Technician Tutorial:
Generic Substitution 101

(Update August 2022)

Many patients and healthcare professionals eagerly wait for generics of expensive brand-name drugs to enter the market. Generic drugs can lead to huge cost savings for pharmacies, patients, and healthcare organizations. About 90% of all Rxs dispensed in the US and over 70% in Canada are for generic drugs. On average, Rxs for generic drugs can cost up to 80% to 85% less than prescriptions for their brand-name counterparts.

You play an important role in filling prescriptions for generic medications. You must know how to select the right products when filling prescriptions, label prescriptions with information to help prevent confusion for patients, and direct patients to the pharmacist for counseling about generics when needed.

e-Rx
RESTASIS MULTIDOSE DAW: 0=NOT SPCFD QTY: 1 BOTTLE REFILLS: 2 SIG: **INSTILL 1 DROP IN EACH EYE TWICE A DAY**

You receive an e-prescription for Restasis MultiDose *for a patient who has filled prescriptions for this medication before. The directions are to instill 1 drop in each eye twice a day. You know that a generic for* Restasis *recently came out, so you check to see if you have any in stock.*

How do generic drugs come to market?

A brand-name drug is a patented product. The patent gives the manufacturer exclusive rights to the brand-name drug for a limited time. Patents usually last about 20 years after the drug is first identified. When this time period is up, the patent expires and generic versions of the brand-name drug can come to market.

The first generic to come to market generally gets six months of exclusivity in the US (this market exclusivity for the first generic does not exist in Canada). This means that no other generic for the brand-name drug can be marketed during that time period. This also means that the first generic probably won't be that much cheaper than the brand-name drug. Some insurance companies may even continue to cover the brand-name drug during this initial six months, but not the new generic. This is because they are likely getting rebates from the brand manufacturer, which makes the brand cheaper for the insurance company. But after six months are up, other generics can be marketed and this competition causes prices to fall.

In the US, generic drug manufacturers must submit an abbreviated new drug application (ANDA) to the US Food and Drug Administration (FDA) for approval. Canada has a similar process for generic drug approval. This shorter process doesn't require costly clinical trials, that were required for approval of the brand-name drugs, to be repeated. But the generic drug manufacturer must show that their drug acts similarly to the brand. Evidence of this might include showing that the drug is stable, dissolves properly, and that the active ingredients get absorbed into a patient's bloodstream in the same quantity and in the same amount of time as the brand drug. But manufacturers of generics don't have to prove clinical outcomes, such as preventing a disease or decreasing a lab value. The idea is that if the generic has the

same active ingredient(s), strength, dosage form, quality, purity, and stability and acts similarly, it will have the same clinical outcomes as the brand drug.

How do generic drugs benefit pharmacies, insurers, and patients?

There is a real financial impact when a generic drug becomes available. Think of it as an economic wave rippling through the entire system. Since generic drug manufacturers don't have the same development costs as brand-name drug manufacturers, generics can be sold at a lower price. The cost of the medication for the pharmacy and the insurer goes down. Often both the pharmacy and insurance company make better profit margins off generic drugs. Pharmacies also benefit from having less money tied up in inventory since lower drug costs mean a smaller investment. Additionally, the insurance company is able to provide the same service to the patient for a lower price.

These cost savings ultimately get passed on to the patient. For example, insurance co-pays for generic drugs are usually less than for brand-name drugs. An insurance co-pay is either a fixed amount or it's calculated as a percentage of the total cost of the prescription. Fixed co-pays are lower because the insurance company assigns lower co-pays for generics to encourage using them over brands. If the co-pay is a percentage, the generic drug co-pay will be cheaper than the brand-name drug because the total cost of the prescription is lower.

Are active ingredients in generic and brand-name drugs the same?

Some patients think generics don't work as well as brand-name drugs. There are often rumors that generics and brands don't contain the same amount of active ingredient(s). This is simply not true. A generic drug must come in the same strength (e.g., milligram strength of tablets or capsules, concentration of liquid) and dosage form (e.g., capsule, suspension, tablet) as the brand-name drug. Plus, the active ingredient in the generic is exactly the same as the active ingredient in the brand-name drug. This is referred to as "**pharmaceutical equivalence**" – drugs with the same active ingredient(s), dosage form, route of administration, and strength or concentration.

