Biosimilars: Overview for the Home and Specialty Infusion Pharmacy Professional

By Desiree A. Shouse, PharmD, Darcy Malard Johnson, PharmD, and Logan G. Kostur, PharmD

Pharmacists and Pharmacy Technicians

This INFUSION article is cosponsored by Educational Review Systems (ERS), which is accredited by the Accreditation Council for Pharmacy Education (ACPE) as a provider of continuing pharmacy education. ERS has assigned 1.0 contact hours (0.1 CEU) of continuing education credit to this article. Eligibility to receive continuing education credit for this article begins January 10, 2020 and expires January 10, 2023. The universal activity numbers for this program are: 0761-9999-20-007-H01-P and 0761-9999-20-007-H01-T. Activity Type: Knowledge-Based.

Nurses

Educational Review Systems is an approved provider of continuing nursing education by the Alabama State Nurses Association (ASNA), an accredited approver of continuing nursing education by the American Nurses Credentialing Center (ANCC), Commission on Accreditation. Program #5-115-20-001. Educational Review Systems is also approved for nursing continuing education by the state of California, the state of Florida, and the District of Columbia. This program is approved for 1.0 hours of continuing nursing education. Eligibility to receive continuing education credit for this article begins January 10, 2020 and expires January 10, 2023.

Dietitians

Educational Review Systems (Provider number ED002) is a Continuing Professional Education (CPE) Accredited Provider with the Commission on Dietetic Registration (CDR). Registered dietitians (RDs) and dietetic technicians, registered (DTRs) will receive 1.0 hour or 0.1 continuing professional education unit (CPEU) for completion of this program/material. Eligibility to receive continuing education credit for this article begins January 10, 2020 and expires January 10, 2023.

Dietitian Knowledge Level: 2

Dietitian Learning Codes:

- 5000

Approval as a provider refers to recognition of educational activities only and does not imply Accreditation Council for Pharmacy Education, ERS, or ANCC Commission on Accreditation approval or endorsement of any product. This continuing education activity is intended for pharmacists, pharmacy technicians, nurses, and other alternate-site infusion professionals. In order to receive credit for this program activity, participants must complete the online post-test and subsequent evaluation questions available at www.nhia.org/CE_Infusion. Participants are allowed two attempts to receive a minimum passing score of 70%.

Learning Objectives

1. *Differentiate between generic drugs and biosimilars.*
2. *Describe the FDA approval criteria for biosimilars.*
3. *Comprehend the factors driving adoption of biosimilars in the home infusion site of care.*
4. *Describe the role of the home infusion pharmacy in facilitating adoption of biosimilars in their patient populations.*

About the Authors

Desiree A. Shouse, PharmD is a PGY1 Pharmacy Resident at Vital Care of Meridian, Mississippi. She was a certified pharmacy technician for 10 years before entering the pre-pharmacy studies program at Middle Tennessee State University and earning her Doctor of Pharmacy from the University of Hawaii at Hilo in 2019. Shouse has experience working in a variety of practice settings, including community independent retail pharmacy, long-term care pharmacy, specialty pharmacy, and home infusion.

Logan G. Kostur, PharmD is a Pharmacist at Walgreens in Denver, Colorado and a Clinical Research Associate at Mountain Blue Cancer Center. He earned a bachelor's of science in Chemistry from the University of Oregon and a Doctor of Pharmacy from the University of Hawaii at Hilo. His graduate research focused on preclinical research and development of pharmaceuticals targeting MAO-B and nAch receptors in the central nervous system.

Darcy Malard Johnson, PharmD is the Oncology Pharmacy Program Mangers at Fairview Health in Minneapolis, Minnesota. She earned her Doctor of Pharmacy degree in Pharmaceutical Sciences from North Dakota State University and holds a Masters Certificate in Organizational Leadership from St. Catherine University in St, Paul.

AUTHOR DISCLOSURE STATEMENT

The authors declare no conflicts of interest or financial interest in any product or service mentioned in this program, including grants, employment, gifts, stock holdings, and honoraria.

Over the last several decades biologic products have vastly transformed pharmacotherapy options for patients with complicated diagnoses, such as autoimmune and inflammatory diseases and cancer. Now, monoclonal antibodies, interferons and cytokines, biological response modifiers, and growth factors allow many patients to experience the resolution of debilitating symptoms and disease remission. With limited side effect profiles and limited interactions with small-molecule drug therapies, biologics have become an important and common treatment alternative to conventional therapies.

Unfortunately, biologic drugs represent an outsized portion of drug spend in the United States. These products are among the most expensive therapies available and represent an increasing share of drug spending. In 2017, U.S. spending on biologics totaled $120.1 billion. That represents a 12.5% increase over 2016 and an increase of at least 10% each year since 2011.[1] According to the American Council on Science and Health, "Biologics provide relief for about 2% of America's population at the cost of about 40% of the money we, as a nation, spend on pharmaceuticals."[2]

Biosimilars, which have been available in Europe since 2006 with more than 50 approvals to date, offer a cost-effective solution. Often called follow-on biologics, biosimilars are estimated to reduce spending in this therapy class by more than $50 billion between 2017 and 2026.[3] They are also expected to improve clinical outcomes as patients can more easily afford treatment regimens, improving accessibility and adherence rates overall.[4]

Since 2015 when the first biosimilar was approved by the U.S. Food and Drug Administration (FDA), an increasing number of lower-cost therapeutic alternatives to brand name biologics have become available to prescribers and patients. There are currently 26 approved biosimilars in the U.S. with more than one-third (36%) of approvals in 2019.[5] Not all of the approved therapies are available on the U.S. market, however, as some product launches have been delayed due to ongoing litigation. Approved biosimilars and those in development fall into the clinical areas of hematology, inflammation and immunology, and oncology.[6] See the charts on pp. 40-44 for a comprehensive listing along with approved indications and essential information.

These products are among the most expensive therapies available and represent an increasing share of drug spending.

In general, the manufacture of biologics and biosimilars consists of cell modification to create a basic cell line from which protein production is possible.

What is a Biosimilar?

Biologics, and in turn, biosimilars, are extremely complex, large-molecule drug products derived from living organisms or their components (see Exhibit 1). As a result, the manufacturing process is quite complicated. Unlike traditional small-molecule drugs, which are produced via chemical synthesis, the replication of exact identical structures is fundamentally impossible to duplicate from manufacturer to manufacturer since the cells used to create these products are unique to each company.[7]

In general, the manufacture of biologics and biosimilars consists of cell modification to create a basic cell line from which protein production is possible. These proteins are then separated from the other cells and purified. However, production of biologics and biosimilars may result in batch-to-batch differences that can influence efficacy and immunogenicity.[8] For example, when Sanofi Genzyme upscaled production of its biologic alglucosidase alfa (Lumizyme®), the FDA determined that the product had changed sufficiently to require a new Biologics License Application.[9] While complex, this process has become more simplified over the past decade due to standardization and increasingly accessible technology, allowing for the reduced cost of production.[10]

FDA Approval Process

The Biologics Price Competition and Innovation Act (BPCIA), signed into law as part of the Affordable Care Act (ACA) in 2010, established an abbreviated approval pathway for biosimilars in the U.S. intended to increase competition among biologics and decrease prices (see Exhibit 2).[8] Using this pathway, a manufacturer doesn't need to demonstrate the full portfolio of safety and efficacy tests that a new biologic requires, thus allowing the manufacturer to avoid duplicating costly clinical trials.[11]

Instead, the manufacturer must show that a biosimilar is 'highly similar to the reference product notwithstanding minor differences in clinically inactive components.' No clinically meaningful differences can exist between the reference and biosimilar product when looking at the key areas of safety, purity, and potency.[8] This is generally demonstrated through human pharmacokinetic (exposure) and pharmacodynamic (response) studies, an assessment of clinical immunogenicity, and, if needed, additional clinical studies.

