FIGHT COLORECTAL CANCER

BIOSIMILARS

Breaking Down the Differences Between Drug Types: Biologic, Biosimilar, Generic, and Brand-Name Drugs

BIOSIMILARS

This resource is designed to help you understand the differences between biosimilar, biologic, generic, and brand-name drugs so that you can be as informed as possible when it comes to treatment decisions.

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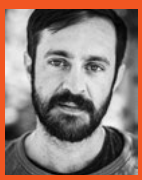

COVER:
Patrick Moote
Stage III survivor

FIGHT CRC

ABOUT FIGHT COLORECTAL CANCER

We FIGHT to cure colorectal cancer and serve as relentless champions of hope for all affected by this disease through informed patient support, impactful policy change, and breakthrough research endeavors.

MEDICAL DISCLAIMER

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INTRODUCTION

WHILE AT THE PHARMACY OR IN YOUR DOCTOR'S OFFICE, you may have heard the terms "generic" and "brand-name." Generic and brand-name drugs will remain staples in our healthcare system, and there's a new kid on the block that you may soon encounter: **biosimilars.**

As a colorectal cancer (CRC) patient, survivor, or loved one of someone diagnosed with cancer, you have had many discussions with your treatment team about which medicines to take and which treatments will be the most beneficial. It is important to know all of your treatment options so you can be involved in shared decision-making.

VOCABULARY

- **Shared decision-making**
  The process in which doctors and patients work together to make decisions about the patient's care, including tests and treatments. Doctors and patients discuss risks, outcomes and patient values to come to a decision together.
- **Rx:** *A symbol that stands for medical prescription.*

AN ANALOGY: COOKIES & BEER

IMAGINE YOU HAVE A RECIPE for double chocolate chip cookies, and another recipe for beer. You make both, and both are delicious. A few months later, you decide to make more of each, following the same recipes.

For the cookies, you follow each direction precisely; however, you use different brands of each ingredient. Still, you use flour, chocolate chips and all of the other ingredients needed. You bake the cookies and they turn out great – exactly the same as they did before.

The beer is a slightly different story. The temperature of your house varied from the first brew to the second brew. You followed the directions exactly, but the beer tasted just a little bit different. It was still delicious and had all the properties expected of beer but the taste was not identical to the first.

Why did the cookies turn out exactly the same and the beer turned out similar, but not identical? Largely this is because beer is a living, fermenting product, which makes it more delicate to its surroundings while being brewed.

The examples of baking cookies and brewing beer are a bit of a stretch, but it's a good way to start thinking about generic and brand-name drugs (in this case, cookies) and biologics and biosimilars (in this case, beer).

BACKGROUND:

WHAT'S THE DIFFERENCE BETWEEN SMALL MOLECULE VS LARGE MOLECULE?

SMALL MOLECULE	LARGE MOLECULE
Brand-Name Drugs example: Xeloda®	**Biologics** example: bevacizumab (Avastin®)
Generic example: capecitabine	**Biosimilars** example: bevacizumab-awwb (Mvasi®)

BRAND-NAME AND GENERIC DRUGS ARE SMALL MOLECULE

Some drugs are smaller in chemical structure than others.

Small molecule drugs are chemically manufactured. They are simple to make, and they are quite common on the market. In fact, they make up about 90% of all medicines on the market! Most often, small molecule drugs are in pill form.

These types of drugs are made up of a well-defined chemical structure that can be easily reproduced. Similar to following a cookie recipe, there are detailed and specific steps that are followed to make the drug so that each time they're produced, they turn out the same. For example: if you take chemical A and mix it with chemical B, filter it down, heat it up and add chemical C, you'll get the exact same drug every time.

The National Cancer Institute (NC) describes a small molecule as…

A substance that is able to enter cells easily because it has a low molecular weight. Once inside the cells, it can affect other molecules, such as proteins, and may cause cancer cells to die. This is different from drugs that have a large molecular weight, such as monoclonal antibodies, which are not able to get inside cells very easily. Many targeted therapies are small-molecule drugs or small molecule inhibitors.

BIOLOGICS AND BIOSIMILARS ARE LARGE MOLECULE

Biologics and biosimilars (used here interchangeably) are large molecule drugs. They are more complex than small molecule drugs because they are made out of or within actual living cells instead of chemicals, which are used for small molecule drug development. These cells could include microorganisms like bacterial, mammalian cell lines, or yeast. Differing from their small molecule counterparts, which are made of chemicals, biologics are made of protein. Because they are created out of living cells, they cannot be recreated exactly. It's the job of the living cells to make the protein (which is the biologic), and scientists have discovered how to make the cells make the biologics. It is called biotechnology. The process can be expensive, as large equipment is needed to produce the biologic.