In the US, generics only get approved by the FDA if they are pharmaceutically equivalent and **bioequivalent**. To be considered bioequivalent, the generic drug manufacturer must show that the average rate and extent of drug absorption into the body is within the statistical range of 80% to 125% of the brand product (the requirements are very similar in Canada). This is the same standard that is used for comparing different batches of brand-name drugs. However, these numbers can be a little misleading, and may still sound like too much variability to a lot of people. Keep in mind that calculating this 80% to 125% range involves complicated statistics. It's not the same as saying that drug levels in the body can vary by 20% or 25%. In fact, if drug levels vary by more than 10%, the product will likely fail the required studies. In reality, most generics don't vary from brand-name drugs by much more than 3% to 5%.

When is it okay for a pharmacy to substitute a generic for a brand-name drug?

The term "generic substitution" refers to the process of filling a prescription for a brand-name drug with an equivalent generic medication. Generic substitution is regulated at the state level in the US, so each state has its own laws for generic substitution. In Canada, generic substitution is regulated by provinces. Generic substitution laws allow a pharmacist to dispense a generic equivalent rather than a brand-name drug when the brand name is written on the Rx.

In the US, the FDA publishes a book that is used as the standard by which many states allow generic substitution. It's called the "Orange Book," or more formally, *Approved Drug Products with Therapeutic Equivalence Evaluations* (https://www.accessdata.fda.gov/scripts/cder/ob/index.cfm). As its title implies, the Orange Book contains ratings that show whether two drugs are "**therapeutically equivalent**." Therapeutically equivalent means that drugs are both **bioequivalent** and **pharmaceutically equivalent**.

Drug products that are therapeutically equivalent are expected to have the same clinical outcomes and the same safety profile.

The Orange Book rates each generic with a code. This "code" has two letters, and it usually begins with an "A" or "B" (e.g., **A**B-rated, **B**N-rated, etc). The first letter "A" designates products that have demonstrated therapeutic equivalence. The first letter "B" indicates those that have **not**. The second letter in the Orange Book rating code can give additional information about the product, such as its dosage form. For example, the second letter "A" indicates an oral dosage form, "N" indicates a product for aerosolization, "P" means a parenteral or injectable product, and "T" stands for topical. Products that have been studied and proven to be bioequivalent are AB-rated, which is the most common code you will see. In some states, only products given an "A" rating (e.g., AB-rated, AT-rated, AP-rated) in the Orange Book can be substituted.

In Canada, generic substitution is also based on therapeutic equivalence. Interchangeability decisions are often based on Health Canada's Declaration of Equivalence, outlined on a Notice of Compliance (NOC) for a generic drug. The Canadian Reference Product is the brand-name comparator product. If a generic drug is interchangeable with the Canadian Reference Product this will be identified on the NOC. The onus of informing pharmacies about the interchangeable status of a drug typically lies with the manufacturer of the generic product. However, some provinces may allow pharmacists to use their professional judgment to determine interchangeability even without a Canadian Reference Product identified.

Generic substitution can be especially tricky for oral contraceptives and is worth mentioning separately. One thing that's especially confusing about oral contraceptive generics is that they often have names that sound like brand names. For example, *Nikki* (US) and *Loryna* (US) are listed as generics for *Yaz* in the Orange Book. A *Yaz* Rx can be filled with either of these products in most states.

It can be difficult to determine which oral contraceptives are equivalent. Usually, it's okay to rely on your computer system to automatically select the appropriate generic when you enter the brand name. But sometimes this might not be possible. For example, if you enter the generic name first instead of the brand name, some systems might not show you other equivalent products. Or, if there's a new generic drug manufacturer it might not be loaded in the system yet. The product may be there, but it might not be linked to the brand. If you're unsure if one product can be substituted for another, check with the pharmacist.

We have charts of available contraceptives in the US and Canada. In our charts, products are grouped together by hormonal content. However, this grouping is **not** meant to indicate which products can be substituted for each other. Review our chart, *Comparison of Oral Contraceptives and Non-Oral Alternatives* (US Subscribers); (Canadian subscribers) to become familiar with available products.

A takeaway point about generic substitution is that in most cases, the pharmacist can dispense either the brand or therapeutically equivalent generic, regardless of which drug product is written on the Rx. The cost of the product or insurance co-pay will likely influence what the patient receives. However, pharmacists may not substitute when prescribers specifically indicate that substitution is not allowed. This will be discussed in more detail later. For more about appropriate generic substitution, check out our CE, *Generic Substitution Laws*.