The goal of FDA approval is to demonstrate biosimilarity between the biosimilar product and a reference product for those conditions which have already been approved for the reference product and for the same mechanism of action, route of administration, dosage form, and strength. A "biosimilarity" determination allows

EXHIBIT 1

Relative Size of Chemical and Biologic Drugs

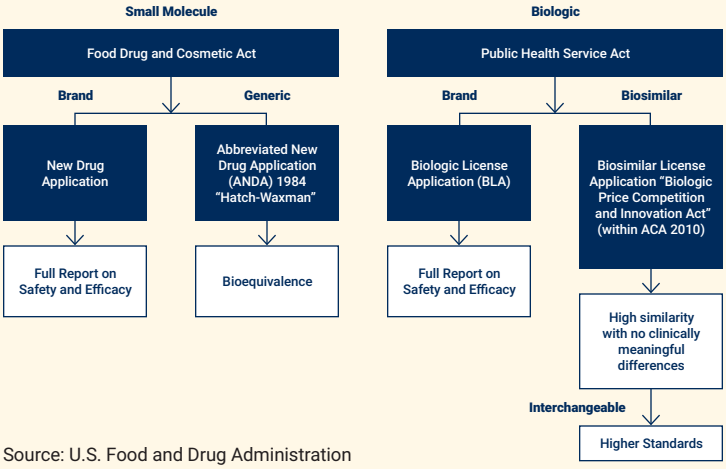
Drug		Molecular Formula
Chemical Drugs	Aspirin Tylenol (acetaminophen) Sovaldi (sofosbuvir)	$C_9H_8O_4$ $C_8H_9NO_2$ $C_{22}H_{29}FN_3O_9P$
Small Biologic Drugs	Lantus (insulin glargine) Epogen (epoetin alpha) Neupogen, Zarxio (filgrastim) Growth hormone (somatropin)	$C_{267}H_{404}N_{72}O_{78}S_6$ $C_{809}H_{1301}N_{229}O_{243}S_5$ $C_{845}H_{1339}N_{223}O_{243}S_9$ $C_{990}H_{1528}N_{262}O_{300}S_7$
Large Biologic Drugs	Enbrel, Erelzi (etanercept) Remicade, Inflectra (infliximab)	$C_{2224}H_{3472}N_{618}O_{701}S_{36}$ $C_{6428}H_{9912}N_{1694}O_{1987}S_{46}$

C – carbon
F – fluorine
H – hydrogen
N – nitrogen
O – oxygen
P – phosphorous
S – sulfur

Source: U.S. Food and Drug Administration

EXHIBIT 2

FDA Approval Pathway Small-Molecule vs. Biologic



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

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

Interchangeable Product
An interchangeable product is a biosimilar product that meets additional requirements.

Source: U.S. Food and Drug Administration

The goal of FDA-approval is to demonstrate biosimilarity between the biosimilar product and a reference product for those conditions which have already been approved for the reference product and for the same mechanism of action, route of administration, dosage form, and strength.

for the product to be on the market, but not for direct pharmacy substitution as we see with generically equivalent medications.

Of note, generic versions of certain biologics do exist, which are therapeutically equivalent to the reference product and have been approved via the abbreviated new drug application (ANDA) process. One example of this is Glatopa, a generic version of Copaxone (glatiramer). Similarly, there can be multiple biologic products with the same active ingredients, each approved separately as new drugs under the traditional approval process for biological drugs, meaning they are not biosimilars, but could be the reference product for future biosimilar development.[12]

The Challenge of Interchangeability

Interchangeable biologic products can be substituted for the reference product without the approval of the prescribing physician, ultimately allowing for pharmacists to choose and dispense more affordable alternatives to patients, if allowed by specific state regulations.[13] To date, however, no biosimilar product has been deemed interchangeable by the FDA. Therefore, standards for substitution have been left to the states.[14,15]

Currently 45 states have biosimilar substitution laws with a variety of standards set forth by each individual state.[15] Components of those standards may include substitution; pharmacy notification (to patient, to provider, others); and recordkeeping.[14,15] Pharmacists need to be aware of their state legislation when adopting biosimilars.

Standards outlined by the FDA for interchangeability are more rigorous than for biosimilar approval. In May 2019, the agency published final guidance for industry on demonstrating interchangeability with a reference product.[16] A biological product may be designated interchangeable if the manufacturer can show: [16]

1. Biosimilar expected to produce the same clinical result as the reference product in all of the reference product's licensed conditions of use in any patient.

2. For products administered to a patient more than once, the risk for adverse events or diminished efficacy of alternating or switching between products is no greater than the risk of continued use of the reference product.

The guidance further recommends that manufacturers "seek licensure for all of the reference product's licensed conditions of use when possible." It also continues to permit manufacturers to provide justification of interchangeability of multiple indications from extrapolated data, provided that the risk of safety or diminished efficacy in the alternating products can be assessed.[16]

The switching study should evaluate changes in treatment that result in two or more alternating exposures (switch intervals) to the proposed interchangeable product and to the reference product.

The FDA considers the totality of the evidence in determining interchangeability and may consider various factors dependent on the nature of the proposed interchangeable product. These factors may include considerations regarding differences in pharmacokinetics and immunogenicity among different patient populations in which the reference product is licensed and the clinical impact of any analytical differences between reference and interchangeable products.[16]

Switching Studies

Biosimilars intended to be administered more than once to an individual will be expected to "include data from a switching study or studies in one or more appropriate conditions of use." [16] The purpose of the switching study is to demonstrate that "the risk in terms of safety or diminished efficacy of alternating or switching between use of the biological product and the reference product is not greater than the risk of using the reference product without such alternation or switch."[16] The switching study should evaluate changes in treatment that result in two or more alternating exposures (switch intervals) to the proposed interchangeable product and to the reference product.[16] The final guidance provides details on the safety and immunogenicity assessments that should be evaluated in a switching study. If a manufacturer of a proposed interchangeable product believes that data from a switching study is not necessary, it will need to provide justification to the FDA for not providing that data.

Dedicated switching studies may incorporate a lead-in period of treatment with the reference product, followed by randomization to either switching treatment to the proposed interchangeable product or continuing treatment with the reference product. The number and duration of switches between products should consider various aspects of the treated condition. The switching arm is expected to incorporate at least two separate exposure periods to each of the two products, resulting in at least three switches from one product to another. The final switch should be from the reference to the interchangeable product, and final assessment should occur during the final exposure period.[16]

The switching study primary endpoint is a pharmacokinetic and pharmacodynamic analysis. These endpoints are recommended over clinical efficacy because they are considered more sensitive in detecting changes in exposure or activity that arise due to the switching or alternating between products. Secondary end points, including immunogenicity and safety end points, should be assessed. Immunogenicity assessment should evaluate incidence of antidrug and neutralizing antibodies, and the impact on pharmacokinetics, pharmacodynamics, safety, and efficacy.[16]

There are published switching studies with a number of biologic agents, including infliximab, erythropoietin-stimulating agents, filgrastim, insulin, adalimumab, rituximab, and etanercept. Results do not show clinically significant differences between the reference and biosimilar agents.[17] It is important to consider any impact that a therapeutic interchange may have on transitions in care. Frequent switching between a biosimilar and branded biologic may have an effect on variability of efficacy and safety. However, it is known that efficacy and safety of biologics can drift over time due to changes in manufacturing as well.

Naming and Labeling

Because biosimilar drug products require the same pharmacovigilance via post-marketing surveillance as any other drug on the market, the chemical name of each biosimilar product needs to be distinguishable from the others in order to provide accurate detail for reporting. The FDA has indicated naming requirements for biological products to include a "core name" followed by a random, non-sensical distinguishing suffix comprised of four lowercase letters attached by a hyphen. Many reference products were approved prior to this naming requirement and do not possess the four-letter suffix. For this reason it is imperative that the exact product is known.[18]

The FDA recommends that biosimilar product labeling (full prescribing information) incorporates relevant data and information from the FDA-approved labeling for the reference product, along with any appropriate modifications specific to the biosimilar product. A biosimilar product is not required to have the same labeling as its reference product, and so biosimilar product labeling may differ from the reference product labeling for a variety of reasons. For example, a

biosimilar applicant may seek licensure for fewer than all of the indications for which the reference product is approved, and this difference would be reflected in product labeling.[19]

Economics Will Drive Adoption

As the pace of approvals picks up and high drug prices continue to confound efforts to bend the cost curve, many health care systems and payers are beginning to adopt biosimilars based on health care economics. Payer coverage and policies are also a factor since benefit structure, formularies, and medical policies can all influence medication selection, site of care, and more.