Because they are made up of living cells, they are far more sensitive to the environment, such as temperature, shelf-life, and more. As a result of this sensitivity, biologics are often made in smaller batches than small molecule drugs, which have a higher threshold for these exposures.

Biologics can be up to 1,000 times larger in structure than a small molecule drug.

Vaccines, insulin, and monoclonal antibodies are excellent examples of biologics. Monoclonal antibodies are proteins that target only cancer cells in an effort to help signal the immune system to destroy them. Examples of monoclonal antibodies are the CRC therapies that target epidermal growth factor receptors (EGFR), like cetuximab and panitumumab, and vascular endothelial growth factor (VEGF), like bevacizumab and ziva flibercep.

Biologics are important in cancer treatment because, generally speaking, they use the patient's own immune system to directly or indirectly fight cancer. Because they can be so precise, biologics don't harm as many healthy cells as other drugs do, like chemotherapy. This reduces the risk of toxicity and side effects. In treating cancer, biologics are often used alongside other drugs.

The FDA approved the first biosimilar to treat colorectal cancer in September 2017.

THE COMPARISONS

GENERIC VS BRAND-NAME

GENERICS AND BRAND-NAME DRUGS ARE CHEMICALLY the same – they have the same active ingredients, the same safety and strength, the same route of administration (for example, orally or intravenously), and they are of the same quality. The term generic drug is applied to small molecular drugs (drugs made from chemical combinations). In manufacturing them, it's about chemistry and following a formula. While generics and brand-name drugs follow the same formula, generics can cost up to 80-85% less than their brand-name counterpart.

Common questions about brand-name and generics:

Q: If they are the same, why do both generic and brand-name drugs exist?

A: When a new drug is developed and clinical trials prove it to be safe and effective, it goes to the Food and Drug Administration (FDA) for approval. Once approved, it receives a 20-year patent, which stops other companies from selling the same drug during that time frame. This allows the companies who invested money in the drug development can start to make some of that money back. After the patent ends, generics are able to go on the market. This helps keep the drug price down by allowing for price competition between companies..

Q: How do we know generics are the same strength and have the same safety as brand-name drugs?

A: Just because the generic is less expensive doesn't mean it's not as good! The FDA has extremely strict rules and regulations to ensure this is the case. All drugs, generic and brand-name, must meet specific standards approved by the FDA.

Q: Do generics have a shorter pathway through the FDA process?

A: "Yes. Since generic drugs are essentially "copies" of the original medication, they do not have to complete all the same high

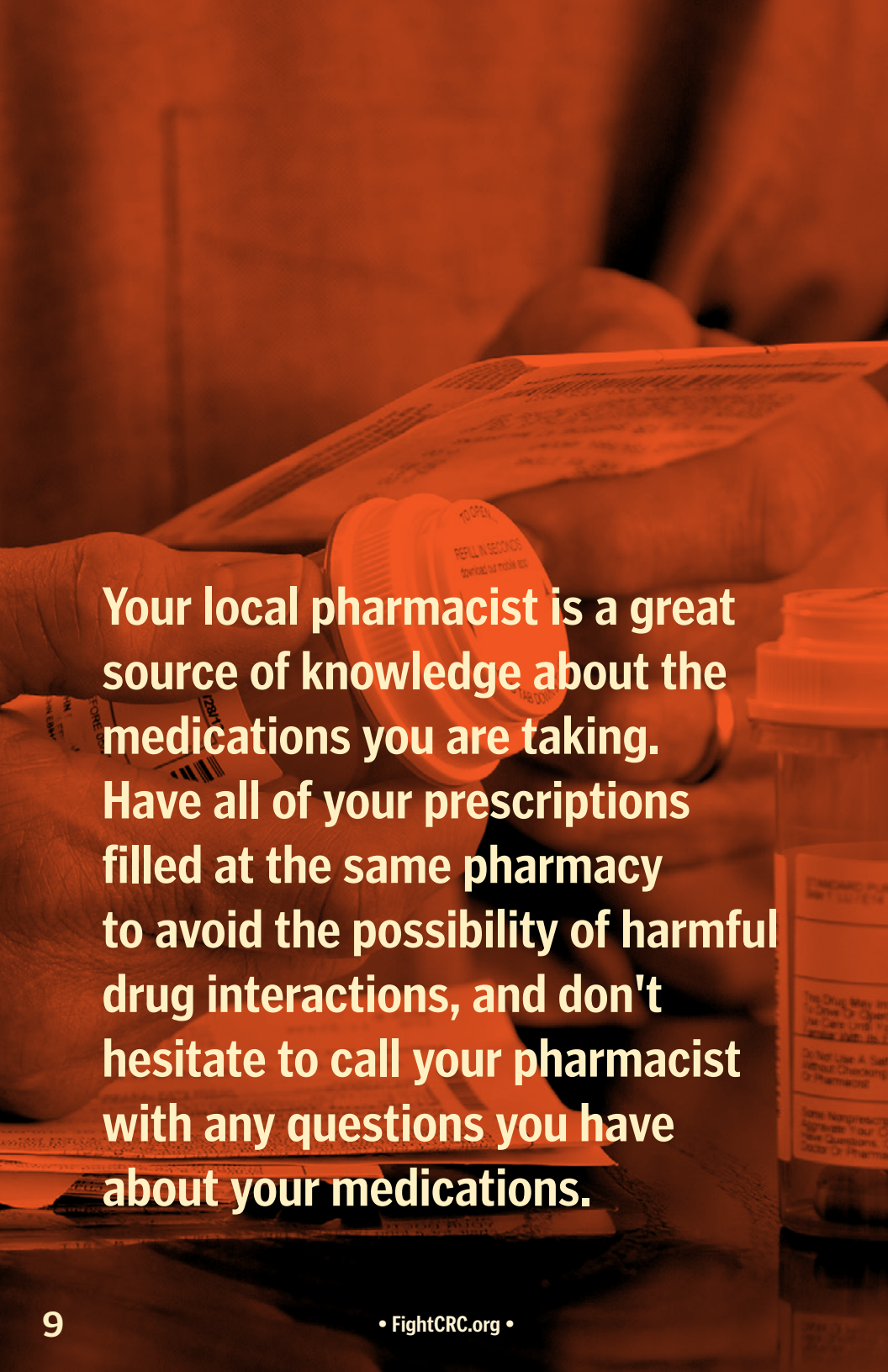
cost clinical trials a new product would have to complete to be approved by the FDA. The FDA uses an Abbreviated New Drug Application (ANDA) to review and approve a generic drug product for 'bioequivalence.'" - Ashley Glode, PharmD, BCOP

