FDA Drug Topics:
Biosimilars: A Review of Scientific, Regulatory, and Clinical Considerations for Health Care Providers

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Office of Therapeutic Biologics and Biosimilars
CDER/FDA
### FDA Approved Biosimilar and Interchangeable Products*

<table>
<thead>
<tr>
<th>Product Class</th>
<th>Approvals</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Supportive Care</strong></td>
<td></td>
</tr>
<tr>
<td>Filgrastim</td>
<td>B B B B B</td>
</tr>
<tr>
<td>Epoetin</td>
<td>B</td>
</tr>
<tr>
<td>Pegfilgrastim</td>
<td>B B B B B</td>
</tr>
<tr>
<td><strong>Oncology</strong></td>
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<tr>
<td>Rituximab</td>
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<tr>
<td>Bevacizumab</td>
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<td>Trastuzumab</td>
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<tr>
<td><strong>Autoimmune</strong></td>
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<tr>
<td>Etanercept</td>
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<tr>
<td>Adalimumab</td>
<td>B I B B B B B B B</td>
</tr>
<tr>
<td>Insulin Glargine</td>
<td>I I</td>
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<tr>
<td><strong>Ophthalmology</strong></td>
<td></td>
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<tr>
<td>Ranibizumab</td>
<td>B I</td>
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</tbody>
</table>

*as of May 31, 2023

- 41 Biosimilars Approved
- 29 Currently marketed
Learning Objectives

1. Review the key definitions, nomenclature, labeling, issues of interchangeability, and similarities and differences between biosimilars and reference biologics.

2. Describe how biologics differ from small molecules (size, complexity, inherent variation) and compare the biosimilar and generic approval pathways.

3. Explain the statutory requirements and approval process for biosimilars and interchangeable biosimilars.

4. Discuss considerations for prescribing and dispensing biosimilars and interchangeable biosimilars.

5. Summarize the new resources available for health care providers and faculty to learn more about biosimilar and interchangeable products and how to use the Purple Book Database of Licensed Biological Products.
Biosimilar and Interchangeable Products: Scientific Concepts and Regulatory Framework
Biological Products

- Biologics are generally large and produced from living systems
- They range in size and complexity
- Examples: therapeutic proteins (hormones, growth factors, monoclonal antibodies), vaccines, blood products

 Modified from Mellstedt H, EJC Supplements II, 2013, 3, I - II
Cells can make exact copies of a protein but other add-ons and changes may occur, resulting in different versions of the molecule (inherent variation).

Millions of slightly different versions of the same protein or antibody per dose or batch.

Biologics manufacturers try to keep a consistent mix of variants across batches of their products and over time.
Biological Product Regulation

• **351(a) “stand alone” Biologics License Application (BLA):** contains all information and data necessary to demonstrate that the proposed biological product is safe, pure and potent.

• **The Biologics Price Competition and Innovation Act of 2009 (BPCI Act)**
  – Created an **abbreviated licensure pathway (351(k))** for biological products shown to be biosimilar to or interchangeable with an FDA-licensed reference product (originator biological product).
Key Definitions from the BPCI Act

**Reference Product**
A reference product is the single biological product, already approved by FDA, against which a proposed biosimilar product is compared.

**Biosimilar Product**
A biosimilar is a biological product that is *highly similar to and has no clinically meaningful differences from* an existing FDA-approved reference product.

**Interchangeable Product**
- Is a biosimilar
- Expected to produce the same clinical result as the reference product (RP) in any given patient
- Switching between the proposed product and the RP does not ↑safety risks or ↓effectiveness compared to using the RP without switching
Why Seek Interchangeability?

An interchangeable biosimilar product can be *substituted for the reference product at pharmacies* without the intervention of the prescribing health care provider, subject to state pharmacy laws.
Biosimilars and Interchangeable Biosimilars

- Applicants request licensure as a biosimilar or interchangeable biosimilar.
- An applicant may be first approved as a biosimilar but later seek interchangeability.
- The analytical similarity and product quality standards are the same for biosimilars and interchangeable biosimilars.
- Statutory criteria related to the potential for substitution without the intervention of the prescriber.