As this article was being written, payers were just starting to release coverage policies for 2020. It's still too early to confirm every plan's biosimilar strategy, but in a few instances, payers are favoring biosimilars in targeted plans. For example, UnitedHealthcare revised its community and commercial plans' coverage of erythropoiesis-stimulating agents. Effective January 1, 2020, patients receiving epoetin alfa reference products, Epogen® (Amgen) and Procrit® (Janssen), will be required to switch to Pfizer's biosimilar, Retacrit® unless they meet medical necessity criteria. United also removed prior authorization requirements for coverage of Retacrit for patients who meet diagnosis-specific criteria. The payer had previously taken similar steps to promote utilization of Amgen's biosimilars bevacizumab (Mvasi™) and trastuzumab (Kanjinti®) over Genentech's reference drugs Avastin® and Herceptin®, respectively.[20]

Payers may be waiting for more biosimilar agents to reach the market, especially in the expensive oncology and rheumatology spaces, before scaling policies that favor these lower-cost alternatives, but it's very likely that they will begin driving utilization away from brand name biologics to biosimilars. In a 2017 survey, 22% of payer respondents had a strategy in place for addressing the use of biosimilars and

Payer coverage and policies are also a factor since benefit structure, formularies, and medical policies can all influence medication selection, site of care, and more.

Health care professionals, especially those working in home and specialty infusion pharmacies can anticipate playing a larger role in the adoption of these products.

67% planned to create a formalized strategy by 2018.[21] And, in 2018, more than half (51%) of payers surveyed required members to step through a biosimilar before utilizing its reference product. For those payers who did not have a step requirement in place, 36% were planning to implement such a policy.[22] Another study from that same time period showed more than half of payers planning to implement management policies, such as prior authorization requirements, step therapy, mandatory conversion for same dosage, and higher cost sharing, by the end of 2018 (see Exhibit 3). The average discount required to prompt payers to mandate switching to biosimilars was 24% for non-oncology drugs and 28% for oncology drugs.[23]

In the medical benefit, the biologics that consistently have highest portion of drug spend are rituximab (Rituxan®, Genentech, Biogen), trastuzumab, (Herceptin®, Genentech), bevacizumab (Avastin®, Genentech), pegfilgrastim (Neulasta®, Amgen), and infliximab (Remicade®, (Janssen).[22] These therapies, which all had FDA-approved biosimilars in 2019, are the most likely to be subject biosimilar adoption—regardless of whether it is driven by payers, health systems, or physician practices, or patients themselves. Home infusion provider organization should begin preparing for these shifts if they have not already.

Prescriber and Patient Education

Health care professionals, especially those working in home and specialty infusion pharmacies can anticipate playing a larger role in the adoption of these products. From the patient perspective, there is clearly an educational gap regarding biosimilars. For example, a 2017 survey indicated that majority (56%) of patients were not at all familiar with the term biosimilar and nearly three-quarters (70%) were concerned that biosimilars are less effective than their reference products. Researchers have studied a "nocebo" effect in patients switching from originator products to biosimilars. A systematic review of literature found insufficient evidence to confirm

a nocebo effect, but authors did note higher discontinuation rates in open-label studies of an infliximab biosimilar that supported the theory.[24]

Awareness of biosimilars among payers is substantially higher with nearly one-quarter (22%) already applying biosimilar adoption policies by 2017. Interestingly, these payers also reported that pharmacists are the most preferred providers (89%, compared to 67% physicians) for educating plan members who were considering switching to a biosimilar.[21]

Yet, prescribers' understanding of biosimilars is far from complete. A review of studies conducted between 2014 and 2017 in the U.S. and Europe showed varied knowledge of biosimilars and overall caution in prescribing them. For example, a 2014 study found that 61% of gastroenterologists had little or no confidence in biosimilars, while a 2016 study found that just 7% of rheumatologists had prescribed a biosimilar. A 2016 study found that 51% of providers limited biosimilar prescribing to biologic-naïve patients. Concerns about immunogenicity and safety also surfaced. A 23% of providers believed biosimilars to have a higher risk of immunogenicity than reference products in a 2016 study, and more than 60% of providers reported similar concerns in a 2017 survey.[25] Prescriber familiarity with biosimilars will likely accelerate with the pace of approvals, but educational gaps are likely to remain.

It is essential for home infusion pharmacy professionals to have a general knowledge of biosimilar products and their utility, how they can improve patient outcomes and adherence, and be prepared to play a role in providing education that eases any apprehension regarding the use of biosimilar products that may be exhibited by either patients or prescribing physicians. Consulting with prescribing physicians on the pharmacological attributes, effectiveness, and clinical outcomes of biosimilars will become a larger part of the home infusion provider's role. As early as 2016, more than half (53%) of health plans had already begun engaging their network providers in discussions about the use of biosimilars. A year later, that number had jumped to 58%.[23] These conversations are sure are sure to lead to prescribers' desire to learn more.

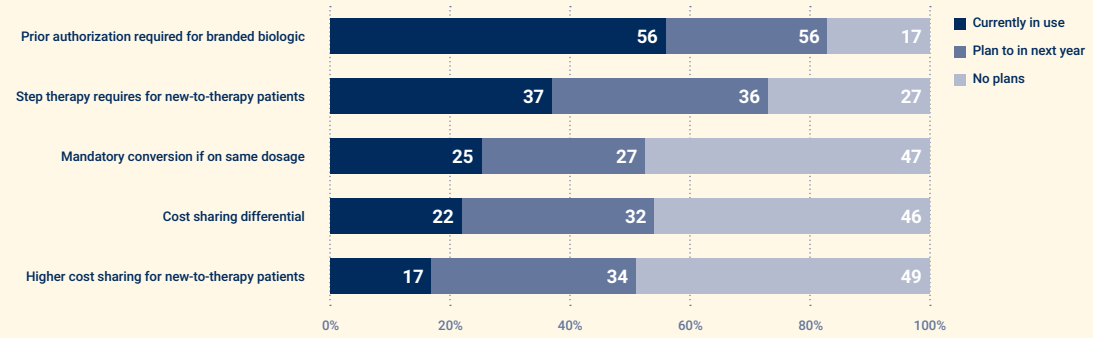
On the federal side, the Centers for Medicare and Medicaid Services (CMS) has taken steps to lay the foundation for biosimilar adoption in the Medicare program. For example, the agency established separate Healthcare Common Procedure Coding System (HCPCS) codes and payment rates for biosimilars. The average sales price (ASP) for each biosimilar will not be combined with that of other biosimilars, and reimbursement rates under Part B are based on the reference product's ASP.[26]

From a practical sense, providers should not be concerned about using biosimilars in the home setting and should expect to manage them as they would the reference product.

EXHIBIT 3

Payer Policies for Biosimilars

More than half of plans either currently use or plan to implement one or more management policies for biosimmiliars



Source: EMD Serono Specialty Digest, 14th Edition

It is essential for home infusion pharmacy professionals to have a general knowledge of biosimilar products.

As Congress and the administration continue to clamp down on soaring U.S. drug prices, several legislative proposals focus directly on increasing biosimilar utilization through price negotiation strategies, changes to patent regulations, new Medicare reimbursement models, and development of education programs for health care providers. Most of the bills apply to government-run programs such as Medicare and Medicaid, but a few apply to manufacturers and could affect the entire marketplace.[27] These legislative and regulatory steps are designed to increase uptake of biosimilars and also point to the need for health care provider understanding of these therapies.

Operational Considerations

Although decisions about substituting a biosimilar for a biologic product can only be made at the prescriber level today, home infusion providers and health systems will want to create strategies around biosimilar adoption—and know that their referral sources may already be doing the same. Eventually as interchangeable product approvals come online, substitutions will be the purview of the pharmacy department. Key deployment activities to support a biosimilar adoption strategy include:

- Clinical and economic analysis
- Engagement of the care team, including physicians, pharmacy, and nursing
- Operational review of functions such as contracting, purchasing, and inventory management
- Policy determination as to whether biosimilars will be promoted for only new orders/patients or for existing patients as well

A thorough project plan might include key goals for implementation, such as maintaining clinical outcomes, maximizing savings for the health system, minimizing impact on patient out-of-pocket expenses, and so on. Policies should be written to reflect the current lack of interchangeability so that steps are in place to address payer-mandated switching and that these processes are compliant with state law.[14,15] Policies should also spell out how to coordinate with ordering physicians, educate patients and staff about therapy changes, secure prior authorization, and make the appropriate changes to revenue cycle management, including collection of patient co-pays.

