AMERICAN COLLEGE OF RHEUMATOLOGY

POSITION STATEMENT

SUBJECT:	Patient Safety and Site of Service for Biologics
PRESENTED BY:	Committee on Rheumatologic Care
FOR DISTRIBUTION TO:	Members of the American College of Rheumatology Medical Societies Members of Congress Health Care Organizations/Third Party Carriers Insurance Companies and Commissioners Pharmacy Benefit Managers Managed Care Entities Other interested parties

POSITIONS

1. The American College of Rheumatology (ACR) supports the safe use of biologic medications for treatment of rheumatic diseases.

2. Adverse drug reactions to biologics may occur and are potentially more severe with intravenous (IV) versus subcutaneous (SC) administration of biologics.

3. Intravenous biologic agents should be administered in a monitored health care setting with onsite supervision by a provider with appropriate training in biologic infusions, ideally one who is actively involved with the patient's care with access to their medical record.

4. The ACR opposes policies that force patients to receive biologic infusions at home because such policies, designed for the sole purpose of cutting costs, undermine patient safety. Recognizing the convenience of home infusion for some patients, the ACR supports shared decision-making by the patient and their provider on the best course of treatment and safest option on a case-by-case basis.

5. Nurse practitioners and physician assistants who supervise infusion centers, or free-standing infusion sites, should have specialized training in the use and administration of biologic therapies and work in the context of a collaborative or supervised relationship with a physician as regulated by state law. The recent development of free-standing infusion centers without clinicians properly versed in the arena of biologic medications, poses an increased risk to patients.

BACKGROUND

The ACR strongly supports the use of biologic agents as necessary treatments for rheumatic diseases. Biologics are highly effective for many diseases; however, their molecular structure, size, manufacturing, and storage, as well as their potential to cause serious adverse events, complicates delivery to patients. As a result, all biologics are considered complex medications by the ACR[1]. Due to their molecular structures, biologic drugs are administered via SC or IV routes. In addition, the tremendous heterogeneity of patients and the diversity of autoimmune conditions treated with biologics multiplies the variety of responses and side effects associated with these medicines, necessitating oversight by highly trained, specialized physicians to ensure their safe and effective administration. The ACR promotes the highest quality guidelines and best practices for treatment with biologics[2].

DISCUSSION

All classes of biologics used in autoimmune diseases have the potential to cause serious adverse events[3]. Adverse events associated with biologics include, but are not limited to, injection site reactions, infusion reactions, exacerbation of heart failure, cytopenias, infections (including lethal tuberculosis and fungal infections), increased risk of skin cancer, psoriasis, demyelinating diseases (such as multiple sclerosis), the development of drug induced systemic lupus erythematosus, anaphylaxis and even death. Serious infections affect 2-5% of patients per year of exposure. Proper screening for occult infections and other comorbidities is required before biologics are prescribed and each time administration occurs. In addition, ongoing expert monitoring for any new or developing conditions is necessary to minimize the potential for harm.

Adverse drug reactions associated with biologics occur in up to 30% of patients in clinical trials[4]. Although injection site reactions caused by SC biologics are generally easily managed, infusion reactions associated with IV biologics are often more serious. These reactions range in severity from a mild rash and myalgia to hypertension, shortness of breath, headaches, and even life-threatening anaphylaxis, and can occur during or after the infusion.

Infusion reactions must be promptly evaluated and treated. For a mild reaction, the infusion rate can often be slowed potentially allowing the patient to complete the infusion. Moderate reactions require cessation of the infusion and either oral or IV medications to prevent clinical decline. Severe reactions can involve multiple organ systems and lead to respiratory and cardiovascular collapse[6]. These medical emergencies require immediate therapy with medications such as epinephrine and IV glucocorticoids. Such interventions are often beyond the scope of home health providers and delays waiting for emergency services further jeopardize patients' lives. Experienced providers, available on site, are most capable of decidine whether it is safe to continue therapy in the setting of mild reactions and providing prompt treatment for moderate or severe reactions.