Q: Are generics or brand-name medications more cost effective?

A: Part of the aim of generic drugs is to reduce the costs of medicine and make more cost-effective treatment options available to patients.

"Typically generic drugs are more cost effective. Patients may receive brand-name therapies at a lower price with programs offered by the manufacturer to help decrease drug prices to make their product more competitive, but generic drugs are usually still cheaper. Companies are able to price generic drugs at such a discount because they do not have to repeat the costly research and development process that is required for a new drug approval."

– Ashley Glode, PharmD, BCOP



Your local pharmacist is a great source of knowledge about the medications you are taking. Have all of your prescriptions filled at the same pharmacy to avoid the possibility of harmful drug interactions, and don't hesitate to call your pharmacist with any questions you have about your medications.

BIOSIMILARS VS BIOLOGIC

JUST AS BRAND-NAME AND GENERIC DRUGS ARE USED to treat the same conditions, so are biologics and biosimilars. Biologics are referred to as "reference medicine." You can think of the original biologic (or reference medicine) as the "brand-name" drug. All biologics that follow suit are called biosimilars. They are similar but not identical because they are organically grown from living organisms. In this case, you cannot replicate the exactness of a formula.

A biosimilar is a copy of an existing biologic that is made in a different cell line (meaning it grew from different living cells than the reference medicine). Often times, biosimilars also are made using different manufacturing and purification processes, located in a different facility, or even in a different country. Even with all these variables, the biosimilars have the same clinical outcomes as their biologic counterparts. Although not identical, through rigorous laboratory work, biosimilars are shown to be just as effective and *just as safe as* biologics.

Q: How do we know biosimilars have the same strength and safety as biologics?

A: The FDA follows strict guidelines to ensure the safety of biosimilars. The guidelines ensure a strict approval process, with additional testing to ensure product safety. The FDA compares the original biologic and the biosimilar in extensive and comprehensive laboratory testing, and may include animal studies and clinical studies, to ensure that biosimilars are just as safe and effective as their biologic counterparts.

Q: If they are the same, why do both biosimilars and biologics exist?

A: Like generics, biosimilars are manufactured to increase price competition in the market and attempt to drive prices down. They are produced at a slightly discounted rate because the manufacturer does not need to conduct research on them to know if the medication will work for a specific indication, just that

continued on next page.

the biosimilar product produces outcomes and safety effects similar to the biologic, reference medicine.

Q: Are biosimilars used in other countries?

A: Yes, biosimilars have been used in Europe for decades.

Q: Do biologics have a shorter pathway through the FDA process?