Biosimilar therapies need to be added to the electronic medical record, inventory systems, order sets and treatment plans—remember that biosimilars may not be approved for all of the indications for which their reference products are approved. There should also be a communications plan for sharing policies and related information with staff, patients, prescribers, and payers.

Clinical Considerations

From a practical sense, providers should not be concerned about using biosimilars in the home setting and should expect to manage them as they would the reference product. Because biological products administered via intravenous infusion can produce infusion-related reactions and other potential toxicities, they should be administered initially according to the provider's first-dose policy. In general, slowing the infusion rate can help to alleviate mild-to-moderate infusion reactions, along with re-initiation at a slower rate if the infusion is stopped. The patient may also receive pre-medication with corticosteroids, acetaminophen, and/or antihistamines when appropriate. Pre-medication protocols will likely already be in place and be provider-specific.

In general, patients will be monitored for at least 30 minutes post-infusion to ensure there will be no residual reactions occurring after completion. Post-infusion monitoring beyond this will be specific to the site, provider, and patient based on individual needs. After a patient demonstrates he or she can tolerate treatment, nurse administration in the home may be considered for some agents. Product-specific requirements will be discussed in further detail in the following charts compiled using each product's manufacturer prescribing information. Other considerations for infusion administration in the home setting include nursing staff competencies with biologic products and patient insurance requirements. ■

JOIN US FOR

NHIA's Annual Conference!

Be a part of the leading education and networking event for the home and specialty infusion community.

APRIL 2020

5-9

Gaylord Rockies in Denver, Colorado

Get **Inspired**

By our keynote speaker John O'Leary and learn from industry experts during educational programming.

NHIA's Expo has industry exhibitors, interactive demonstrations, networking receptions, exhibitor theatre and the Sterile Compounding Clinic — all designed to maximize education and opportunity for attendees.

Register **Now**

Register now and learn more about the conference at: **http://bit.ly/2YpKsHT**.

With limited side effect profiles and limited interactions with small-molecule drug therapies, biologics have become an important and common treatment alternative to conventional therapies.

REFERENCES

1 Quintiles IMS Institute, Medicine use and spending in the U.S.: A review of 2017 and outlook to 2022. April 2018:11.

2 American Council of Science and Health. Biosimilars are not 'generic' versions of expensive biologic medicines. February 2018. Available at: www.acsh.org/ news/ 2018/ 02/ 15/ biosimilars-are-not-generic-versions-expensive-biologic-medicines-12577 (accessed 12/4/19).

3 Mulcahy AW, Hlavka JP, Case SR. Biosimilar cost savings in the United States: Initial experience and future potential. *Rand Health Q.* 2018;7(4):3.

4 Association for Accessible Medications. 2018 Generic drug access and savings in the U.S. Available at: https://accessiblemeds.org/sites/default/files/2018_aam_generic_drug_access_and_savings_report.pdf (accessed 12/4/19).

5 U.S. Food and Drug Administration (FDA). Biosimilar product information. Available at: www.fda.gov/ drugs/ biosimilars/ biosimilar-product-information (accessed 12/4/19).

6 Amgen. Biosimilars: Current state of the market, 2019 report (sixth edition). Available at: https://www.amgenbiosimilars.com/pdfs/2019%20Trends%20in%20Biosimilars%20Report%20Electronic%20Version%20-%20USA-BIO-80182.pdf (accessed 12/4/19).

7 FDA. Novel drug approvals for 2018. Available at: https://www.fda.gov/drugs/developmentapprovalprocess/druginnovation/ucm592464.htm (accessed 12/4/19).

8 FDA. Development of therapeutic protein biosimilars: Comparative analytical assessment and other quality-related considerations. Guidance for industry. May 2019. Available at: https://www.fda.gov/media/125484/download (accessed 12/4/19).

9 Taylor N. Myozyme becomes Lumizyme after biologics scale-up. February 16, 2009. Available at: https://www.in-pharmatechnologist.com/Article/2009/02/16/Myozyme-becomes-Lumizyme-after-biologics-scale-up (accessed 12/4/19).

10 About biosimilar manufacturing. Available at: https://www.biosimilardevelopment.com/doc/about-biosimilar-manufacturing-0001 (accessed 12/4/19).

11 FDA. Biological product definitions. Available at: https://www.fda.gov/files/drugs/published/Biological-Product-Definitions.pdf (accessed 12/4/19).

12 FDA. Approved drug products Available at: http://www.accessdata.fda.gov/Scripts/cder/DrugsatFDA/index.cfm (accessed 12/4/19).

13 FDA Center for Drug Evaluation and Research. Implementation of the biologics price competition and innovation act of 2009: Available at: https://www.fda.gov/drugs/guidance-compliance-regulatory-information/implementation-biologics-price-competition-and-innovation-act-2009 (accessed 12/14/19).

14 Cauchi R. State laws and legislation related to biologic medications and substitution of biosimilars. National Conference of State Legislatures. June 2016. Available at: http://www.ncsl.org/documents/health/Biologics_BiosimilarsNCSLReport2015.pdf (accessed 12/4/19).

15 Kuyers SB. 45 states now have biosimilar substitution laws. February 11, 2019. Available at: https://www.mintz.com/insights-center/viewpoints/2801/2019-02-_5-states-now-have-biosimilar-substitution-laws (accessed 12/4/19).

16 FDA. Considerations in demonstrating interchangeability with a reference product. Guidance for industry. May 2019. Available at: https://www.fda.gov/media/124907/download (accessed 12/4/19).

17 McKinnon RA, Cook M, Liauw W, et al. Biosimilarity and interchangeability: Principles and evidence: A systematic review. *BioDrugs*. 2018;32(1):27-52.

18 FDA Center for Drug Evaluation and Research. Nonproprietary naming of biological products guidance for industry. January 2017. Available at: https://www.fda.gov/media/93218/download (accessed 12/4/19).

19 FDA. Labeling for biosimilar products. Guidance for industry. July 2018. Available at: https://www.fda.gov/media/96894/download (accessed 12/4/19).

20 Davio K. UnitedHealthcare Patients will switch to biosimilar epoetin alfa in 2020. November 4, 2019. Available at: https://www.centerforbiosimilars.com/news/unitedhealthcare-patients-will-switch-to-biosimilar-epoetin-alfa-in-2020 (accessed 12/4/19).

21 Reyes R, Lott S, et al. Looking into the future of biosimilars. *Pharmacy Today*. July 2017;23(7):42-3. https://www.pharmacytoday.org/article/S1042-0991(17)30964-7/pdf (accessed 12/4/19).

22 Magellan Rx Management. Medical pharmacy management report, 2018, 9th edition. Available at: https://www1.magellanrx.com/documents/2019/03/medical-pharmacy-trend-report_2018.pdf/ (accessed 12/4/19).

23 EMD Serono Specialty Digest. Managed care strategies for specialty pharmaceuticals, 14th edition. 2018.

24 Odinet J, Day C, Cruz J, et. Al. The biosimilar nocebo effect: A systematic review of double-blinded versus open-label studies. *J Manag Care Spec Pharm*, 2018;24(10::952-959.

25 Leonard E, Wascovich M, Oskouei S, et. al. Factors affecting health care provider knowledge and acceptance of biosimilar medicines: A systematic review. *J Manag Care Spec Pharm*. 2019;25(1):102-112.

26 Centers for Medicare and Medicaid Services. Medicare program: Revisions to payment policies under the physician fee schedule and other revisions to Part B for CY 2018; Medicare Shared Savings Program requirements; and Medicare Diabetes Prevention Program. Final rule. November 15, 2017.*Federal Register*;82(219):52976-53371

27 Bangua I. Drug pricing proposals and implications for biosimilars. November 25.2019. Available at: https://www.centerforbiosimilars.com/contributor/isha-bangia/2019/11/drug-pricing-proposals-and-implications-for-biosimilars (accessed 12/4/19).