High product quality standards

No Clinically Meaningful Differences

Analytically Highly Similar

Biosimilars

Interchangeable Biosimilars

Statutory criteria related to potential for substitution without the intervention of the prescriber
- "any given patient"
- "risk of alternating or switching"
A 351(k) application must include information demonstrating that the biological product:

- Is **biosimilar** to a reference product
  - Highly similar to and has no clinically meaningful differences from the FDA-approved reference product
- Utilizes the **same mechanism(s) of action** for the proposed condition(s) of use -- but only to the extent the mechanism(s) are known for the reference product;
- **Condition(s) of use** proposed in labeling have been previously approved for the reference product;
- Has the **same route of administration, dosage form, and strength** as the reference product; and
- Is manufactured, processed, packed, or held in a facility that **meets standards** designed to assure that the biological product continues to be **safe, pure, and potent**.
Different Goals for “Stand-alone” vs. Biosimilar Development

“Stand-alone”: 351(a) BLA
Goal: To establish *de novo* safety and efficacy of a new product

- Clinical Safety & Efficacy Study for Each Indication
- Clinical Pharmacology
- Animal
- Product Quality

“Abbreviated”: 351(k) BLA
Goal: To demonstrate biosimilarity (or interchangeability) to a reference product based on comparative assessments

- Additional Clinical Studies
- Clinical Pharmacology
- Comparative Analytical Assessment
- Product Quality
## Generic vs. Biosimilar

<table>
<thead>
<tr>
<th>Assessment</th>
<th><strong>Generic (Orange Book)</strong></th>
<th><strong>Biosimilar (Purple Book)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>“Same” Active Ingredient PK Bioequivalence</td>
<td>“Highly Similar” No Clinically Meaningful Differences</td>
</tr>
</tbody>
</table>

**Example schematic of product comparisons. Comparative Analytical data expected for both products**

Reference Listed Drug = Generic Drug

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**Clinical Pharmacology Studies**
- Compare PK, when applicable
- Compare PK, and PD, when applicable

**Other clinical study(ies)**
- Assess immunogenicity; may further evaluate safety and efficacy

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Both are “abbreviated” development pathways that have distinct statutory requirements and scientific expectations supporting their approval.
FDA’s Recommended Approach to the Development of Biosimilars and Interchangeable Biosimilars
Comparative Analytical Assessment is the Foundation

• Compare multiple physicochemical and biological attributes of each product
  – Analytical studies are generally more sensitive than clinical studies in detecting differences between products, should differences exist
  – A biosimilar product with highly similar structure and function to the reference product should behave like the reference product
• Analyze multiple lots of the reference product and proposed biosimilar for product quality attributes, including:
  – Primary amino acid sequence
  – Higher order structure (protein folding)
  – Post-translational modifications (glycosylation, etc.)
  – Heterogeneity (charge, size, aggregates, etc.)
  – Biological activity - evaluation of attributes that affect the known MoAs
## CAA Example 1: Semglee (insulin glargine-yfgn) vs US-Lantus: Quality Attributes Compared*

<table>
<thead>
<tr>
<th><strong>Primary structure</strong></th>
<th><strong>Mitogenic Activity</strong></th>
<th><strong>Protein Concentration</strong></th>
<th><strong>Other</strong></th>
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</thead>
<tbody>
<tr>
<td>• Amino acid sequence and mass</td>
<td>• IR-A phosphorylation</td>
<td>• Activity and concentration in U/mL</td>
<td>• Zinc content</td>
</tr>
<tr>
<td><strong>Higher order structure</strong></td>
<td>• Mitogenic assay (Sao2 cells)</td>
<td></td>
<td>• Aggregates/High molecular weight proteins</td>
</tr>
<tr>
<td>• Conformation</td>
<td>• IR-A binding kinetics</td>
<td></td>
<td>• Isoelectric point</td>
</tr>
<tr>
<td>• Secondary structure</td>
<td>• IGF1R binding kinetics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Tertiary and higher order structures</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>• Hydrodynamic radius</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Disulfide bonds</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><strong>Product Variants</strong></td>
<td><strong>Metabolic Activity</strong></td>
<td></td>
<td></td>
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<tr>
<td>• Deamidation</td>
<td>• IR-B phosphorylation</td>
<td></td>
<td></td>
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<tr>
<td>• Glycerol ester</td>
<td>• Glucose uptake assay</td>
<td></td>
<td></td>
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<tr>
<td>• Citric acid conjugate</td>
<td>• IR long form receptor binding kinetics</td>
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<td></td>
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<tr>
<td>• Acetylation</td>
<td>• IR autophosphorylation</td>
<td></td>
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</table>

