Maryland
DEPARTMENT OF HEALTH

PHARMACY
News & Views

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Biosimilars

In the eight years since the FDA's approval of the first biosimilar, there have been 40 additional products authorized. Much like the ANDA for generic drug approval, biosimilar medications must provide pharmacokinetic, pharmacodynamic and other data to demonstrate that the product is "highly similar" to the reference product with no clinically significant differences. Despite this, inactive ingredients may vary between a biosimilar and the reference product, so it is possible that a small portion of patients would experience differences in adverse reactions or response to therapy.[1]

In 2020, legal changes made to the classification of some hormones allowed for the development of insulin biosimilars such as those referencing the long-acting insulin Lantus-Rezvoglar and Semglee. Semglee also marked the first FDA approval of a biosimilar as an "interchangeable biosimilar." [2] Prior to this, all insulin generics were unbranded generics with the reference biologic product being repackaged and sold at a lower cost than its branded counterpart. A portion of approved biosimilar medications are designated as "interchangeable biosimilars", meaning manufacturers have conducted additional testing and clinical studies to establish their product delivers the same clinical results as the reference product. In addition, studies are required to demonstrate no additional safety risk is present if the patient were to switch between the reference biologic and the biosimilar product as opposed to using the reference biologic alone. Depending on what studies were conducted for the product, an interchangeable biosimilar may not be approved for all the indications of the reference biologic. While there are currently only three approved interchangeable products, several of the currently approved biosimilar medications are performing additional studies with the intention of pursuing interchangeable status at a later date.[1,2]

In Maryland, a pharmacist is permitted to dispense an FDA-designated interchangeable biosimilar drug product without prior approval from the provider, with the exception of prescriptions marked "Dispense as Written".

(continued page 2)

Reference Biologic	Biosimilar Product(s)
Avastin (bevacizumab)	Alymsys, Mvasi, Vegzelma, Zirabev
Procrit (epoetin alfa)	Retacrit
Enbrel (etanercept)	Erelzi, Eticovo
Herceptin (trastuzumab)	Herzuma, Kanjinti, Ogivri, Ontruzant, Trazimera
Humira (adalimumab)	Abrilada, Amjevita, Cyltezo[A], Hadlima, Hadlima HC, Hulio, Hyrimoz, Idacio, Yusimry
Lucentis (ranibizumab)	Byooviz, Cimerli[B]
Lantus (insulin glargine)	Basaglar[C], Rezvoglar[D], Semglee[D]
Neulasta (pegfilgrastim)	Fulphila, Fylnetra, Nyvepria, Stimufend, Udenyca, Ziextenzo
Neupogen (filgrastim)	Granix[C], Nivestym, Releuko, Zarxio
Remicade (infliximab)	Avsola, Inflectra, Ixifi, Renflexis
Rituxan (rituximab)	Riabni, Ruxience, Truxima

[A]: Interchangeable biosimilar, approved for interchangeable use in RA, JIA, PsA, AS, CD, UC,PsO.
[B]: Interchangeable biosimilar, approved for interchangeable use in NVAMD, DED, MEfRVO, mCNV.
[C]: Basaglar and Granix are not considered to be biosimilar products as these drugs were approved under the FD&C Act section 505(b) new drug pathway.
[D]: Interchangeable biosimilar, approved for interchangeable use in DM.

Not all FDA approved biosimilar medications are currently available due to patent and loss of exclusivity (LOE) litigation, however it is expected in 2023 to see a significant increase in biosimilar use with the release of several Humira biosimilars following settlement agreements.[3]

Biosimilars *(continued)*

The patient must be notified of the substitution at the time of dispensing in writing, and the provider must be notified within five business days. Pharmacists who dispense interchangeable biosimilar products in accordance with Maryland law incur no greater liability in filling the prescription than would be incurred in filling the prescription by dispensing the prescribed brand name drug or device.[4]

More information about FDA-approved biologics and biosimilars can be found through their searchable Purple Book Database at https://purplebooksearch.fda.gov/.

