kay is a Fellow of the American College of Rheumatology and of the American College of Physicians. In 2018, he was awarded honorary membership in EULAR. He is an ad hoc reviewer for many journals, an advisory editor of *Arthritis & Rheumatology*, and a member of the editorial boards of *Best Practice and Research Clinical Rheumatology*, *Journal of Clinical Rheumatology*, and *RMD Open*.

Dr. Kay's clinical interests span the spectrum of rheumatic diseases, with special interest in rheumatoid arthritis, spondyloarthropathies, and other forms of inflammatory arthritis. He was a member of the group that developed the 2010 ACR/EULAR Diagnostic and Classification Criteria for Rheumatoid Arthritis. He chaired the Rheumatology Working Group and was a member of the Internal Medicine and Musculoskeletal Topic Advisory Groups for the World Health Organization in its Revision of the International Classification of Diseases (ICD)-11.

Over the past three decades, his clinical research has focused on nephrogenic systemic fibrosis (formerly known as nephrogenic fibrosing dermopathy), β_2 -microglobulin amyloidosis, and other rheumatologic problems of patients with chronic kidney disease. He has been a principal investigator on more than 50 clinical trials of novel therapies for rheumatoid arthritis, axial spondyloarthritis, gout, and osteoarthritis. Over the past several years, he has been involved in the development of biosimilars to treat rheumatic diseases. Dr. Kay lectures internationally and is the author of more than 160 publications.

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