*Not an exhaustive list; Information summarized and adapted from the [Product Quality Review](#) available on drugs@fda
CAA Example 1: Semglee (insulin glargine-yfgn) vs US-Lantus: Insulin Receptor IR-B Phosphorylation

These studies provide data to support the physiochemical structural and functional similarity of MYL-1501D to US-Lantus and evaluate the impact of any differences identified.

- Green lines represent the quality range (QR) limits (mean ± 3SD of US-Lantus).
- The values of relative IR-B phosphorylation activity for all MYL-1501D lots are 100% within the QR of US-Lantus

Adapted from the Product Quality Review available on drugs@fda
CAA Example 2: CT-P10 vs US-Rituximab: Potency and Charge Variants

The black bars represent the mean percentages. The orange lines represent the QR limits (mean ± 3SD of the US-rituximab).

Additional Analytical Studies Showed:
- Charge peaks contain same variants
- Similar biological activity between both products for each peak

Adapted from Oct. 10, 18 FDA ODAC Slides: Slides from the October 10, 2018 Meeting of the Oncologic Drugs Advisory Committee
Role of Clinical Studies

• As a scientific matter, FDA expects an adequate clinical PK, and PD if relevant, comparison between the proposed biosimilar product and reference product and a clinical immunogenicity assessment.

• Additional clinical studies are not considered “pivotal” in the way Phase 3 clinical trials are for standalone development.

• Add to the totality-of-the-evidence that supports a demonstration of biosimilarity.
Type of Clinical Data

• Clinical Pharmacology Studies
  – PK and/or PD is generally considered the most sensitive *clinical study/assay* in which to assess for differences between products, should they exist
  – PK and PD similarity data supports a demonstration of biosimilarity with the assumption that similar exposure (and pharmacodynamic response, if applicable) will provide *similar efficacy and safety* (i.e., an exposure-response relationship exists)
  – Use of a single scientifically appropriate PD biomarker or a composite of more than one relevant PD biomarker to demonstrate PD similarity can reduce residual uncertainty.

• At least 1 clinical study that includes a comparison of the immunogenicity of the proposed and reference product generally will be expected

• A comparative clinical study that compares safety and efficacy in patients is currently expected if there are residual uncertainties about whether there are clinically meaningful differences between the proposed and reference products based on structural and functional characterization, human PK and PD data, and clinical immunogenicity assessment.
Focused Efforts to Streamline Biosimilar Development

Current
“Abbreviated”: 351(k) BLA

- Additional Clinical Studies
- Clinical Pharmacology
- Comparative Analytical Assessment
- Product Quality

Potential Future
“Abbreviated”: 351(k) BLA

- Additional Clinical Studies
- Clinical Pharmacology
- Comparative Analytical Assessment
- Product Quality

Goals

- Develop alternatives to and/or reduce the size of studies involving human subjects
- Enhance the efficiency of the analytical and CMC characterization
Clinical Program Example 1: Semglee (insulin glargine-yfgn) vs US-Lantus PK/PD Compared

PK/PD Similarity Study
Euglycemic clamp study in healthy subjects

<table>
<thead>
<tr>
<th>Parameter</th>
<th>GMR (%)</th>
<th>90% CI</th>
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<tbody>
<tr>
<td>PK similarity</td>
<td></td>
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</tr>
<tr>
<td>AUC0-24h</td>
<td>99.08</td>
<td>95.11 – 103.22</td>
</tr>
<tr>
<td>Cmax</td>
<td>99.63</td>
<td>94.94 – 104.55</td>
</tr>
<tr>
<td>PD similarity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GIR AUC0-24h</td>
<td>94.92</td>
<td>86.95 – 103.62</td>
</tr>
<tr>
<td>GIRmax</td>
<td>96.44</td>
<td>89.33 – 104.11</td>
</tr>
</tbody>
</table>

Adapted from the Multi-Discipline Review available on drugs@FDA
Clinical Program Example 2: CT-P10 vs US-Rituximab

