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 sites of service for administration of infusible rheumatologic therapies that provide the safest outcomes while respecting costs of care.

2. Intravenous biologic agents should be administered in a monitored health care setting with onsite supervision by a rheumatologist or rheumatology care team licensed professional who are appropriately trained in biologic infusions. The individual should ideally be actively involved in the patient's care and have access to the patient's medical record.

3. 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.

4. Advanced Practice Providers (APPs) who supervise infusion centers, or free-standing infusion sites, should receive specialized training in the use and administration of biologic therapies and work in the context of a supervised relationship with a physician as regulated by applicable laws. The recent development of free-standing infusion centers staffed by clinicians without proper training regarding biologic medications poses an unnecessary risk to patients.

BACKGROUND:

The ACR strongly supports the use of biologic agents as necessary treatments for rheumatic diseases. Biologic medications 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. All biologics are considered complex medications by the ACR (1). Due to their molecular structures, biologic drugs are administered via subcutaneous (SC) or intravenous (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 and necessitates 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, drops in blood counts (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 death. Serious infections affect 2-4% of patients per year of exposure. Proper screening for occult infections and other comorbidities is required before biologics are prescribed and routinely during the course of treatment. In addition, ongoing expert monitoring for any new or developing conditions is necessary to minimize the potential for harm.

Infusion Site and Patient Safety:

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 (5). These medical emergencies require immediate therapy with medications such as epinephrine and IV glucocorticoids. Such interventions are beyond the scope of home health providers and delayed response when waiting for emergency services further jeopardizes the patient's life. Experienced care team members, 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 biologic administration by a trained rheumatologist or care team member

remains the standard of care. The administration of biologics requires detailed patient evaluation by specially trained healthcare professionals, 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 or care team interprofessionals.

Safety concerns with home infusions include drug reactions, increased risk of hospital visits, and concerns with drug storage and handling. In a cohort study of 57,220 patients with immune-mediated disease who received biologic infusions, home infusions were associated with 25% increased odds of emergency department or hospital admission after infusion on the same or following day when compared with facility infusions (6). Compared to facility or clinic-based infusions, home infusions do not allow for rigorous maintenance of recommended drug temperature, storage away from sunlight, and proper reconstitution or dosing. Lack of control around these important variables puts patients at risk and undermines confidence.

Infusion Site and Patient Compliance:

Compelling patients to receive infusions at home or in facilities not supervised by a rheumatologist or rheumatology-trained care team interprofessional 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 cited reason among patients for choosing IV as opposed to SC therapy is the availability of enhanced safety monitoring (7); 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, unplanned hospital visits, or death.

Compliance to maintain disease control is affected by the patient infusion experience. Those who experience an adverse reaction are less likely to continue prescribed treatment. Of patients who had a reaction leading to hospitalization within 48 hours of infusion, there was 28% increased odds of discontinuing biologic therapy after emergency department or hospital admission (8). Rheumatologists, by virtue of their training and extensive experience, are highly qualified to provide a high level of control, care and expertise to ensure patient safety when administering infusions in their clinic setting.

Infusion Site and Reduction in Overall Healthcare Cost:

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 or care

team interprofessional in an office setting, 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.

Importance of Advanced Training to Oversee Biologic Infusion:

Advanced Practice Providers should receive specialized training in the use and administration of biologic therapies and work in the context of a collaborative or supervised relationship with a physician. The ACR recommends that APPs who oversee infusion of biologics have advanced training in rheumatology. Understanding that basic training does not fully cover the rheumatology subspecialty, in 2024 the ACR and Association of Rheumatology Professionals (ARP) established a curriculum to provide training for the specific rheumatologic needs and complications that are unique to the rheumatology patient population (9). Additional training on mitigating infusion reactions is also encouraged, such as the ACR's infusion reaction mini curriculum (10). By receiving specialized training, all members of the rheumatology care team are equipped to infuse biologic therapies adhering to the highest standard of patient safety.

In summary, the ACR promotes the highest quality guidelines and best practices for treatment with biologics. This requires infusion sites that are overseen by physicians and care team interprofessionals with specific training unique to the rheumatology patient population and infusion nurses who are familiar with the infusion reactions that can cause life threatening complications. Infusions overseen by a rheumatologist or rheumatology interprofessional administered in a clinical setting are cost effective and improves patient safety and medical compliance.

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