AMERICAN COLLEGE OF RHEUMATOLOGY
POSITION STATEMENT

SUBJECT: Patient Access to Disease Modifying Therapies

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. Conventional synthetic DMARDs, biologic DMARDs and targeted synthetic DMARDS are vitally important therapeutic options for patients with rheumatic diseases. Given their effectiveness and potential to reduce long-term disability, patients should have affordable access to all forms of DMARD therapy without undue delay.

2. The documentation for medical necessity should include the diagnosis and rationale for choice of treatment. The ACR opposes documentation requirements that place undue administrative burden on the treating provider.

3. Reimbursement for biologic DMARD therapy given in the clinical setting for rheumatic diseases should be fair and equal and take into account FDA labeling and peer-reviewed literature.

4. The ACR opposes step edits, fail-first policies, tiering, forced switching, or excessive out of pocket costs for biologics for insured patients.

5. ACR opposes policies that provide payments to patients as financial incentive to switch treatments to a payer-preferred alternative.

6. Polices regarding the location of the administration of biologic DMARDs should promote the highest standards of safety and allow patients to obtain their treatments in physician offices or medical facilities with rheumatologist or rheumatology professional-supervised infusions.

7. The choice of conventional synthetic DMARD, biologic DMARD or targeted synthetic DMARD therapy is a complex decision that is made between the patient and the rheumatologist and rheumatology professional. Policies should be based on the best interests of the patient and allow for continuation of therapy for patients whose disease is well controlled.

BACKGROUND

Disease modifying anti-rheumatic drugs (DMARDs) are therapies which are the mainstay in the treatment of many rheumatic conditions. They can be further subdivided into conventional synthetic DMARDs (csDMARDs), biologic DMARDs (bDMARDs) and targeted synthetic DMARDs (tsDMARDs). While all DMARDs slow disease progression in inflammatory arthritis, their subdivisions correspond to differences in mechanisms of action and manufacturing. Conventional DMARDs restrict the immune system more broadly and examples include methotrexate and hydroxychloroquine. Biologic DMARD, or biologics, are large complex molecules made using organic sources modified to target specific cytokine signaling proteins, cytokine receptors, and other cellular molecules. Examples of drugs in this class include TNF inhibitors and IL-6 inhibitors. In contrast, targeted synthetic DMARDs are small, chemically synthesized, orally active drugs that suppress multiple cytokine and growth factor receptor signaling pathways. Janus Kinase (JAK) inhibitors are classified as tsDMARDs.

Most often, csDMARDs are the first line therapy of choice. When disease activity is not adequately controlled or a csDMARD is otherwise not appropriate,the use of bDMARDs or tsDMARDs can be life altering and prevent significant morbidity and even mortality. While access to all DMARDs is of utmost importance, bDMARDs and tsDMARDs are relatively newly developed and often very expensive, making their access more limited due to payer and formulary restrictions.

The ACR provides guidelines on the use of all DMARDs in the treatment of many rheumatic conditions and publishes medication guides and guidelines that include information on all types of DMARDs. The use of these medications requires an understanding of their mechanisms of action, unique toxicities, proper screening, proper monitoring measures, and contraindications. The principles for patient access to all DMARDs are based on clinical standards of practice.

DOCUMENTATION AND DISEASE ACTIVITY MEASURES

The overreaching goal of all treatment is to treat to a target of low disease activity or full clinical remission. Thus, it is common practice to include statements about achieving remission in the medical record. In fact, documenting the status of these goals has become a mainstay in physician reporting for quality of care. Early, aggressive, treat-to-target therapy is the recommended approach for rheumatoid arthritis, and emerging data suggest the benefits of this approach for other rheumatic conditions as well. Biologic DMARDs and tsDMARDs are often necessary when csDMARDs are either ineffective or not tolerated by the patient. In addition, bDMARDs and tsDMARDs tend to work rapidly and may achieve control of the disease more quickly which is important when facing a brief window of opportunity for maximum therapeutic efficacy. Delayed treatment leads to reduced mobility and daily function, reduced performance at work, progression of disability, and other complications of rheumatic disease. Therefore, patients require timely access to these medications to achieve the best outcome. Processes for approval of all DMARDs, such as prior authorizations, should not delay medically necessary treatment with biologics.

Conventional synthetic DMARD therapy is often the initial treatment for those with rheumatic disease and bDMARDs and tsDMARDs are used for those with resistant, moderate and severe rheumatic disease states and are approved based on specific disease states and clinical criteria.

