

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 are not uncommon 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.
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.
5. Nurse practitioners and physician assistants who supervise infusion centers 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.

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 by the ACR¹. Due to their inherent complexity, biologic drugs can only be 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, thus requiring that highly trained, specialized physicians oversee their safe and effective administration. The ACR promotes the highest quality guidelines and best practices for treatment with biologics².

DISCUSSION

All classes of biologics used in autoimmune diseases may cause serious adverse events³. 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 trials⁴. Although injection site reactions caused by SC biologics have the potential to be easily managed, infusion reactions associated with IV biologics are often more serious. For example, the administration of infliximab is associated with acute infusion reactions in 10% of patients⁵. These reactions range in severity from a mild rash and myalgia to hypertension, shortness of breath, headaches and even life-threatening anaphylaxis. Infusion reactions 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 collapse⁶. These medical emergencies require immediate therapy with medications such as epinephrine and IV glucocorticoids. Such interventions are beyond the scope of untrained and inexperienced home health providers and delays waiting for emergency services further jeopardize patients' lives. Experienced providers, available on site, are most

capable of deciding 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 biologics by a trained provider remains the standard of care for the administration of these medications. The administration of biologics requires a safety checklist and 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. Patients are also reassured by the presence of a physician during acute and potentially severe reactions. Given the black box warnings for serious infusion reactions and infections, the safest location for the administration of these drugs remains a setting supervised by a provider with advanced training in the use of biologic agents. Effective clinical monitoring and mitigation of risk is best accomplished when these drugs are infused in medical facilities supervised by on-site trained physicians.

The risk of serious drug reactions requires that infusible biologic agents be administered in a medically controlled environment. Home infusions do not allow for control of important variables such as whether a drug is maintained at the recommended temperature, away from sunlight, properly reconstituted or dosed appropriately. Lack of control around these important variables puts patients at risk and undermines patient confidence. Rheumatologists, by virtue of their fellowship 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. The ACR opposes policies that require home infusion. Routine 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 (lack of transportation, medical comorbidities, etc.) and that the risks of home infusion are outweighed by the benefits, is an unnecessary risk to patients and violates current clinical standards of practice.

In addition to safety considerations, forcing patients to perform infusions at home in facilities not supervised by a trained provider threatens to reduce access to these critical therapies. Specially trained providers are unlikely to prescribe treatments that are not properly administered in the safest clinical setting. Patient fear of biologic therapy may lead to noncompliance and inadequate control of disease. In fact, the most commonly cited reason among patients for choosing IV as opposed to SC therapy is the availability of enhanced safety monitoring⁷. Undertreated autoimmune disease can result in organ damage or death.

As mentioned above, the ACR has issued separate statements on the complexity of biologics. Related position statements addressing patient access to biologics, biosimilars, step edit therapies, and therapeutic substitution are also available on the ACR website⁸.

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 AntiRheumatic 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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