You see that you have generic Restasis*, cyclosporine 0.05% ophthalmic emulsion, in stock, but the product packaging looks significantly different than the prescribed* Restasis MultiDose. *The prescribed product comes in a small box and is supplied in a 5.5 mL bottle, while the generic version of* Restasis *comes in a larger box and is supplied as 30 single-use vials. Even though both products list the same active ingredient, cyclosporine 0.05% ophthalmic emulsion, the dosage forms seem so different that you don't think you'll be able to substitute* Restasis MultiDose *with the generic. You ask the pharmacist to make sure.*

Why do generic drugs look different from the brand-name drug?

The company that makes a brand-name drug will trademark or patent the appearance of the drug. This means that by law, a generic drug cannot look exactly like the brand-name drug. As a result, generics may be different in color, shape, or size than brand-name products. The exception to this rule is seen with an "authorized generic," which will be explained in the next section.

Generics can have different inactive ingredients (e.g., colors, fillers, flavors) than the brand-name drug. This doesn't affect the amount of drug in the body, how the drug works, or the safety of the drug. However, rarely a patient may be allergic or intolerant to a specific inactive ingredient in either a generic or brand-name drug. Stay alert for patients who may require the brand or a specific generic that they can tolerate.

Having different-looking products can actually be advantageous in the pharmacy. This can help lessen confusion and mix-ups between generic and brand-name products. On the other hand, the different appearances of generic and brand-name drugs can be confusing to patients. Reassure patients that the active ingredients in the generic drug are the same as those in the brand-name drug.

What is an authorized generic?

An authorized generic is the actual brand-name drug product that has been relabeled and marketed as a generic drug. Because the product is the actual brand-name drug, authorized generics sometimes look exactly the same as the brand-name drug. An authorized generic may be marketed by the same company that makes the brand-name drug or by its subsidiary. The brand-name drug company can also license the product to another company for marketing in return for royalties. Brand-name drug manufacturers are able to market authorized generics along with a generic that has been granted six-month exclusivity. This allows them to compete with the first generic, which may lead to lower prices. The authorized generics available in the market vary at any given time. In the US, FDA maintains a list of authorized generics on their website (https://www.fda.gov/about-fda/center-drug-evaluation-and-research-cder/fda-listing-authorized-generics). Keep in mind, most states allow you to dispense authorized generics for the brand, even though they're not in the Orange Book and may not be automatically substituted by your computer system.

What steps can be taken to ensure appropriate generic substitution?

It's sometimes a challenge to determine when a generic drug is equivalent to the brand-name drug, especially when multiple generics or brands are on the shelves. Some common situations where confusion may arise are listed below.

Extended- and immediate-release brand and generic forms of the same drug are available. Some drugs are available in both immediate- and extended-release forms. The different forms of the brand-name drug may have different names, while the generic names are very similar. For example, *Lopressor* is a brand name for metoprolol tartrate, a short-acting form of metoprolol. *Toprol-XL* (US) is the brand name for metoprolol succinate, a long-acting form of metoprolol. In Canada, there's both an immediate-release and sustained-release version of metoprolol tartrate. An Rx written for 'metoprolol' may lead to confusion in the pharmacy, since it's unclear if it should be filled with the short- or long-acting form.

Another similar example is seen with bupropion formulations. Bupropion is available as both brands and generics in immediate-release (US only), sustained-release (SR), and extended-release (XL) forms. This can cause confusion when dispensing either the brands (e.g., *Wellbutrin SR*, *Zyban*) or their generics since the names can look and sound very similar.

In addition to those listed above, other common examples include *Paxil* (paroxetine) and *Paxil CR* (paroxetine controlled-release), *Effexor* (venlafaxine [US]) and *Effexor XR* (venlafaxine extended-release), *Depakote* (divalproex delayed-release; *Epival* [Canada]) and *Depakote ER* (divalproex extended-release

[US]). If these products are often confused in your pharmacy, talk to your pharmacist about adding a visual alert such as shelf tags or a colored sticker or highlight on the bottle. It may also be helpful to separate these products on pharmacy shelves.

Multiple brand and generic forms are available, but only some are equivalent. One drug may be available as multiple brand-name products. An example is the thyroid medicine levothyroxine, which is available in the US as *Synthroid*, *Unithroid*, *Levoxyl*, and others; and in Canada as *Eltroxin* and *Synthroid*. There are also a number of generic levothyroxine products in the US, but all of the generics aren't necessarily appropriate substitutes for any of the brand-name products.