References:

1. US Food and Drug Administration. Biosimilars. Published December 19, 2022. https://www.fda.gov/drugs/biosimilars
2. FDA. Information for patients about regulatory changes for certain biological product medications. Published February 20, 2020. https://www.fda.gov/media/135341/download
3. Center for Biosimilars. Biosimilar Approvals. Updated February 16, 2023. https://www.centerforbiosimilars.com/biosimilar-approvals
4. Code Citation: Md. HEALTH OCCUPATIONS Code Ann. § 12-504; https://mgaleg.maryland.gov/mgawebsite/Laws/StatuteText?article=gho§ion=12-504&enactments=true

Gene Therapies

Cell and gene therapies are one of the fastest growing areas of treatment, especially for patients with rare and refractory diseases. These products range in cost from tens of thousands of dollars per dose to several million dollars per dose, and in some cases may be curative. A disease is a good target for cell or gene therapy if occurrence of the disease is primarily linked to a known single genetic mutation. Viral vectors are used to transport the desired gene or correctional DNA or RNA into the target cells. These cells can be either extracted from the patient and then returned after being genetically modified as with CAR-T therapy, or the viral vectors may be administered directly into the patient. Currently there are over one-thousand clinical trials in the United States looking at a variety of cell and gene therapy products and disease states.[1] Currently approved cell and gene therapies are listed in the table.

Some of these products, such as Abecma, are CAR-T cell therapies made from the patient's own white blood cells in a process that takes 4-6 weeks and may only be administered at a REMS-approved treatment center.[2] Treatments like Zolgensma arrive in frozen vial kits based on patient weight.[3] Like other biologic products, cell and gene therapies are kept refrigerated or frozen until time of use.

The Center for Biologics Evaluation and Research (CBER) at the FDA regulates and approves both gene and cellular therapies, as well as devices related to them. Permission to produce a biologic product such as a gene or cellular therapy is requested through a Biologics License Application (BLA) submitted to CBER, and a decision is granted within ten months (six months if granted priority review designation).[4]

Prior to and throughout the administration process many of these products require high dose systemic corticosteroids, close monitoring, and inpatient hospitalization due to the risk of serious systemic immune response, in particular cytokine release syndrome (CRS). For CAR-T therapies, at least two doses of Actemra (tocilizumab) must be kept on hand in case of severe or life-threatening CRS.[1,2]

Several cell and gene therapies have been submitted for FDA consideration in 2023, including Vyjuvek (beremagene geperpavec) for epidermolysis bullosa, Roctavian (valoctocogene roxaparvovec) for Hemophilia A, and SRP-9001 (delandistrogene moxeparvovec) for Duchenne muscular dystrophy. Additional companies have indicated intentions to file BLA for gene therapies for sickle cell disease, hemophilia A and B, aromatic l-amino acid decarboxylase (AADC) deficiency, metachromatic leukodystrophy (MLD) and Fanconi anemia.[1]

References:

1. American Society of Gene and Cell Therapy. Updated October 31, 2022. https://patienteducation.asgct.org/
2. Abecma. Package insert. Celgene Corporation; 2021.
3. Zolgensma. Package insert. Novartis Gene Therapies, Inc.; 2021.
4. US Food and Drug Administration. Published July 25, 2018. https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/what-gene-therapy
5. US Food and Drug Administration. Updated December 16, 2022. https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/approved-cellular-and-gene-therapy-products