When a rheumatology professional evaluates a patient, he or she uses an integrated history, physical exam, laboratory values, and imaging studies to determine the degree of disease activity. There are also commonly used disease activity measures that may be calculated and documented separately (ex. Health Assessment Questionnaire (HAQ), Routine Assessment of Patient Index Data (RAPID), Clinical Disease Activity Index (CDAI)). Disease measures such as these are one of many tools employed in rheumatology practice. They should not be used to deny approval for a chosen biologic treatment. The ACR distinguishes among disease activity measures for routine clinical use in most clinic settings.

In addition, there are formal measures of disease activity utilized during clinical trials that are not used in routine clinical practice. For example, the Psoriasis Area Severity Index (PASI), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), and Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) scores define parameters for research purposes but do not incorporate complex factors that influence therapeutic decisions. These tools are neither sensitive nor specific for factors that influence choices between biologics. They are not intended to determine medical necessity for a drug. They do not always capture an individual's response to treatment. A patient may reach important clinical goals but these may be accompanied by only small numerical changes in these measures. These tools are not used as the sole determinant for treatment decisions in the clinical practice of rheumatology.

The ACR recommends clinicians follow the AMA and CPT guidelines for documentation. The treating rheumatologist and rheumatology professional must clearly indicate in the medical record the diagnosis of the rheumatic condition. Where necessary, previous treatment failures for lack of efficacy or poor tolerability, or contraindications to other medications (such as DMARDs) need to be adequately documented in the medical record.

MEDICAL DECISION-MAKING FOR TREATMENT

The decision to choose one treatment option over another requires careful clinical evaluation and consideration by a physician, rheumatology professional, and patient. Patient factors that strongly influence this choice include but are not limited to an individual patient’s age, gender, diagnosis and comorbid conditions, concomitant medications, specific organ manifestations, antibody status, disease severity and burden, physical or psychological abilities, access to transportation, and ability to tolerate a particular route of administration.

For example, susceptibility to infection, heart or lung conditions, malignancy, and other disease manifestations may drive the choice between agents. Thus, both individual patient characteristics and differences in disease states for rheumatic populations will determine the choice of medication. DMARDs are complex, rheumatic diseases are complex, and the choice of treatment may be complex. Medical decision-making and subsequent risks associated with these medications fall on the physician and the patient. Therefore, insurance plans must leave the clinical decision-making for medical necessity to the rheumatologist and rheumatology professional. Payers should not determine the treatment of the patient, nor should they mandate the use of one therapy over another based-on cost alone.

Presently, there is a paucity of peer-reviewed literature addressing the comparative efficacy and safety of bDMARDS and tsDMARDs. Given the safety concerns with these drugs and lack of

evidence for clinical superiority or safety of one versus another, access and coverage for bDMARDs and tsDMARDs should remain fair and equal. Forcing a stable patient to switch to another medication for the sake of cost control needlessly disrupts continuity of care and puts patients at significant risk for loss of disease control (see Reggia et al.) and potentially life-threatening complications.

In contrast, there is a large body of research demonstrating that each of these drugs is unique in terms of their molecular structure, immunogenicity, mechanism of action, safety, and efficacy. For example, between classes of bDMARDS, there are enormous differences in therapeutic pathways and FDA indications. Even within the most used class of biologics, TNF inhibitors, differences in responses and adverse events are commonly observed. Again, individual patient considerations, overlapping medical and immune conditions, safety and other considerations will drive the clinician and patient's decision for appropriate therapy. While some biologics may have similar mechanisms of action, this does not confer equivalent adherence, tolerability, or safety profiles. Moreover, individual bDMARDs and tsDMARDs can differ in time to remission, need for concurrent csDMARD therapy, frequency of administration, type of administration, frequency of infusion and injection site reactions, and many other characteristics.

Additionally, the influence of anti-drug antibodies and immunogenicity can influence the choice of a bDMARD. Due to their very large molecular size, some patients on bDMARDs develop drug-specific antibodies that influence the efficacy of subsequent therapies. Inadvertent drug holidays, class switching, and retreatment after cessation of a drug increase the risk of disease relapse, drug resistance, and serious reactions. Therefore, forced switches in bDMARD therapy due to formulary changes may harm patients and lead to disease relapse.

Formulary policy must be supported by high-quality research and remain in accordance with best clinical practices. It must also make exceptions for patient characteristics and current status (including remission status). Policies related to treatment choices must include a "grandfather" provision that allows stable patients to continue their current treatment at affordable prices.

AFFORDABLE ACCESS TO DMARDs

The ACR recognizes that biologic DMARDs and targeted synthetic DMARDs are costly medications, and that rheumatologists and rheumatology professionals must consider this choice carefully. Given the high value of this class of drug in achieving disease remission and improvements in overall patient wellness, employer health plans, other payers, and pharmacy benefit managers must allow affordable coverage options. Importantly, the cost of the drug is not the only financial consideration. A growing body of evidence indicates that by slowing disease progression these medications may reduce costly disease-related complications including adverse outcomes related to cardiovascular disease, metabolic syndrome, and expensive procedures and surgeries. Early use of aggressive therapy in rheumatic conditions also reduces costs by preventing missed work, improving work performance, and avoiding long-term disability. Although the ACR recognizes that drug costs are a factor in health care delivery, it believes that restricting access not only adversely affects patients' health but impacts important public health outcomes as well.