This type of situation can occur for a number of reasons. Most of the time, it's because a generic drug is tested against one brand or "reference" drug when it's being approved. When these tests are completed, the drug is rated based on its comparison to the reference drug it was tested against. The result is that some generics are equivalent to one brand, but not another, even though both brands contain the same drug entity.

The calcium channel blocking drugs diltiazem, verapamil, and nifedipine are also available as multiple brand and generic products. For example, diltiazem is available in the US as *Tiazac* and *Cardizem CD*. However, US generics that are AB-rated (therapeutically equivalent) to *Tiazac* cannot be substituted for *Cardizem CD*. Some generic forms of extended-release nifedipine are AB-rated to both *Adalat CC* (US) AND *Procardia XL* (US), while others can only be substituted for one or the other, but not both.

In addition to paying attention to which generic can be substituted for which brand, remember that different brand-name drugs (and their generics) with the same ingredient usually cannot be automatically substituted for each other. This is the case with the following drugs:

- Fluoxetine – Brand name of *Prozac* for the treatment of depression and *Sarafem* (US) for the treatment of premenstrual dysphoric disorder (PMDD).
- Sildenafil – Brand name of *Revatio* for the treatment of pulmonary arterial hypertension and *Viagra* for erectile dysfunction.
- Sotalol – Brand name of *Betapace* (US) for the treatment of one kind of heart rhythm disturbance and *Betapace AF* (US) for a different kind of heart rhythm disturbance.
- Tretinoin – Brand name of *Renova* (US) for the treatment of wrinkles and *Retin-A* for the treatment of acne.

These are just some examples, but there are other similar situations out there. Despite the fact that these brand products have the same ingredients, they often come in different strengths and are approved for different uses. Substitution will require the pharmacist to intervene and the prescriber to approve. If you are unsure about substitution, always check with your pharmacist.

The same ingredient exists but as different salts. There are drugs that have the same name but come in different salt forms. The earlier example of metoprolol tartrate and metoprolol succinate is one example of this. Another example in the US is with bupropion hydrochloride and bupropion hydrobromide (*Aplenzin*). Desvenlafaxine can also cause confusion since it is available as desvenlafaxine base and desvenlafaxine succinate. If an Rx just says "desvenlafaxine," it won't be clear which product is being prescribed. Always check with the pharmacist if it isn't clear which product should be dispensed. Also, be careful to select the correct product off of the shelf. Generic drugs that have the same name but come in different salts may be next to each other.

What steps are needed to dispense a brand-name drug when a generic is available?

There are some cases when it may be necessary to dispense a brand-name drug even though a generic is available. A patient may simply request the brand-name drug. Or, as mentioned above, a patient may be

intolerant to inactive ingredients in a generic (although this is very rare). In some cases, the prescriber may request a brand-name drug be dispensed by checking a box on the prescription blank or including the phrases "Do not substitute" or "Dispense as written" on the face of the prescription.

It's important to indicate the reason a brand is being chosen instead of an available generic when entering a prescription order into the computer. In the US, this is usually done using "Dispense as Written" or "DAW" codes in the pharmacy computer system. DAW codes are a nationally recognized code set that are transmitted with the pharmacy claim to the insurance provider. The DAW code tells the insurance provider if there are special circumstances that affect product selection for the prescription. A list of DAW codes and their meaning is provided below:

0 = No product selection indicated
1 = Substitution not allowed by prescriber
2 = Substitution allowed-patient requested that brand product be dispensed
3 = Substitution allowed-pharmacist selected product dispensed
4 = Substitution allowed-generic drug not in stock
5 = Substitution allowed-brand drug dispensed as generic
6 = Override
7 = Substitution not allowed-brand drug mandated by law
8 = Substitution allowed-generic drug not available in marketplace
9 = Other

In most cases, you are not required to enter DAW codes with every Rx. Pharmacy computer systems generally default to a DAW code of "0" when a prescription order is entered and the claim is transmitted.

It's important to always use the correct DAW code when submitting a claim. DAW codes may affect insurance reimbursement, audits, and co-pay determination for a prescription if a brand-name drug is dispensed when a generic is available. Never use DAW "1" if the prescriber has not in fact documented that the brand is requested. This could be a big financial hit for pharmacies during insurance audits if there isn't proper documentation. Make a habit to document additional explanations whenever possible for using DAW codes "2" through "9."