Register now for NHIA's Sterile Compounding Clinic

Learn the latest information and best practices for sterile compounding standards and methods, all while earning more than 20 ACPE-approved continuing education credits

Our industry experts address critical aspects of sterile compounding, including:

- Aseptic practices
- Facility design and maintenance
- Environmental monitoring
- Developing compliant SOPs
- Determining BUD
- Hazardous drug compounding
- Decontamination, cleaning, and disinfecting
- Employee training and qualification

At the Gaylord Rockies in Denver, Colorado

April 5-9, 2020

Learn more today at http://bit.ly/2Zdo8T7.

Currently Approved Biosimilar Products*

By Desiree A. Shouse, PharmD, Darcy Malard Johnson, PharmD, and Logan G. Kostur, PharmD

HCPCS Code	CURRENTLY APPROVED BIOSIMILAR PRODUCTS			
	Product	**Indication(s)**	**Administration**	**Clinical Considerations**
	Reference Product: Remicade (infliximab), *Janssen*			
N/A	**Avsola** (infliximab-axxq) 100 mg/20 mL lyphilized vial Anticipated availability currently unknown *Amgen*	• **Ulcerative Colitis (UC)** 5 mg/kg at 0, 2, and 6 weeks, then every 8 weeks • **Crohn's Disease (CD)** 5 mg/kg at 0, 2, and 6 weeks, then every 8 weeks / (May ↑ to 10 mg/kg if loss of response occurs) • **Rheumatoid Arthritis (RA)** 3 mg/kg at 0, 2. And 6 weeks, then every 8 weeks in combination with methotrexate (MTX) / (May ↑ to 10 mg/kg every 4 weeks for added benefit) • **Psoriatic Arthritis (PsA)** 5 mg/kg at 0, 2, and 6 weeks, then every 8 weeks • **Plaque Psoriasis** 5 mg/kg at 0, 2, and 6 weeks, then every 8 weeks • **Ankylosing Spondylitis (AS)** 5 mg/kg at 0, 2, and 6 weeks, then every 6 weeks • **Pediatric Ulcerative Colitis** 5 mg/kg at 0, 2, and 6 weeks, then every 8 weeks • **Pediatric Crohn's Disease** 5 mg/kg at 0, 2, and 6 weeks, then every 8 weeks	Vascular Access: peripheral IV infusion over ≥ 2 hours using in-line low protein binding filter (≤1.2 micron) Infusion-reactions and/or anaphylaxis may occur at any time during infusion. Slowing infusion rate may help to alleviate mild-to-moderate reactions. Consider premedication with acetaminophen and diphenhydramine 90 min prior to infusion in all patients with prior infusion reaction Consider corticosteroid premedication in patients with prior severe infusion reaction • PO Prednisone 50 mg Q12h x 3 doses • IV hydrocortisone 100 mg or IV methylprednisolone 20-40 mg once, 20 mins prior to infusion Upon initiation, start with a test dose at 10 mL/h x 15 min, increasing at 15 min intervals, as tolerated, to completion For prior mild-to-moderate infusion reactions, max rate of 125 mL/h recommended DO NOT rechallenge in the event of a serious hypersensitivity reaction	Used in combination with Methotrexate (MTX) for RA **Boxed Warning:** • Increased risk for development of severe infections • Lymphoma and other malignancies, some fatal, have been reported in children and adolescent patients **Contraindications:** • Doses > 5 mg/kg in moderate/severe heart failure • Previous hypersensitivity to infliximab product, inactive components of Ixifi, or to any murine proteins **Warnings:** • Do not administer during an active infection • Risk for invasive fungal infections • Risk for malignancies • Hepatitis B (HBV) reactivation - STOP infliximab • Hepatotoxicity - STOP infliximab with jaundice and/or marked liver enzyme elevations • Heart failure, new onset or worsening • Cytopenias - STOP infliximab • Cardiovascular/Cerebrovascular Reactions • Demyelinating disease, new onset or worsening • Lupus-like syndrome - STOP infliximab • Do not administer LIVE vaccines while on therapy Prior to initiation of therapy, patients should be tested for latent tuberculosis and hepatitis B virus infection Prior to initiation of therapy, ensure all necessary LIVE vaccinations are up to date **Monitoring:** Vital signs should be monitored upon arrival, after start of infusion, upon discontinuation, and before patient leaves from facility. If prior acute infusion reaction, vitals should be monitored every 10 min for 30 min, then every 30 min, and for 30 min after infusion Most common ADRs include: upper respiratory tract infections, infusion-related reactions, headache, and abdominal pain Consider home infusion for subsequent dosing
Q5103	**Inflectra** (infliximab-dyyb) 100 mg/20 mL lyophilized vial *Pfizer*			
Q5104	**Renflexis** (Infliximab-abda) 100 mg/20 mL lyophilized vial *Merck*			
Q5109	**Ixifi** (infliximab-qbtx) 100 mg/15 mL lyophilized vial *Anticipated availability currently unknown* Not approved for pediatric UC *Pfizer*			