Presently the cost of drugs is determined by pharmaceutical companies and may be negotiated (for example, between a manufacturer and a pharmacy benefit manager). Unfortunately, there is a lack of transparency in pricing in the eyes of the patients, rheumatologists and rheumatology professionals, and the public. Pricing differences between companies or plans are not based on clinical decision-making or standards of practice and are subject to change with tremendous frequency. While rebates and price fixing in particular contracts may reduce the cost of a drug for the plan, privately negotiated cost savings to the insurance company should not be allowed to undermine the important clinical considerations and decisions made by patients and rheumatologists and rheumatology professionals when choosing a treatment option. Essentially, plan savings should not override medical necessity or intrude on safe medical practice.

The ACR is concerned that patients are susceptible to adverse events that result from changes in these negotiations from year to year, inconsistencies between plans, and the dangers of third-party negotiations driven by profit rather than by safe and sound medical practice. The ACR finds that step therapies, fail first, and tiering policies may disregard the appropriate clinical decisions made between rheumatologists and rheumatology professionals and patients and may contradict the current standard of care and practice guidelines. Affordable access to these drugs, in the absence of excessive copayments, coinsurance, and other subversive financial restrictions, for patients who suffer from chronic, disabling conditions is a necessity. Additionally, the practice of financial payment from an insurer to a patient to entice a switch in therapy is inappropriate and unnecessarily risks a flare of well-controlled disease. Clinical guidelines should drive these discussions and not the other way around.

The ACR supports efforts to reduce costs and improve access to all DMARDs. If a newly chosen bDMARD has an available biosimilar option, then the ACR supports the initiation of a biosimilar. However, if no biosimilar is available for the appropriate medication, then the ACR opposes any requirement to choose a medication from a different class. Furthermore, patients who receive biologic therapy and achieve an acceptable clinical response should be allowed to remain on that therapy. Continuation of therapy for stable patients is particularly important for aging patients transitioning from private health insurance to Medicare plans. This vulnerable population of patients is frequently forced to change biologic DMARD or targeted synthetic DMARD therapies despite years of stable, well-controlled disease on a particular medication, purely due to differences in prescription coverage in Medicare plans versus private insurance, in addition to loss of access for Medicare beneficiaries to copay support from manufacturers. While the ACR recognizes the importance of addressing the increasing costs of these medications, efforts to curb costs must not result in increased financial burdens for sick patients or increase the risk of disease flare in an otherwise stable patient due to cost-driven switch of therapy.

ADMINISTERING BIOLOGICS IN MEDICAL SETTINGS

Biologic DMARDs carry a high risk of dangerous adverse and allergic reactions, both at the point of care and remotely. As detailed in peer-reviewed research articles, ACR position papers on biologic administration, and FDA labeling, direct supervision of the infusion of biologics remains the standard of care for the administration of these medications. The administration of infusible biologic DMARDs requires a safety checklist and detailed patient history and evaluation prior to their infusion by specially trained rheumatologists and rheumatology

professionals. 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 rheumatologist and rheumatology professional. The clinical monitoring is best accomplished and risks are best mitigated when these drugs are infused in medical facilities rather than at a patient's residence. Given the level of care and required expertise, the position of the ACR is that proper administration of biologic DMARDs should take place under the close supervision of a trained rheumatologist and rheumatology professional. Biologics should be given in a physician's office or medical facility whenever possible to ensure the highest standards of safety for patients. Financial matters related to potential cost savings of home infusions should not override the safety of the patients and standards of practice.

Biologics are currently administered and coded according to the CPT manual, and in accordance with this definition, these agents require direct rheumatologist and rheumatology professional supervision. Thus, not only does the ACR recognize the safest standards of practice, the AMA and CPT have defined the coding regulations requiring oversight by a trained provider. Again, managed plans and specialty pharmacies should comply with coding regulations set forth by these associations.

There may be rare circumstances in which home infusions could be medically necessary for a particular patient to have access to biologic treatment. In these highly unusual situations, the increased risk of a home infusion may be outweighed by the risks associated with a lack of access to biologic therapy at all. The ACR encourages rheumatologists and rheumatology professionals in such situations to make the best medical decision based on the individual needs of the patient. The ACR believes that home infusion for the sake of cost-cutting undermines patient safety. Home infusion of biologic DMARDs is considered an unnecessary and dangerous risk to patients and violates our current clinical standards of practice.