PK Similarity Study in patients with rheumatoid arthritis using the therapeutic dosing

Comparative Clinical Study in patients with low tumor burden follicular lymphoma for comparing efficacy, safety, and immunogenicity

<table>
<thead>
<tr>
<th></th>
<th>CT-P10</th>
<th>US-Rituxan</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall Response, n (%)</td>
<td>108/130 (83.1%)</td>
<td>104/128 (81.3%)</td>
</tr>
<tr>
<td>ORR Difference, (90% CI)</td>
<td>0.7981-1.0796</td>
<td></td>
</tr>
<tr>
<td>Equivalence margin</td>
<td>0.83 – 1.17</td>
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</tr>
<tr>
<td>Immunogenicity</td>
<td>Similar</td>
<td></td>
</tr>
<tr>
<td>Adverse events</td>
<td>Similar</td>
<td></td>
</tr>
</tbody>
</table>

Adapted from Oct. 10, 18 FDA ODAC Slides: Slides from the October 10, 2018 Meeting of the Oncologic Drugs Advisory Committee
Rituximab-abbs (CT-P10) Licensed for Multiple Indications 1, 2:

- Adult patients with Non-Hodgkin’s Lymphoma (NHL)
- Adult patients with Chronic Lymphocytic Leukemia (CLL)
- Rheumatoid Arthritis (RA)
- Granulomatosis with Polyangiitis (GPA) and Microscopic Polyangiitis (MPA) in adult patients

1 See USPI for full indication text: Nov 28, 2018 USPI
2 See USPI for full indication text: Feb 04, 2022 USPI
Interchangeable Biosimilars

To date, FDA has approved 4 interchangeable biosimilars to 3 different reference products

- **Lantus**
  - Semglee (insulin glargine-yfgn)
  - Rezvoglar (insulin glargine-aglr)

- **Humira**
  - Cyltezo (adalimumab-abdm)

- **Lucentis**
  - Cimerli (ranibizumab-eqrn)

Clinical immunogenicity study comparing these products and U.S. Lantus was not considered necessary*

Based on product-dependent factors, switching study was conducted for interchangeability determination

Based on product-dependent factors scientific justification supported switching study was not needed

*Draft Guidance for Industry: Clinical Immunogenicity Considerations for Biosimilar and Interchangeable Insulin Products, 2019 [https://www.fda.gov/media/133014/download](https://www.fda.gov/media/133014/download);

Review Documents available at: Drugs@FDA: FDA-Approved Drugs
Switching Between Products – Literature Highlights & Conclusions

• Reviews* of randomized and real-world studies do not suggest that switching from a reference product to a biosimilar results in efficacy, safety, or immunological issues

• Reviews# of randomized and real-world studies show that single or multiple switches between the reference product and its biosimilars had no negative impact on efficacy, safety, or immunogenicity

• Nocebo effect: Some studies report higher discontinuations in switched patients based on patient-reported outcomes without changes in objective parameters

• Based on available data from randomized and real-world studies, no differences are observed in efficacy, safety, or immunogenicity following one or more switches, with the exception of nocebo effects.

• Theoretical safety and immunological concerns with switching have not been demonstrated in patients

*Selected publication: Barbier et al. 2020 reviewed 178 studies with one or more switches between RP and BP totaling nearly 21,000 switched patients.
#Selected publication: Kurki et al. 2021 includes analyses for 23 biosimilar mAb and fusion proteins and represents over 2 billion treatment days
Using Biosimilar and Interchangeable Products
Patients and health care providers can be confident in the safety and effectiveness of a biosimilar and interchangeable product and prescribe them by name, just as for the reference product.

Biosimilar and interchangeable biosimilar products can be used in patients who have previously been treated with the reference product (i.e., treatment-experienced), and in patients who have not previously been treated with the reference product (i.e., treatment-naïve).

Interchangeable biosimilars may be substituted for the reference product without the intervention of the prescribing health care provider, subject to state laws.
Biosimilar and Interchangeable Labeling

• The labeling summarizes the scientific information health care practitioners need for safe and effective use of the product.

• A biosimilar is not required to have the same labeling as its reference product (e.g., a biosimilar can be labeled for fewer than all conditions of use or there may be differences in storage/preparation, or presentation).