As detailed in peer-reviewed research articles, ACR position papers, and FDA labeling, direct supervision of IV biologic administration by a trained provider remains the standard of care. The administration of biologics requires detailed patient evaluation by specially trained providers, familiar with these drugs and the diseases being treated, to determine if the patient is fit each time a biologic is administered. Effective clinical monitoring and mitigation of risk is best accomplished when these drugs are infused in medical facilities supervised by on-site trained physicians.

In addition, home infusions do not allow for rigorous maintenance of conditions such as recommended temperature, storage away from sunlight, and proper reconstitution or dosing. Lack of control around these important variables puts patients at risk and undermines patient confidence. Rheumatologists, by virtue of their training and extensive experience with these drugs, are highly qualified to provide this high level of control, care, and expertise.

Those responsible for access to treatment must ensure the highest standards of safety for patients. Financial considerations related to potential cost savings of home infusions should not override patient safety and standards of care. The position of the ACR is that proper administration of biologics should take place under the close supervision of a physician in a provider's office, infusion center or hospital rather than in a patient's home, unless the patient and provider decide that home infusion is in the patient's best interest.

In addition to safety considerations, forcing patients to receive infusions at home or in facilities not supervised by a trained provider may reduce access to these critical therapies. Moving the site of administration to the patient's home creates obstacles to communication regarding dose adjustments, interruptions, or therapy change. In the clinic setting, direct access to the patient's chart by the treating clinician facilitates timeliness of necessary adjustments and interventions. The most commonly cited reason among patients for choosing IV as opposed to SC therapy is the availability of enhanced safety monitoring7; the absence of the treating physician may impact patients' trust and adherence to therapy. Use of home infusion may thus lead to delays in therapy and inadequate control of disease. Undertreated autoimmune disease can result in serious adverse consequences, including organ damage or death.

The ACR opposes policies that require home infusion of biologics. In the absence of an agreement between the provider and the patient that home infusion is the best option due to extenuating circumstances (i.e., lack of transportation or medical comorbidities) and that the risks of home infusion are outweighed by the benefits, required home infusion is an unnecessary risk to patients and violates current clinical standards of practice.

RESOURCES

1. The Complexity of Biologics and their Coverage and Payment. ACR position statement available at: http://www.rheumatology.org/Portals/0/Files/Complexity%20of%20Biologics.pdf
2. Singh JA, Furst DE, Bharat A, Curtis J, Kavanaugh A, Kremer J, et al. 2012 Update of the 2008 Recommendations for the use of Disease-Modifying Anti-Rheumatic Drugs and Biologics in the treatment of Rheumatoid Arthritis. Arthritis Care Res 2012;64:625-39.
3. Rubbert-Roth A. Assessing the safety of biologic agents in patients with rheumatoid arthritis. Rheumatology 2012;51:v38-47.
4. Pappas DA, Geraldino-Pardilla L, Bathon JM. Immune modulation of rheumatoid arthritis. 2011;25:873-889.
5. Cheifetz A, Smedley M, Martin S, Reiter M, Leone G, Mayer L, Plevy S. The incidence and management of infusion reactions to infliximab: a large center experience. Am J Gastroenterol 2003;98: 1315-24.
6. Lichtenstein L, Ron Y, Kivity S, Ben-Horin S, Israeli E, Fraser GM, et al. Infliximab-related infusion reactions: systematic review. J Crohn's Colitis 2015: 805-815.
7. Huynh TK, Ostergaard A, Egsmose C, Madsen OR. Preferences of patients and health professionals for route and frequency of administration of biologic agents in the treatment of rheumatoid arthritis. Patient Prefer Adherence 2014;8:93-99.
8. http://www.rheumatology.org/Practice-Quality/Administrative-Support/PositionStatements

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