*As of January 1, 2020

HCPCS	Product	Indication(s)	Administration	Clinical Considerations
Reference Product: Neupogen (filgrastim), *Amgen*				
Q5110	**Nivestym** (filgrastim-aafi) 300 mcg/mL soln 480 mcg/mL soln 300 mcg/0.5 mL PFS 480 mcg/0.8 mL PFS *Pfizer*	• **Acute Myeloid Leukemia (AML) following induction or consolidation chemotherapy** 5 mcg/kg/day SQ, short IV (15-30 min), or continuous IV infusion; may ↑ by 5 mcg/kg for each chemo cycle Continue for up to 2 weeks until ANC ≥ 10,000/mm^3 Discontinue when ANC ≥ 10,000/mm^3 • **Bone marrow transplantation** 10 mcg/kg/day IV infusion over no longer than 24h, given 24h or more after chemo and bone marrow infusion Reduce dose to 5 mcg/kg/day if ANC > 1,000/mm^3 for 3 consecutive days. If during reduced dose ANC < 1,000/mm^3, increase back to 10 mcg/kg/day Discontinue if ANC > 1,000/mm^3 for 3 more consecutive days • **Chemotherapy-induced myelosuppression in nonmyeloid malignancies** 5 mcg/kg/day SQ, short IV (15-30 min), or continuous IV infusion; may ↑ by 5 mcg/kg for each chemo cycle Continue for up to 2 weeks until ANC ≥ 10,000/mm^3 Discontinue when ANC ≥ 10,000/mm^3 • **Peripheral blood progenitor cell collection and therapy** 10 mcg/kg/day SQ, beginning at least 4d before first apheresis, continued until last apheresis (6 to 7 days) Discontinue if WBC > 100,000/mm^3 • **Severe chronic neutropenia** Congenital neutropenia: 6 mcg/kg/day SQ divided twice daily Cyclic neutropenia: Initial: 5 mcg/kg SQ daily Usual: 2.1 mcg/kg/day Idiopathic neutropenia: Initial: 5 mcg/kg SQ daily Usual: 1.2 mcg/kg/day Adjust dose based on ANC and clinical response	Vascular Access: peripheral Do not administer earlier than 24 hours after or in the 24 hours prior to cytotoxic chemotherapy Subcutaneous administration into upper arm, abdomen, thighs, or upper outer areas of buttocks available for certain indications with patient/caregiver demonstration of ability to measure and administer appropriate dose using BD UltraSafe Plus Passive Needle Guard DO NOT rechallenge in the event of a serious hypersensitivity reaction	**Warnings:** • Fatal splenic rupture: evaluate patients who report left upper abdominal or shoulder pain for enlarged spleen or splenic rupture • Acute respiratory distress syndrome (ARDS): evaluate patients who develop fever and lung infiltrates or respiratory distress ◦ Discontinue use in patients with ARDS • Fatal sickle cell crisis • Glomerulonephritis: evaluate and consider dose-reduction or interruption if causality is likely STORE under refrigeration DISCARD if left at room temp for > 24 hours IV soln should only be reconstituted with 5% dextrose or 5% Dextrose plus albumin (human) and is only compatible in glass, polyvinyl chloride (PVC), polyolefin IV bags, or polypropylene syringes **INCOMPATIBLE with saline (precipitation occurs)** Diluted product is stable at room temp for up to 24 hours which includes infusion time **Monitoring:** Obtain a CBC and platelet count prior to initiation and twice weekly during therapy, with dose adjustments being made based on ANC ADRs reported vary with each indication for use and were of low incidence and mild in nature Consider home infusion for subsequent dosing
Q5101	**Zarxio** (filgrastim-sndz) 300 mcg/0.5 mL PFS 400 mcg/0.8 mL PFS 480 mcg/0.8 mL PFS SQ formulation only *Sandoz*			
Reference Product: Herceptin (trastuzumab), *Genentech*				
Q5113	**Herzuma** (trastuzumab-pkrb) 420 mg lyophilized multi-dose vial *Anticipated availability currently unknown* *Teva*	• **HER2+ Breast cancer, adjuvant treatment** *During and following paclitaxel, docetaxel, or docetaxel/carboplatin:* Initial: 4 mg/kg IV infusion over 90 min, then 2 mg/kg IV infusion over 30 min weekly during chemo for first 12 weeks (paclitaxel or docetaxel) or 18 weeks (docetaxel/carboplatin) Maintenance: 6 mg/kg IV infusion over 30-90 min every 3 weeks starting one week after last weekly dose Total duration: 52 wks *Following completion of anthracycline-based chemo:* Initial: 8 mg/kg IV infusion over 90 min w/in 3 weeks Maintenance: 6 mg/kg IV infusion over 30-90 min every 3 weeks Total duration: 52 wks • **HER2+ Breast cancer, metastatic** Initial: 4 mg/kg IV infusion over 90 min given alone or in combination with paclitaxel Maintenance: 2 mg/kg IV infusion over 30 min once weekly until disease progression • **HER2+ Gastric cancer, metastatic** Initial: 8 mg/kg IV infusion over 90 min Maintenance: 6 mg/kg IV infusion over 30-90 min every 3 weeks until disease progression	Vascular Access: peripheral, PICC, or mediport based on concurrent therapies and continued need for access For mild-to-moderate infusion reactions, decrease infusion rate. Interrupt infusion for dyspnea or clinically significant hypotension. Discontinue for infusion reactions manifesting as anaphylaxis, angioedema, interstitial pneumonitis, or acute respiratory distress syndrome. Manage symptoms with diphenhydramine, acetaminophen, epinephrine, corticosteroids, oxygen, bronchodilators, or IV fluids when appropriate Monitor until complete resolution of signs/symptoms Patients who experience reactions may be rechallenged, but strongly consider permanent discontinuation in all patients with severe infusion reactions Consider premedication with antihistamines or corticosteroids with subsequent doses where appropriate A dose delay >1 week would require ~6 weeks to return to steady state range; if a maintenance dose is missed by >1 week, a reloading dose is required	**Boxed Warning:** • Cardiomyopathy ◦ Withhold trastuzumab for ≥ 4 weeks if there is a ≥ 16% absolute decrease in LVEF from baseline or if LVEF falls below institutional limits of normal and there is a ≥10% absolute decrease in LVEF from baseline ◦ Permanently discontinue for a persistent (>8 weeks) LVEF decline or for suspension of dosing on > 3 occasions for cardiomyopathy • Infusion reactions, pulmonary toxicity • Embryo-Fetal Toxicity **Warnings:** • Exacerbation of chemo-induced neutropenia DO NOT administer with 5% dextrose in water DO NOT substitute with ado-trastuzumab emtansine Reconstitute with Bacteriostatic Water for Injection. If patient has allergy or intolerance to benzoyl alcohol, can use Sterile Water for Injection but must be used immediately after reconstitution (except for Ontruzant, which can be reconstituted with sterile water for injection). STORE under refrigeration Reconstituted vials may be refrigerated for up to 4-24 hours (depending on specific product and/or vial size); 28 days for reconstituted 480 mg multi-dose vial DISCARD after 4-24 hours (depending on specific product and/or vial size) **Monitoring:** Vital signs during infusion, signs/symptoms of cardiac dysfunction, LVEF (baseline, Q3 mo during treatment, upon therapy completion, Q6 mo for ≥ 2 years; if treatment withheld for LVEF dysfunction, monitor LVEF at 4-week intervals), signs/symptoms of infusion reactions or pulmonary toxicity ADRs reported ranged from mild to severe in nature but trastuzumab is generally well-tolerated. Consider home infusion for subsequent dosing
Q5117	**Kanjinti** (trastuzumab-anns) 420 mg lyophilized multi-dose vial *Amgen*			
Q514	**Ogivri** (trastuzumab-dkst) 420 mg lyophilized multi-dose vial *Anticipated availability currently unknown* *Mylan*			
Q5112	**Ontruzant** (trastuzumab-dttb) 150 mg lyophilized vial *Merck*			
Q5116	**Trazimera** (trastuzumab-qyyp) 420 mg lyophilized multi-dose vial *Anticipated availability currently unknown* *Pfizer*			