• Health care professionals are advised to review the labeling (i.e., prescribing information) of the biosimilar to determine the conditions of use (e.g., indications, dosing regimens) and routes of administration for which the biosimilar is approved.

• FDA recommends that Highlights of Prescribing Information contain a “Biosimilarity Statement” describing the product’s relationship to its reference product.
Biosimilar Labeling cont.

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use PROPRIETARY NAME safely and effectively. See full prescribing information for PROPRIETARY NAME.

PROPRIETARY NAME (nonproprietary name) dosage form, route of administration, controlled substance symbol
Initial U.S. Approval: YYYY
NEXSYMEO (replicamab-czmnh) is biosimilar* to JUNEXANT (replicamab-hjxf).

WARNING: TITLE OF WARNING
See full prescribing information for complete boxed warning.
- Text (4)
- Text (5.x)

RECENT MAJOR CHANGES
Section Title, Subsection Title (x.x)     M/YYYY
Section Title, Subsection Title (x.x)     M/YYYY

INDICATIONS AND USAGE
PROPRIETARY NAME is a (Insert FDA established pharmacologic class text phrase) indicated for ... (1)
- Indication #1
- Indication #2
- Indication #3

DOSAGE FORMS AND STRENGTHS
- Strength 1, in a single-dose prefilled syringe
- Strength 1, in a single-dose prefilled autoinjector

CONTRAINdications
- Text (4)
- Text (4)

WARNINGS AND PRECAUTIONS
- Text (5.x)
- Text (5.x)

ADVERSE REACTIONS
Most common adverse reactions (incidence > x%) are text (6.x)

To report SUSPECTED ADVERSE REACTIONS, contact name of manufacturer at toll-free phone # or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS
- Text (7.x)
- Text (7.x)

USE IN SPECIFIC POPULATIONS
* Biosimilar means that the biological product is approved based on data demonstrating that it is highly similar to an FDA-approved biological product, known as a reference product, and that there are no clinically meaningful differences between the biosimilar product and the reference product. Biosimilarity of NEXSYMEO as been demonstrated for the condition(s) of use (e.g., indication(s), dosing regimen(s)), strength(s), dosage form(s), and route(s) of administration described in its Full Prescribing Information.

Revised: M/YYYY
Key Takeaways

**Fact:** FDA-approved biosimilars are as safe and effective as their original biologic and you can expect biosimilars to have the same benefits and risks as the original biologic.

**Fact:** FDA’s approval of an interchangeable biosimilar does not indicate a higher standard than biosimilarity (all interchangeables are also biosimilar), but that it underwent further evaluation to allow it to be substituted for the reference product without consulting the health care prescriber.

**Fact:** Patients and healthcare providers do not need to wait for a biosimilar product to be approved as an interchangeable product. Biosimilars are safe and effective, just like the reference product to which they were compared.

**Fact:** Biosimilar and Interchangeable labeling is not required to be the same as the reference product, but is expected to incorporate relevant data and information from reference product labeling.
Resources for Health Care Providers
Purple Book: Database of Licensed Biological Products
The Purple Book Database

The Purple Book Database contains information on all FDA-licensed (approved) biological products regulated by the Center for Drug Evaluation and Research (CDER), including licensed biosimilar and interchangeable products, and their reference products.

The Purple Book also contains information about all FDA-licensed allergenic, cellular and gene therapy, hematologic, and vaccine products regulated by the Center for Biologics Evaluation and Research (CBER).

The database can be found at PurpleBookSearch.fda.gov
The database provides patients, payors, clinicians, and others with an accessible, easy-to-use online search engine with more information about FDA-approved biological products, including biosimilar and interchangeable biological products, and their reference products.

Features tailored to different user needs, including:

- Simple Search and Advanced Search
- User Guide with detailed instructions for site location functions
- Auto-populated search results
- Additional advanced search filters
- Data download and export options
- Product label links
- Show/hide sortable data column options
- Searchable glossary of terms
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Enter a product's proprietary (brand) name or the nonproprietary (proper) name to find biological products. As you type, a list of potential results will begin to appear below the search box based on what you are typing. Click on a product from the auto-populated results list below to view the results page. The results page for your selected product will include all biological products that share a core name (i.e., biosimilar, interchangeable, reference, and related biological products).