Note that in Canada, there are fewer of these types of codes. Typically you will need to indicate whether a brand-name drug is dispensed because of the patient's choice, the prescriber's choice, the pharmacist's choice, or because it is existing therapy.

What must be done when switching from a brand to a generic or from one generic to another?

A patient may be switched from a brand-name drug to a generic drug when a generic finally becomes available. There may be a number of generics from different companies for the same brand-name drug. So it may also be necessary at times to switch from one generic manufacturer to another. For example, generic simvastatin is manufactured by at least ten companies. Depending on pricing issues, product availability, and pharmacy inventory, your pharmacy may stock generics from different manufacturers at different times. When a patient switches from a brand-name drug to a generic or from one generic to another, you can help prevent patient confusion or mix-ups in the pharmacy by taking the steps outlined below.

Select the correct drug product in the pharmacy computer. Whenever a switch is made from a brand-name drug to a generic or from one generic to another, make sure to choose the correct product in the computer inventory list when entering the prescription. The NDC (National Drug Code [US]) or DIN (Drug Identification Number [Canada]) that is selected in the computer should match that of the actual product dispensed. This ensures that product inventory levels in the pharmacy computer match what is actually on

pharmacy shelves and helps prevent inventory errors. It can also help track down specific NDC/DIN or lot numbers in the case of a drug recall.

Include brand and generic names on the prescription label when possible. Including the generic and brand name of the drug on the Rx label can help prevent patient confusion when dispensing generics. Many computer systems do this automatically. For example, "varenicline" may be followed by "*Chantix*" (or "*Champix*" in Canada) to let patients who are used to taking the brand-name drug know that this is the generic. If your computer system doesn't automatically include the brand name when dispensing a generic, it may be helpful to input the brand name manually on the label. Keep in mind that labeling requirements for prescriptions vary from state to state and province to province. Generally, when a generic is dispensed, only the generic name is actually required. But some states may require both generic and brand names on the label when the brand-name drug is dispensed. Other states may require specific language when substituting a generic drug for a brand-name drug. Check with your pharmacist or the board of pharmacy for requirements in your state.

Use auxiliary labels to indicate that a generic is being substituted for a brand. It's important to reinforce information about a product change by letting patients know verbally and/or in writing when a switch is made. This ensures that patients will expect their medications to look different and can help decrease confusion if, for example, a patient is used to taking a "small, round, blue" tablet that is switched to an "oval, green" tablet. Auxiliary labels are a good way to let patients know you are filling the same medication they have been taking, even though the appearance of the medication may have changed.

What can I tell patients who ask when their brand-name drug will be available as a generic?

Sometimes this is hard to find out, since patent laws can be complicated and legal battles over a manufacturer's right to produce a generic drug are not uncommon. Generally, generics are available earlier in Canada than in the US. We have a chart, *Anticipated Availability of First-Time Generics*, that can give you an idea of when generics will be available for different brand-name drugs in the US. Even if there isn't a generic alternative available yet, in many cases the pharmacist can work with the prescriber to find a similar drug that is more affordable. Also, brand manufacturers often provide coupons and other types of co-pay assistance for their drugs.

The pharmacist confirms that the generic Restasis *product cannot be used to fill a prescription for* Restasis MultiDose *without obtaining authorization from the prescriber. You fill the prescription for* Restasis MultiDose *and get a co-pay of $40, which is what the patient has paid in the past for this product.*

What about "biosimilar" drugs and substitution?

You may have heard some buzz about "biosimilar" drugs and their ability to be substituted for brand-name biological drugs. Biological drugs (or biologics) come from a natural source, and are generally of human, animal, or microbiological origin. Biologics are made of proteins, nucleic acids, and/or sugars, and may even be living things, such as cells or tissues. Biologics are much larger and more complex molecules than a traditional drug. So, it's harder to make identical copies of biologics. Examples of biologics include vaccines, insulins, *Humira* (adalimumab), *Neupogen* (filgrastim), and *Aranesp* (darbepoetin alfa).

Biosimilars are **not** the same as "generics" because they go through a different approval process. They do still need to show that there are NO clinically meaningful differences in safety, effectiveness, purity, and potency compared to the original biologic. Biosimilars can usually only be substituted if FDA approves them to also be "interchangeable." To prove interchangeability, the biosimilar manufacturer needs to perform studies showing the same clinical result as the original brand. Unlike generic drugs, information on interchangeability with biosimilars can be found in FDA's "Purple Book" or more formally, *Lists of Licensed Biological Products with Reference Product Exclusivity and Biosimilarity or Interchangeability*

Evaluations (https://www.fda.gov/drugs/therapeutic-biologics-applications-bla/purple-book-lists-licensed-biological-products-reference-product-exclusivity-and-biosimilarity-or).