Gene Therapies		
Product / *Approval Year*	**Indication**	**Therapy**
Abecma (idecabtagene vicleucel) *2021*	For treatment of relapsed or refractory multiple myeloma after four or more prior lines of therapy.	CAR-T Therapy; one-time IV infusion
Adstiladrin (nadofaragene firadenovec-vncg) *2022*	For treatment of high-risk Bacillus Calmette-Guérin (BCG)-unresponsive non-muscle invasive bladder cancer (NMIBC) with carcinoma in situ (CIS) with or without papillary tumors.	Gene therapy; intravesical administration every 3 months
Breyanzi (lisocabtagene maraleucel) *2021*	For treatment of relapsed or refractory large B-cell lymphoma (LBCL), including diffuse large B-cell lymphoma (DLBCL) not otherwise specified (including DLBCL arising from indolent lymphoma), high-grade B-cell lymphoma, primary mediastinal large B-cell lymphoma, and follicular lymphoma grade 3B.	CAR-T Therapy; one-time IV infusion
Carvykti (ciltacabtagene autoleucel) *2022*	For treatment of relapsed or refractory multiple myeloma, who previously received a proteasome inhibitor (PI), an immunomodulatory agent (IMiD) and an anti-CD38 antibody.	CAR-T Therapy; one-time IV infusion
Hemgenix (etranacogene dezaparvovec-drlb) *2022*	For treatment of Hemophilia B (congenital Factor IX deficiency) who currently use Factor IX prophylaxis therapy, or have current or historical life-threatening hemorrhage, or have repeated, serious spontaneous bleeding episodes.	Gene therapy; one-time IV infusion
Imlygic (talimogene laherparepvec) *2015*	For treatment of unresectable cutaneous, subcutaneous, and nodal lesions in patients with melanoma recurrent after initial surgery.	Oncolytic virus; cutaneous, subcutaneous and/or nodal injection given every 2 weeks for at least 6 months
Kymriah (tisagenlecleucel) *2017*	For treatment of relapsed or refractory follicular lymphoma after two or more lines of therapy or for b-cell precursor ALL that is refractory or in second or later relapse.	CAR-T Therapy; one-time IV infusion
Luxturna (voretigene neparvovec-rzyl) 2017	For treatment of confirmed biallelic *RPE65* mutation-associated retinal dystrophy.	Gene therapy; one-time ophthalmic sub-retinal injection per eye
Provenge (sipuleucel-T) 2010	For treatment of asymptomatic or minimally symptomatic metastatic castrate resistant (hormone refractory) prostate cancer.	Cellular therapy; 3 dose IV infusion scheduled 2 weeks apart
Skysona (elivaldogene autotemcel) 2022	To slow the progression of neurologic dysfunction in boys 4-17 years of age with early, active cerebral adrenoleukodystrophy (CALD).	Gene-modified cell therapy; one-time IV infusion
Tecartus (brexucabtagene autoleucel) 2020	For treatment of relapsed or refractory mantle cell lymphoma (MCL), or with relapsed or refractory (r/r) B-cell precursor acute lymphoblastic leukemia (ALL).	CAR-T Therapy; one-time IV infusion
Yescarta (axicabtagene ciloleucel) 2017	For the treatment of relapsed or refractory large B-cell lymphoma.	CAR-T Therapy; one-time IV infusion
Zolgensma (onasemnogene abeparvovec-xioi) 2019	For the treatment of Spinal Muscular Atrophy (Type I) in patients less than 2 years of age	Gene therapy; one time IV infusion
Zynteglo (betibeglogene autotemcel) 2022	For treatment of patients with ß-thalassemia who require regular red blood cell (RBC) transfusions.	Gene-modified cell therapy; one-time IV infusion

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  Monday-Friday, 8:00 am - 5:00 pm
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- **Maryland AIDS Drug Assistance Program**
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  Monday-Friday, 8:30 am - 4:30 pm
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  855-283-0876
  Monday-Friday, 8:00 am - 6:00 pm

Web Portal PA Process

Web Portal PA is available in Maryland. To sign up for secured access to the portal visit: www.mdhrxprograms.com and click on the *Web Portal Signup Link* at the top right corner of the page.

To register, prescribers need:

1. Maryland Medicaid and NPI Numbers
2. First and Last Name
3. Email Address
4. Mailing Address
5. Phone and Fax Numbers
6. Three security questions answered

Once your profile has been created, as a prescriber you will have access to:

- Submit Prior Authorizations via the portal (Conduent handled PA forms only)
- Check the status of Prior Authorizations submitted via the portal
- Access, download and print Prior Authorization fax forms
- Access the Provider Manual and any available Provider Trainings and Provider information posted on the portal
- View Provider specific messages and announcements from MDH in the Message Center