Search results:
- **Enbrel (etanercept)**
  - BLA Number: N03795
  - 351(a)
- **Enbrel Mini (etanercept)**
  - BLA Number: N03795
  - 351(a)
- **Erelzi (etanercept-szszs)**
  - BLA Number: 767042
  - 351(k) Biosimilar
- **Erelzi Sensoready (etanercept-szszs)**
  - BLA Number: 767042
  - 351(k) Biosimilar
- **Elicovo (etanercept-ykro)**
  - BLA Number: 767056
  - 351(k) Biosimilar

Advanced Search

Database last updated: May 09, 2023
Simple Search Results
## Advanced Search

Enter data into the search box to search all products in the Purple Book. Click 'Additional Search Filters' to expand your search by entering additional terms or selecting from the drop-down list. The Advanced Search table below will update in real time and display all products that match any of the terms entered.

### Search

- **Search:** etanercept

### Table: Purple Book Database of Licensed Biological Products

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<th>Product Label</th>
<th>Applicant</th>
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<th>Dosage Form</th>
<th>Route of Administration</th>
<th>Product Presentation</th>
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Interchangeable Products

https://purplebooksearch.fda.gov
Glossary of Terms

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The Purple Book database contains information on all FDA-licensed (approved) biological products regulated by the Center for Drug Evaluation and Research (CDER), including licensed biosimilar and interchangeable products, and their reference products.

The Purple Book also contains information about all FDA-licensed allergenic, cellular and gene therapy, hematologic, and vaccine products licensed by the Center for Biologics Evaluation and Research (CBER).

Enter a product's proprietary (brand name) or the nonproprietary (proper) name to find biological products. As you type, a list of matching products will appear below the search box based on what you are typing. Click on a product from the auto-populated results list below to view the detailed page for your selected product, which will include all biological products that share a core name (i.e., biosimilar, interchangeable, reference products).
Biosimilar Education and Outreach
**Education and Outreach**

- FDA is committed to developing effective communications to improve understanding of biosimilars among patients, health care providers and payors
  
  - **Engaging** with health care professional and patient stakeholders
  
  - **Developing** educational materials for health care prescribers, pharmacists, and patients

- Education is an undertaking that requires **multi-stakeholder engagement**

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_FDA is committed to fulfilling their important role as one of many stakeholders_
Communication Challenges

• Lack of awareness and information gaps
• Low health literacy
• Concerns about safety and efficacy
• Lack of trust
• Concerns about cost and equivalency to existing treatment
• Negative perceptions and expectations leading to nocebo effect
Health Care Provider Materials

Overview of Biosimilar Products

Biosimilars are safe and effective biological medications for treating many illnesses, including chronic skin diseases, such as psoriasis; inflammatory bowel diseases, such as Crohn’s disease and ulcerative colitis; arthritis; kidney conditions; diabetes; and cancer. These medications can provide more treatment options and potentially reduce costs for patients.

Biosimilars Are Biological Products

- Biological products, or biologics, are generally large, complex molecules that are made from tissues such as bacteria, yeast, and animal cells. On the other hand, drugs made from chemicals are smaller molecules and include small molecules such as aspirin.
- Because they generally come from living organisms, biologic therapeutics often show more immunogenicity from batch to batch, and their structures are generally more complex than those of other medications. As a result, being more often more complicated to purity, process, and manufacture.
- There are many types of biologics approved for use in the United States, including monoclonal antibodies, allergens products, and monoclonal antibodies.

Overview of the Approval Process

- An FDA-approved biosimilar undergoes rigorous and constant evaluation of its safety and potential benefits throughout the product life cycle.
- The approval of a biosimilar is based on the safety and potential benefits throughout the product life cycle.
- The goal of a biosimilar development program is to demonstrate that the product is safe and effective.
- A regulatory manufacturer must submit data to the FDA for approval.
- The FDA assesses the safety and potential benefits throughout the product life cycle.
- The FDA reviews the approval of a biosimilar product.

Interchangeable Biosimilar Approval Process

- Although a reference product, which is approved by the FDA, undergoes rigorous and constant evaluation of its safety and potential benefits throughout the product life cycle.
- The approval of an interchangeable biologic product is based on its safety and potential benefits throughout the product life cycle.
- The approval of an interchangeable biologic product is based on its safety and potential benefits throughout the product life cycle.
- The approval of an interchangeable biologic product is based on its safety and potential benefits throughout the product life cycle.