Semglee (insulin glargine) is an example of a commercially available interchangeable biosimilar (interchangeable for *Lantus*) in the US. However, most biosimilars are not designated as interchangeable with the original biologic at this time. For instance, in the US, *Zarxio* (filgrastim-sndz) is a biosimilar for the original brand *Neupogen*. However, the two drugs aren't interchangeable. For now, stick with dispensing exactly what's on the Rx and avoid automatically substituting a biosimilar for the original biologic. In many cases, depending on your state, a biosimilar can't be substituted without involving the pharmacist and/or prescriber. Watch drug names closely on prescriptions. For example, dispense *Neupogen* or "filgrastim" for orders written with these names. Dispense *Zarxio* or "filgrastim-sndz" for Rxs written with these names.

In Canada, biosimilars are defined similarly and also go through a different approval process than generic drugs. Biosimilar authorization by Health Canada is not a declaration of equivalence to the reference biologic drug, and therefore does not determine interchangeability. The authority to declare two products interchangeable rests with each province and territory according to its own rules and regulations.

—Continue for a "Cheat Sheet" for Generic Substitution —

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"Cheat Sheet" for Generic Substitution

(Update August 2022)

What is a generic drug?

A generic drug has the same active ingredient(s), dosage form, route of administration, and strength or concentration as a brand-name drug (often referred to as pharmaceutical equivalence). Generic drugs can be marketed at a lower price than the brand-name drug because generic drug manufacturers don't have the same development costs. While generic drugs still have to be approved by FDA and Health Canada, the process for approval is shorter and doesn't require the costly clinical trials that were required for the brand-name drug.

When can a generic drug be substituted for a brand-name drug?

This ultimately depends on state and provincial laws. However, in most cases, states and provinces will require a generic drug to be both pharmaceutically equivalent and bioequivalent to the brand-name drug before it can be substituted without prescriber authorization. Bioequivalence means that a pharmaceutically equivalent drug gets absorbed into the body at a similar rate and extent as the brand-name drug. Drugs that are both pharmaceutically equivalent and bioequivalent are considered therapeutic equivalents and are expected to have the same clinical outcomes and safety profile. In the US, the Orange Book has information on drug products that are therapeutically equivalent. In Canada, information on drug interchangeability is identified on the Notice of Compliance for a generic drug product.

What steps should be taken to prevent substitution errors?

- Watch for situations where confusion may arise when determining if a drug can be substituted, and get the pharmacist involved if you are ever unsure, such as:
  - Extended- and immediate-release brand and generic forms of the same ingredient
  - Multiple brand and generic forms of the same ingredient are available, but only some are equivalent due to different doses, dosage forms, or indications
  - Different salt forms of the same ingredient
- If a generic cannot or should not be substituted for any reason, document this, such as with DAW codes in the US.
- Do not substitute any drug when the prescriber has indicated "Do not substitute" or "Dispense as written" on the prescription, and document this appropriately as mentioned above.
- Include brand and generic names on the prescription label when possible, to prevent confusion.
- Make sure that the NDC/DIN entered into the computer to fill the Rx matches up with the NDC/DIN of the actual product dispensed, even if switching from one generic company to another.
- Use auxiliary labels to indicate that a generic is being substituted for a brand so that patients know to expect their medication to look different but work the same.
- Separate products that seem similar but shouldn't be substituted for each other on the shelf or add visual alerts such as shelf tags or a colored sticker or highlight on the package.

When can biosimilar drugs be substituted?

Biosimilars are drugs that are highly similar to an approved biologic drug. Biologic drugs come from a natural source (e.g., human, animal, or microbiological origin) and are much larger and more complex molecules than a traditional drug. Because of this, it's harder to make identical copies of biologics, and biosimilars must go through a different approval process than generic drugs. However, similar to generics, biosimilar manufacturers must show that there are NO clinically meaningful differences in safety, effectiveness, purity, and potency compared to the original biologic. Biosimilars can usually only be substituted if they have also been found to be "interchangeable," which means studies have been done to prove the same clinical result as the original brand. In the US, interchangeability information is published in the Purple Book. In Canada, interchangeability is determined by each individual province and territory.

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