HCPCS	Product	Indication(s)	Administration	Clinical Considerations
	Reference Product: Rituxan (rituximab), *Genentech/Biogen*			
N/A	**Ruxience** (rituximab-pvvr) 100 mg/10 mL soln 500 mg/50 mL soln *Anticipated availability currently unknown* *Pfizer*	• **Non-Hodgkin's Lymphoma (NHL)** 375 mg/m^2 IV once weekly for 4-8 doses Duration of therapy depends on specific type of NHL • **Chronic Lymphocytic Leukemia (CLL)** Usual: 375 mg/m^2 IV day prior to initiation of fludarabine and cyclophosphamide chemotherapy, then 500 mg/m^2 on day 1 of cycles 2 to 6 (every 28 days) • **Granulomatosis with Polyangiitis (GPA) (Wegener's Granulomatosis) and Microscopic polyangiitis (MPA)** Initial: 375 mg/m^2 IV once weekly for 4 weeks in combination with methylprednisolone IV for 1-3 days followed by a prednisone taper Corticosteroids should begin within 14 days prior to or with rituximab initiation and may continue during and after the 4-week course of therapy Maintenance (after disease control achieved): 500 mg IV as two infusions separated by 2 weeks followed by 500 mg IV once every 6 months thereafter If induction for active disease was with rituximab, begin rituximab follow-up therapy within 24 weeks of the last rituximab induction dose (or based on clinical evaluation), but no sooner than 16 weeks following the last rituximab induction dose. If induction therapy for active disease was with another agent (not rituximab), then initiate rituximab follow-up therapy within the 4-week period following achievement of disease control. Premedication with methylprednisolone 100 mg IV is recommended 30 minutes prior to each rituximab dose	Vascular Access: peripheral Initial Infusion: Start infusion at a rate of 50 mg/hour; if there is no infusion-related reaction, increase the rate by 50 mg/hour increments every 30 minutes, to a maximum rate of 400 mg/hour Subsequent infusions: If patient tolerated initial infusion, start at 100 mg/hour; if there is no infusion-related reaction, increase the rate by 100 mg/hour increments every 30 minutes, to a maximum rate of 400 mg/hour Some patients may be eligible for an accelerated infusion rate (90 min) based on certain criteria Premedicate before each infusion with acetaminophen and an antihistamine If an infusion-related reaction occurs, slow or stop the infusion. If the reaction improves, restart infusion at 50% of the previous rate. Discontinue infusion in the event of serious or life-threatening cardiac arrhythmias	**Boxed Warning:** • Fatal infusion-related reactions w/in 24h of infusion; approximately 80% occurred with first infusion • Severe mucocutaneous reactions, some fatal • Hepatitis B virus (HBV) reactivation • Progressive multifocal leukoencephalopathy (PML) **Warnings:** • Tumor lysis syndrome: Give aggressive IV hydration, anti-hyperuricemic agents, monitor renal function • Infections • Cardiac ADRs: STOP if life-threatening • Renal toxicity: STOP if rising SCr or oliguria • Bowel obstruction/perforation • Immunizations: Live virus vaccines prior to or during therapy not recommended • Embryo-fetal toxicity DO NOT use in combination with cisplatin STORE under refrigeration STABLE after reconstitution under refrigeration for 24 hours and at room temp for an additional 24 hours (does not contain a preservative so refrigeration is preferred) *P. jirovecii* pneumonia prophylaxis is recommended during treatment and for at least 6 months following the last rituximab infusion **Monitoring:** CBC with differential and platelets (prior to initiation, prior to each treatment course, and weekly-monthly intervals in patients with lymphoid malignancies or at 2- to 4-month intervals in patients with GPA/MPA), monitor for cytopenias after final dose and until resolution, electrolytes (in patients at risk for tumor lysis syndrome), renal function, fluid/hydration status, blood pressure, and vital signs Vital signs should be monitored upon arrival, after start of infusion, upon discontinuation, and before patient leaves from facility. If prior acute infusion reaction, vitals should be monitored every 10 min for 30 min, then every 30 min, and for 30 min after infusion ADRs reported ranged from mild to severe in nature Would not recommend for home infusion
Q5115	**Truxima** (rituximab-abbs) 100 mg/10 mL soln 500 mg/50 mL soln *Anticipated availability currently unknown* Approved for NHL and CLL *Genentech*			
	Reference Product: Avastin (bevacizumab), *Genentech*			
Q5107	**Mvasi** (bevacizumab-awwb) 100 mg/4 mL Soln 400 mg/16 mL Soln *Genentech*	• **Metastatic colorectal cancer** 5 mg/kg every 2 weeks with bolus-IFL 10 mg/kg every 2 weeks with FOLFOX4 5 mg/kg every 2 weeks or 7.5 mg/kg every 3 weeks with fluoropyrimidine-irinotecan or fluoropyrimidine-oxaliplatin based chemotherapy after progression on a first-line bevacizumab product-containing regimen • **Non-squamous non-small cell lung cancer, first-line** 15 mg/kg every 3 weeks with carboplatin and paclitaxel • **Glioblastoma, recurrent** 10 mg/kg every 2 weeks • **Metastatic renal cell carcinoma** 10 mg/kg every 2 weeks with IFN-alfa • **Persistent, recurrent, or metastatic cervical cancer** 15 mg/kg every 3 weeks with paclitaxel and cisplatin or paclitaxel and topotecan	Vascular Access: peripheral First dose: Infuse over 90 min Subsequent doses: Infuse over 60 min if first dose tolerated. If second dose tolerated, all others can be infused over 30 mins After tolerance at the 90-, 60-, and 30-minute infusion rates has been established, some institutions use an off-label 10-minute infusion rate (0.5 mg/kg/minute) in adults for bevacizumab dosed at 5 mg/kg Decrease infusion rate for mild (clinically insignificant) infusion reaction; interrupt infusion for clinically significant infusion reaction (after symptoms resolve, resume at a decreased infusion rate); discontinue bevacizumab for severe infusion reaction	DO NOT administer for 28 days following surgery and until surgical wound is fully healed **Warnings:** • GI perforations and fistula: STOP • Surgery and wound healing complications • Hemorrhage: do not administer for recent hemoptysis; STOP for grade 3-4 hemorrhage • Arterial thromboembolic events: STOP if severe • Venous thromboembolic events: STOP for grade 4 • Hypertension: monitor, withholding until medically controlled; STOP for crisis/urgency • Posterior reversible encephalopathy syndrome: STOP • Renal injury and proteinuria: monitor; STOP for nephrotic syndrome; withhold until < 2 gm protein in urine • Embryo-fetal toxicity • Ovarian failure • Congestive heart failure: STOP if develops INCOMPATIBLE with dextrose-containing solutions STORE under refrigeration STABLE after reconstitution under refrigeration for 8 hours **Monitoring:** Monitor for proteinuria/nephrotic syndrome with urine dipstick; collect 24-hour urine in patients with ≥2+ reading. Monitor blood pressure every 2 to 3 weeks; more frequently if hypertension develops during therapy; continue to monitor blood pressure after discontinuing due to bevacizumab-induced hypertension. Monitor closely during the infusion for signs/symptoms of an infusion reaction. Monitor for signs/symptoms of gastrointestinal perforation or fistula (including abdominal pain, constipation, vomiting, and fever), bleeding (including epistaxis, hemoptysis, GI, and/or CNS bleeding), thromboembolism (arterial and venous), wound healing complications, and heart failure ADRs reported ranged from mild to severe in nature and varied depending on concurrent regimen
Q5118	**Zirabev** (bevacizumab-bvzr) *Anticipated availability currently unknown* *Pfizer*			

HCPCS	Product	Indication(s)	Administration	Clinical Considerations
	Reference Product: Epogen (epoetin alfa), *Amgen*			
Q5105	**Retacrit** (epoetin alfa-epbx) 2,000 units/mL Soln 3,000 units/mL Soln 4,000 units/mL Soln 10,000 units/mL Soln 40,000 units/mL Soln *Pfizer*	• **Anemia due to chemotherapy in patients with cancer** 40,000 units weekly or 150 units/kg three times weekly • **Anemia due to chemotherapy in patients with cancer, pediatric (≥ 5 years)** 600 units/kg weekly • **Anemia due to chronic kidney disease** Initial: 50-100 units/kg three times weekly Maintenance dose is individualized • **Anemia due to chronic kidney disease, pediatric** Initial: 50 units/kg three times weekly Maintenance dose is individualized • **Anemia due to zidovudine in HIV-infected patients** 100 units/kg three times weekly • **Reduction of allogeneic RBC transfusion in patients undergoing elective, noncardiac, nonvascular surgery** 300 units/kg daily for 15 days or 600 units/kg weekly	Vascular Access: peripheral IV preferred for hemodialysis patients; SQ preferred for all others No dilution required prior to administration Initiate when hemoglobin (Hgb) < 10 g/dL (cancer); Hgb < 10 g/dL, rate of Hgb decline indicates likelihood of needing RBC transfusion, and reducing risk of alloimmunization and/or other RBC transfusion-related risks is a goal A single Hb excursion may not require a dosing change STOP when hemoglobin (Hgb) approaches > 11 g/dL Potentially serious allergic reactions (including anaphylactic reactions, angioedema, bronchospasm, rash, and urticaria) have been reported rarely with epoetin alfa. Discontinue immediately (and permanently) in patients who experience serious allergic/anaphylactic reactions	**Boxed Warning:** • Chronic kidney disease • Cancer • Perisurgery **Contraindications:** • Uncontrolled hypertension • Pure red cell aplasia (PRCA) that begins after treatment **Warnings:** • Increased mortality, myocardial infarction, stroke, and thromboembolism when targeting HgB > 11 g/dL • Increased mortality and/or increased risk of tumor progression or recurrence in patients with cancer • Hypertension • Increased risk for seizures in patients with CKD • If severe anemia and low reticulocyte count develop, STOP and evaluate for PRCA • Severe cutaneous reactions: STOP • Phenylketonurics: contains phenylalanine Evaluate iron status before and during treatment and maintain iron repletion STORE under refrigeration **Monitoring:** Transferrin saturation and serum ferritin (prior to and during treatment); Hb (weekly after initiation and following dose adjustments until stable and sufficient to minimize need for RBC transfusion, chronic kidney disease (CKD) patients should be also be monitored at least monthly following Hb stability); blood pressure; monitor for signs of seizures (CKD patients following initiation for first few months, includes new-onset or change in seizure frequency or premonitory symptoms) After 8 weeks of therapy, if there is no response as measured by Hgb levels or if RBC transfusions are still required, DISCONTINUE ADRs reported were mild in nature Consider home infusion for subsequent dosing when IV administration is necessary (hemodialysis)
	SUBCUTANEOUS ADMINISTRATION			
	Reference Product: Humira (adalimumab), *AbbVie*			
N/A	**Abrilada** (adalimumab-afzb) 40 mg/0.8 mL PEN 40 mg/0.8 mL PFS 40 mg/0.8 mL SDV 20 mg/0.4 mL PFS 10 mg/0.2 mL PFS Anticipated availability 2023 Approved for Psoriatic Arthritis *Pfizer*	• **Adult Ulcerative Colitis (UC)** Initial: 160 mg on day 1, 80 mg on day 15 Maintenance: 40 mg every other week beginning on day 29 Only continue in patients showing evidence of clinical remission by eight weeks (day 57) of therapy • **Juvenile Idiopathic Arthritis** *Amjevita, Cyltezo, Hadlima, Hyrimoz* ≥ 30 kg: 40 mg every other week 10 kg (22 lbs) to <15 kg (33 lbs): 10 mg every other week 15 kg (33 lbs) to <30 kg (66 lbs): 20 mg every other week *Amjevita* 15 kg to <30 kg: 20 mg every other week • **Adult Crohn's Disease (CD)** Initial: 160 mg on day 1, 80 mg on day 15 Maintenance: 40 mg every other week beginning on day 29 • **Rheumatoid Arthritis (RA)** 40 mg every other week (up to weekly) Psoriatic Arthritis (PsA) 40 mg every other week • **Plaque Psoriasis** Initial: 80 mg once Maintenance: 40 mg every other week beginning week after initial dose • **Ankylosing Spondylitis (AS)** 40 mg every other week	Allow to reach room temp for about 15-30 minutes prior to administration Inject SQ into abdomen or thigh, rotating injection sites with each dose	**Boxed Warning:** • Increased risk for development of severe infections • Lymphoma and other malignancies, some fatal, have been reported in children and adolescent patients **Warnings:** • Do not administer during an active infection • Risk for invasive fungal infections • Risk for malignancies • Hepatitis B (HBV) reactivation - STOP infliximab • Cytopenias, pancytopenia: consider stopping • Demyelinating disease, new onset or worsening • Lupus-like syndrome - STOP infliximab • Heart failure: new onset or worsening Prior to initiation of therapy, patients should be tested for latent tuberculosis and hepatitis B virus infection Prior to initiation of therapy, ensure all necessary LIVE vaccinations are up to date; DO NOT administer LIVE vaccines while on therapy STORE under refrigeration DISCARD after 14 days at room temp **Monitoring:** Most common ADRs reported were mild in nature and include: injection site reaction, headache, rash, and upper respiratory tract infections
N/A	**Amjevita** (adalimumab-atto) 40 mg/0.8 mL PEN 40 mg/0.8 mL PFS 20 mg/0.4 mL PFS Anticipated availability currently unknown *Amgen*			
N/A	**Cyltezo** (adalimumab-adbm) 40 mg/0.8 mL PFS Anticipated availability currently unknown *Boehringer Ingelheim*			
N/A	**Hadlima** (adalimumab-bwwd) 40 mg/0.8 mL PFS 40 mg/0.8 mL PEN Anticipated availability currently unknown *Samsung Bioepis*			
N/A	**Hyrimoz** (adalimumab-adaz) 40 mg/0.8 mL PFS 40 mg/0.8 mL PEN Anticipated availability currently unknown *Sandoz*			