Interchangeable Biological Products

An interchangeable biologic product is a biosimilar that meets additional requirements and may be substituted for the reference product. In other words, depending on the therapeutic armament of different products, interchangeable biological products may help increase patient access to biologics.

Interchangeable Biosimilars

- An interchangeable biologic product is approved by the FDA for the reference product or for the new product. This includes similar g gravy drugs, nearly identical substitutions for the new product.

Pharmacy-Level Substitution

- In the United States, the FDA has approved the use of an interchangeable biologic product for pharmacy-level substitution.

Explore FDA’s biosimilar resources for health care professionals at www.fda.gov/biosimilars.
FDA Biosimilar Materials for Patients

www.fda.gov/drugs/biosimilars/basics-patients

- English and Spanish fact sheets, infographics, articles, and more
Los biosimilares

La Administración de Alimentos y Medicamentos de los EE.UU. (FDA, por sus siglas en inglés) ha aprobado medicamentos biosimilares para tratar enfermedades como el cáncer, la enfermedad de Crohn, la colitis, la artritis reumatoide, la psoriasis y otras.

Pero, ¿qué son los medicamentos biosimilares y biológicos intercambiables? Para
Curriculum for Health Care Degree Programs

• The Biosimilar Curriculum Toolkit contains multiple types of resources to assist teaching faculty who would like to integrate topics about biosimilars into the training they provide students.

• The materials included in the toolkit were designed to meet a variety of teaching needs and contain foundational and more in-depth information by levels.
  — Level 1 is foundational and provides a high-level overview of foundational topics.
  — Level 2 materials provide an in-depth look at scientific and regulatory topics and their practical applications.

• Materials include information sheets, slide decks, videos, case studies, discussion questions, and more.

Topics covered:
• Biologics, biosimilars, and interchangeability
• The approval pathways for biological products
• Manufacturing and variation in biological products
• Labeling and prescribing biosimilar and interchangeable biosimilar products
Medscape Continuing Education

FDA is supporting the development of a series of continuing education (CE) courses through Medscape about biosimilar and interchangeable products. This includes 4 courses in 2022 and a dedicated website for the content.
FDA works with government and non-government stakeholders to support uptake and utilization of biosimilars.

- USP/FDA Infographic on biosimilars and quality
- FDA/FTC educational resource for patients about biosimilar treatment options

Conducting stakeholder outreach and offering education to stakeholders including patient advocacy organizations, medical and professional associations, payors, pharmacy organizations, and state and federal governments partners.
Future Education and Outreach Plans

• Materials and resources for **patients**:
  – Videos
  – Additional infographics and graphics

• Materials and resources for **health care providers**:
  – Videos
  – More continuing Education course options through Medscape
  – Updated educational curriculum/teaching resources for HCP schools

• Continue work with multiple stakeholders to increase educational opportunities and ensure unbiased, truthful information about biosimilars is available.
Resources

- [www.fda.gov/biosimilars](http://www.fda.gov/biosimilars) for access to all the education materials and information about biosimilar and interchangeable products.

- [https://purplebooksearch.fda.gov/](https://purplebooksearch.fda.gov/) The Purple Book: Database of Licensed Biological Products for information on biological products, including if products are biosimilar to a reference product.

- [www.fda.gov/drugsatfda](http://www.fda.gov/drugsatfda) (Drugs@FDA) for information on all FDA approved drug products, including labeling and review information.


- Guidance Webpage for guidance related to BsUFA, including details on BPCI (search on “biosimilar”)

- [CDERLearn Training and Education](http://cderelearn.fda.gov) for FDA CE, Medscape CE, and other education content- select "biosimilars" under topics.
2. Purple Book: [https://purplebooksearch.fda.gov/](https://purplebooksearch.fda.gov/)
7. Oncology Drugs Advisory Committee meeting on October 10, 2018. Meeting materials
8. Curriculum Materials for Health Care Degree Programs | Biosimilars
Questions?

Thank you

Visit www.FDA.gov/biosimilars to learn more about biosimilars.