teva | Biosimilars

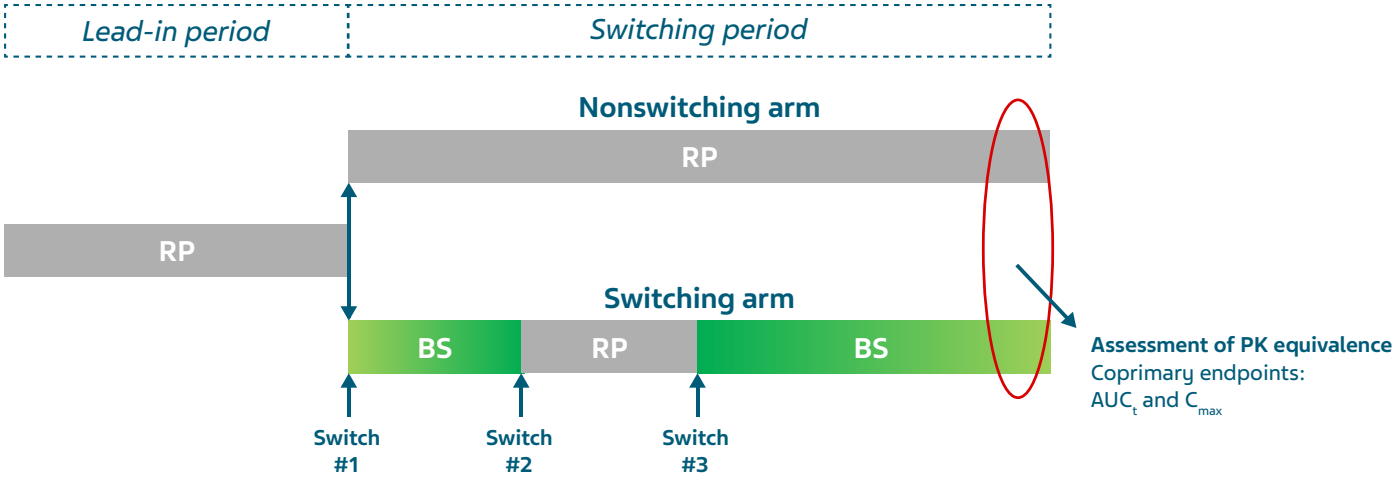
# Key differences between generics and biosimilars

| WHAT'S DIFFERENT | GENERIC | BIOSIMILAR |
|---|---|---|
| **Reference medication** | A small-molecule drug, simple in structure[1] | A large-molecule drug with a complex protein structure[1] |
| **Structural comparison to reference product** | Generic and brand-name medications are structurally identical[1] | A biosimilar is highly similar to the reference product; they both share the same main amino acid sequence but differ in minor parts of the structure[1] |
| **Manufacturing process** | Active ingredient is identical to the brand-name medication, as it is made using the same chemical processes[1] | Made from living cells and using different manufacturing processes than reference products, which are patent protected[1] |
| **Pathway for FDA approval** | • Approved via the Food, Drug, and Cosmetic Act[2]<br>• Active ingredient must be identical in strength, dosage, form, and route of administration[1]<br>• Manufacturing standards for purity, quality, and stability must be the same as the brand-name medication[1]<br>• Bioequivalence studies are required[1] | • Approved via the Public Health Service Act[3]<br>• Biosimilars must demonstrate no clinically meaningful differences in safety and effectiveness compared with the reference product[1]<br>• Clinical studies comparing the toxicity, pharmacokinetics, pharmacodynamics, and immunogenicity to the reference product are required for FDA approval[1] |
| **Pharmacy-level automatic substitution** | • Generics with an A-rated designation have no known bioequivalence problems with the brand-name medication and are AA, AN, AO, AP, or AT rated (depending on dosage form)—or have met the necessary bioequivalence requirements and are AB rated[4]<br>• Depending on state law, pharmacists may automatically substitute the A-rated generic equivalent for the brand-name medication[5]<br>• Most generics are AB rated, so they can be automatically substituted at the pharmacy level[6] | • The FDA determines the interchangeability of a biosimilar based on an additional clinical switch study that demonstrates no differences in clinical outcomes in any given patient when alternating between the reference product and the proposed interchangeable biosimilar (see back panel for details)[7]<br>• Depending on state law, pharmacists may automatically substitute the interchangeable biosimilar for the reference product[3] |
| **FDA resource** | The Orange Book[1] | The Purple Book[1] |

FDA=Food and Drug Administration; The Orange Book=Approved Drug Products With Therapeutic Equivalence Evaluations; The Purple Book=Lists of Licensed Biological Products With Reference Product Exclusivity and Biosimilarity or Interchangeability Evaluations.

## Biosimilar interchangeability study design[8,9]

To assess the safety of switching, manufacturers conduct studies in which patients alternate between the reference product and the proposed interchangeable biosimilar and compare those patients with patients who are only being treated with the reference product. The results must show no decrease in effectiveness or increase in safety risk associated with switching.




AUC=area under the concentration versus time curve in the dosing period; BS=biosimilar; $C_{max}$=maximum concentration; PK=pharmacokinetics; RP=reference product.

## Biosimilar interchangeability substitution by state[10]

| State | Can pharmacists substitute without prescriber approval? | Can prescribers prevent substitution with dispense as written requests? | Are pharmacists required to notify prescribers afterwards about substitution? | Communication time frame to prescribers? |
|---|---|---|---|---|
| **Most states** | ✔ | ✔ | ✔ | Varies by state (≤24 hours to ≤10 days) |
| **AL, SC, WA, IN** | ✘ | Not applicable | ✔ | |
| **NC, VA** | ✔ | ✔ | ✘ | |

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