HCPCS	Product	Indication(s)	Administration	Clinical Considerations
	Reference Product: Enbrel (etanercept), *Amgen*			
N/A	**Eticovo** (etanercept-ykro) 25 mg/0.5 mL PFS 50 mg/mL PFS Anticipated availability currently unknown *Samsung Bioepis*	• **Rheumatoid Arthritis (RA)** 50 mg once weekly with or without methotrexate • **Psoriatic Arthritis (PsA)** 50 mg once weekly with or without methotrexate • **Ankylosing Spondylitis (AS)** 50 mg once weekly • **Plaque Psoriasis (PsO)** 50 mg twice weekly for 3 months, then 50 mg once weekly thereafter • **Juvenile Idiopathic Arthritis (JIA)** ≥ 63kg: 50 mg once weekly ≥ 2 years old	Allow to reach room temp for about 15-30 minutes prior to administration Inject SQ into thigh, abdomen, or outer areas of upper arm, rotating injection sites with each dose	**Boxed Warning:** • Increased risk for development of severe infections • Lymphoma and other malignancies, some fatal, have been reported in children and adolescent patients **Warnings:** • Do not administer during an active infection • Risk for invasive fungal infections • Risk for malignancies • Hepatitis B (HBV) reactivation - STOP infliximab • Heart failure, new onset or worsening • Cytopenias - STOP infliximab • Demyelinating disease, new onset or worsening • Lupus-like syndrome - STOP infliximab • Do not administer LIVE vaccines while on therapy Prior to initiation of therapy, patients should be tested for latent tuberculosis and hepatitis B virus infection Prior to initiation of therapy, ensure all necessary LIVE vaccinations are up to date; DO NOT administer LIVE vaccines while on therapy STORE under refrigeration DISCARD after 28 days at room temp **Monitoring:** Monitor improvement of symptoms and physical function assessments. Latent TB screening prior to initiating and during therapy; signs/symptoms of infection (prior to, during, and following therapy); CBC with differential; signs/symptoms/worsening of heart failure; HBV screening prior to initiating (all patients), HBV carriers (during and for several months following therapy); signs and symptoms of hypersensitivity reaction; symptoms of lupus-like syndrome; signs/symptoms of malignancy (eg, splenomegaly, hepatomegaly, abdominal pain, persistent fever, night sweats, weight loss). Most common ADRs reported were mild and included: injection site reactions
N/A	**Erelzi** (etanercept-szzs) 25 mg/0.5 mL PFS 50 mg/mL PFS 50 mg/mL PEN Anticipated availability currently unknown *Sandoz*			
	Reference Product: Neulasta (pegfilgrastim), *Amgen*			
N/A	**Ziextenzo** (pegfilgrastim-bmez) 6 mg/0.6 mL PFS *Anticipated availability currently unknown* *Sandoz*	• **Prevention of chemotherapy-induced neutropenia** 6 mg SQ once per chemotherapy cycle, beginning at least 24 h after administration of cytotoxic chemo • **Prevention of chemo-induced neutropenia (Pediatric)** SQ once per chemo cycle, beginning at least 24 h after completion of chemo (dose/volume based on weight) < 10 kg: 0.1 mg/kg, 0.01 mL/kg 10-20 kg: 1.5 mg, 0.15 mL 21-30 kg: 2.5 mg, 0.25 mL 31-44 kg: 4 mg, 0.4 mL ≥ 45 kg: 6 mg, 0.6 mL	Do not administer earlier than 24 hours after or in the 24 hours prior to cytotoxic chemotherapy Subcutaneous administration into upper arm, abdomen, thighs, or upper outer areas of buttocks, rotating injection sites with each dose DO NOT rechallenge in the event of a serious hypersensitivity reaction	**Warnings:** • Fatal splenic rupture: evaluate patients who report left upper abdominal or shoulder pain for enlarged spleen or splenic rupture • Acute respiratory distress syndrome (ARDS): evaluate patients who develop fever and lung infiltrates or respiratory distress ◦ Discontinue use in patients with ARDS • Fatal sickle cell crisis • Glomerulonephritis: evaluate and consider dose-reduction or interruption if causality is likely STORE under refrigeration DISCARD if left at room temp for > 48 hours **Monitoring:** Chemotherapy-induced neutropenia: Complete blood count (with differential) and platelet count should be obtained prior to chemotherapy and as clinically necessary. Hematopoietic radiation injury syndrome: CBC at baseline (do not delay administration if CBC not readily available); estimate absorbed radiation dose. Evaluate fever, pulmonary infiltrates, and respiratory distress; evaluate for left upper abdominal pain, shoulder tip pain, or splenomegaly. Monitor for signs/symptoms of allergic reactions, aortitis, glomerulonephritis (azotemia, hematuria, proteinuria), and capillary leak syndrome (hypotension, hypoalbuminemia, edema, and hemoconcentration). Monitor for sickle cell crisis (in patients with sickle cell anemia). Most common ADR reported included bone pain
N/A	**Udenyca** (pegfilgrastim-cbqv) 6 mg/0.6 mL PFS *Coherus Biosciences*			
Q5108	**Fulphila** (pegfilgrastim-jmdb) 6 mg/0.6 mL PFS *Mylan/Biocon*			

■