EXECUTIVE SUMMARY

Given the high value of csDMARDs, bDMARDs, and tsDMARDs, their tremendous positive impact on health outcomes, and the safety concerns and complexity surrounding these agents, access to and coverage of all DMARDs should remain fair and equal according to the labeling and standard of care as described in peer-reviewed literature. Access to these life-altering therapies should be affordable to patients. Step therapies, fail-first policies, tiering, and class-switching requirements create unnecessary obstacles for patients and their physicians, delays in appropriate therapy, potentially dangerous outcomes for patients, and can undermine careful and collaborative decisions made by patients and their rheumatologists and rheumatology professionals. In the interest of patient safety, the administration of biologic DMARDs not labeled for self-administration should take place in medical facilities rather than at home. All policies should grandfather patients on stable therapy in such a way that they can affordably continue effective biologic treatment.

RESOURCES

1. Singh 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 and Research 2012; 64 (5): 625-639. doi:10.1002/acr.21641

2. Saag et al. American College of Rheumatology 2008 recommendations for the use of nonbiologic and biologic disease modifying antirheumatic drugs in rheumatoid arthritis. Arthritis Rheum 2008; 59 (6):762-84. doi:10.1002/art.23721
3. Van der Heijde et al. Probability to Achieve Low Disease Activity at 52 Weeks in Rheumatoid Arthritis Patients Treated With Certolizumab Pegol Depend DOI: https://doi.org/10.3899/jrheum.111171
4. Sepriano et al. Safety of synthetic and biological DMARDs: a systematic literature review informing the 2019 update of the EULAR recommendations for the management of rheumatoid arthritis. Ann Rheum Dis. 2020;79(6):760-770. doi:10.1136/annrheumdis-2019-216653
5. Katchamart W, Trudeau J, Phumethum V, Bombardier C. Efficacy and toxicity of methotrexate (MTX) monotherapy versus MTX combination therapy with non-biological disease-modifying antirheumatic drugs in rheumatoid arthritis: a systematic review and meta-analysis. Ann Rheum Dis. 2009;68(7):1105-1112. doi:10.1136/ard.2008.099861
6. Smolen JS, Van Der Heijde DM, St Clair EW, et al. Predictors of joint damage in patients with early rheumatoid arthritis treated with high-dose methotrexate with or without concomitant infliximab: results from the ASPIRE trial. *Arthritis Rheum*. 2006;54(3):702-710. doi:10.1002/art.21678
7. Singh JA, Hossain A, Mudano AS, et al. Biologics or tofacitinib for people with rheumatoid arthritis naive to methotrexate: a systematic review and network meta-analysis. Cochrane Database Syst Rev. 2017;5(5):CD012657. Published 2017 May 8. doi:10.1002/14651858.CD012657
8. Schiff M et al. Efficacy and Safety of abatacept or infliximab vs placebo in ATTEST: a phase III, multi- centre, randomized, double blind, placebo-controlled study in patients with rheumatoid arthritis and an inadequate response to methotrexate. Ann Rheum Dis 2008 Aug:67(8): 1096-1103. doi:10.1136/ard.2007.080002
9. Hetland et al. Direct comparison of treatment responses, remission rates, and drug adherence in patients with rheumatoid arthritis treated with adalimumab, etanercept, or infliximab: results from eight years of surveillance of clinical practice in the nationwide Danish DANBIO registry. Arthritis Rheum. 2010;62:22-32. doi:10.1002/art.27227
10. Kristensen LE, Saxne T, Geborek P. The LUNDEX, a new index of drug efficacy in clinical practice: results of a five-year observational study of treatment with infliximab and etanercept among rheumatoid arthritis patients in southern Sweden. Arthritis Rheum. 2006;54(2):600-606. doi:10.1002/art.21570
11. Reggia R, Franceschini F, Tincani A, Cavazzana I Switching from intravenous to subcutaneous formulation of abatacept: a single-center Italian experience on efficacy and safety. J Rheumatol. 2015 Feb;42(2):193-5. doi:10.3899/jrheum.141042
12. American College of Rheumatology Position Statement: Biosimilars. https://www.rheumatology.org/Portals/0/Files/Biosimilars-Position-Statement.pdf
13. Anderson J, Caplan L, Yazdany J, et al. Rheumatoid arthritis disease activity measures: American College of Rheumatology recommendations for use in clinical practice. *Arthritis Care Res (Hoboken)*. 2012;64(5):640-647. doi:10.1002/acr.21649
14. Fraenkel L, Bathon JM, England BR, et al. 2021 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. Arthritis Rheumatol. 2021;73(7):1108-1123. doi:10.1002/art.41752

Note: This position statement was previously titled "Model Biologics Access Policy" and "Patient Access to Biologics"

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