A: Yes. Both the original biologic and the biosimilar go through the biologic license application (BLA) pathway. The original goes through the 351(a) BLA and the biosimilar goes through the 351(k) BLA. Because biosimilars prove their product is highly similar in structure and function to the original biologic product it is referencing, the company does not need to repeat extensive and costly clinical trials to get it approved.

Q: Are biosimilars or biologics more cost effective?

A: Part of the aim of biosimilars are to reduce the costs of medicine and make more, cost-effective treatment options available to patients.

Q: Are there biosimilars for treating colorectal cancer?

A: There are currently two biosimilars approved for colorectal cancer patients. These include Mvasi™ (bevacizumab-awwb) and Zirabev (bevacizumab-bvzr). Bevacizumab is the reference medicine for both.

"Biosimilars are deemed to be safe and effective products by the FDA, and should be incorporated into routine clinical practice. Biosimilars are intended to be priced less than the reference biologic, and should create some price competition to decrease the cost of cancer care for patients. Due to the complex process required to manufacture biosimilars, these medications do not have the same level of cost savings as generic medications."

– Ashley Glode, PharmD, BCOP

"As a stage IV and on maintenance treatment for life, having biosimlars as a new treatment option means if and when my current treatment stops working, I now have more than one option available. Knowing biosimilars are similar to their biological counterpart gives me hope that the side effects will be equally manageable. Having a new treatment option means I get more time. Time with my loved ones, and time for research to produce more effective treatment options...this means, as long as research keeps producing new and better options, a stage IV diagnosis can be viewed as a chronic illness."

– Heather Schiller
Stage IV survivor

Fred Schiller
& Heather Schiller
Stage IV survivor

MAKING YOUR DECISION

WHILE GENERIC, BRAND-NAME, AND BIOLOGIC DRUGS HAVE BEEN available to cancer patients for many years, the option to be given a biosimilar for colorectal cancer treatment is on the horizon. **When making decisions about your treatment, it is imperative to know and understand all of your options so that you can make the decision that's best for you!** Like any other medicine approved by the FDA, biosimilars are expected to be safe and effective when used under the guidance of your doctor. Here are some tips to follow when considering treatment decisions:

- **Talk to your doctor.** Ask your doctor to explain the treatments and how they may affect your body.
- **Do your research.** Visit ***FightCRC.org*** to learn about the latest treatments available for colorectal cancer patients. Seek a second opinion.
- **Consider the cost effectiveness.** Work with your family and/or social worker to learn about how the cost of treatment may affect you.
- **Consider your values and talk to your doctor about them.** Always be open with your treatment team about what you value when it comes to your medical care.
- **Prepare a list of questions for your next visit.** Here is a list to help you start the conversation:

Q: Are there risks or benefits if I switch to a biosimilar?
Q: Do I have to switch my medicine?
Q: What are the side effects?
Q: How long has the biosimilar been available?
Q: Was the biosimilar studied in my condition?
Q: How long will it take to see if the biosimilar is working for me?
Q: Will my insurance cover the biosimilar? Will Medicare cover a switch?
Q: Where can I find financial assistance?

Make sure your oncologist knows of any other medical conditions you have, or any pain you are experiencing, so they can consult with your primary care physician or your specialist if needed.

FIGHT COLORECTAL CANCER

FOR MORE INFORMATION & SUPPORT

Fight Colorectal Cancer is a trusted, nonprofit advocacy organization dedicated to empowering patients to be their own health advocates.

RESEARCH

At Fight CRC, we fight to make breakthrough research a reality. We fund innovative research grants, convene meetings with national and global experts on the biggest issues in CRC, and we train survivors and caregivers to be a part of the scientific discussions. To get involved in research and stay up to date on the latest scientific breakthroughs, follow ***@FightCRC*** on Twitter, or visit us at ***FightCRC.org/research.***

ADVOCACY

Are you ready to turn your pain into purpose? By sharing your story and raising awareness, you can help change policy around colorectal cancer. That's what the Fight CRC Advocacy Program is all about! We advocate on Capitol Hill. We engage and teach grassroots advocates like you to get involved in your communities. To learn more about how to raise your voice for CRC advocacy, visit ***FightCRC.org/action-center.***

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RESOURCES

To download or request print materials, go to:
FightCRC.org/Resources

REFERENCES

- *National Cancer Institute. https://www.cancer.gov*
- *US Food and Drug Administration (2019). Generic drugs. Retrieved from https://www.fda.gov/drugs/buying-using-medicine-safely/generic-drugs*
- *US Food and Drug Administration (2019). Biosimilars. Retrieved from https://www.fda.gov/drugs/therapeutic-biologics-applications-bla/biosimilars*
- *For more on biosimilars, visit the Biosimilars Resource Center at www.biosimilarsresourcecenter.org*

SPONSORS

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