INDIAN HEALTH SERVICE
National Pharmacy and Therapeutics Committee
Formulary Brief: ***Biologic DMARDs for RA***
-November 2025-

Background:

The Indian Health Service (IHS) National Pharmacy & Therapeutics Committee (NPTC) provided a pharmacotherapeutic review of biologic disease-modifying antirheumatic drugs (DMARDs) for rheumatoid arthritis (RA) during its November 2025 meeting. Medications listed on the IHS National Core Formulary (NCF) relevant to this review include adalimumab-bwwd and etanercept. Following clinical review and analysis, the NPTC made **no modifications** to the NCF.

Discussion:

Prevalence of RA in the Europe and North America is 0.5% for males and 1% for females. Other than sex, risk factors for RA include older age (peak incidence is at around age 50), family history, obesity, and both current and prior cigarette smoking. RA is a significant cause of morbidity among American Indian and Alaska Native (AI/AN) communities, with multiple studies demonstrating prevalence rates equal to, or substantially exceeding, those of the general U.S. population. Chippewa and Pima populations historically have some of the highest documented rates globally at 6.9% and 5.3%, respectively. Several regional reports, including findings in Yakama, Tlingit, and Navajo populations show RA rates three to five times the national average, further underscoring a disproportionate disease burden in these communities.[1-5]

Given this elevated prevalence, early, effective, and accessible RA management is essential. First-line therapy for most patients with RA is the conventional synthetic DMARD, methotrexate. Patients who have a high-moderate to high disease activity 3-months after methotrexate initiation should receive a tumor necrosis factor inhibitor (TNFi), ideally added to methotrexate. Currently available TNFi's include adalimumab, certolizumab, etanercept, golimumab, and infliximab. All TNFi medications demonstrate similar efficacy in treating RA, with no meaningful difference in adverse event risk across agents.[5,6] Selection of a specific TNFi for RA can therefore be guided by accessibility and cost. TNFi's such as adalimumab and etanercept have convenient dosing subcutaneous dosing options, such as pens and prefilled syringes, allowing for self-administration of these medications at home, avoiding resource intensive infusions. Recognizing the health disparities among AI/AN communities and the need for accessibility beyond methotrexate, the NPTC voted to add "adalimumab -or- etanercept" to the NCF in 2016, allowing local sites to choose one or the other.

In 2021, the Rheumatology Access Expansion (RAE) Initiative was established to provide support to those who have RA with limited access to specialized rheumatologic care. Their mission is to "promote access to evidence-based, culturally-specific care for people living with rheumatic diseases in underserved communities, with a particular focus on improving health for Native American communities." Through Project ECHO, the RAE Initiative provides support and resources to primary care providers who wish to develop expertise in diagnosing and managing RA and other common rheumatologic conditions. Their resources include a RA treatment algorithm, including screening, monitoring, drug selection, and follow up parameters, among other resources. Consistent with other treatment guidelines, the RAE Initiative's treatment algorithm recommends a trial of two TNFi's before specialist referral to consider other treatment options. [5,6]

Adalimumab and etanercept remain commonly used agents across the IHS. Etanercept offers a relatively lower risk of tuberculosis and certain infections, though it is a less favorable choice in patients with concomitant inflammatory bowel disease or inflammatory eye disease. Certolizumab carries unique advantages in pregnancy due to minimal placental transfer, making it the preferred TNFi in this setting, although adalimumab and etanercept are also considered safe in pregnancy.[5,6]

Adalimumab biosimilars are now widely accessible in the U.S. market, improving affordability for the agency. **A large systematic review and meta-analysis of 24 randomized controlled trials (N=10,259) confirmed equivalent therapeutic outcomes between biosimilars and reference biologics.**[7] In 2024, the NPTC re-reviewed this topic and replaced adalimumab on the NCF with the biosimilar adalimumab-bwwd (Hadlima™) based on consistent, demonstrated efficacy and improved value-based metrics. Although no etanercept biosimilar exists on the market, it was determined that etanercept should remain on the NCF.

Since its inclusion, utilization trends of adalimumab-bwwd support substantial cost savings for the IHS. Despite the significant cost avoidance opportunity for the IHS through the addition of adalimumab-bwwd to the NCF, many sites continue to utilize the branded product (i.e., Humira®) or other adalimumab biosimilars at a much greater cost.

Etanercept biosimilars, while approved in Europe in 2016 and 2019, are not expected to reach the U.S. market until 2029.[8] Nationally, in 2024, biologic medications made up only 5% of prescriptions in the U.S. but accounted for 51% of total drug spending. Comparatively, the U.S. Food and Drug Administration (FDA) approved 42 biosimilars in 2024 whereas the European Medical Agency approved 110.[9] In October 2025, the FDA announced that it was planning to accelerate approvals of biosimilars in the U.S.[10] It is unclear whether this will impact etanercept biosimilars entering the market soon.

Overall, the high burden of RA in AI/AN populations, combined with therapeutic equivalence across the TNFi agents and biosimilars, support continued emphasis on access, affordability, and primary care-based clinical management. Resources through the RAE Initiative help support increased provider capacity and treatment capabilities across Indian Country.

Findings:

RA prevalence among many AI/AN populations is higher than the general U.S. population, with some tribal communities exhibiting prevalence several times the national average. This disparity highlights the need for consistent access to effective RA treatment across the Indian health system. [1-4]

The REA Initiative provides training and treatment guidelines, tailored to the needs of the AI/AN, for primary care providers care for people who have limited access to a rheumatologist. Treatment guidelines consistently recommend the availability of two TNFIs for patients who are controlled on methotrexate monotherapy.[5]

Across the TNFi class for the treatment of RA, evidence demonstrates equivalent efficacy and safety.[5] Adalimumab biosimilars now provide cost-effective alternatives supported by strong evidence confirming therapeutic equivalence.[7] Given the substantial cost savings of adalimumab-bwwd (Hadlima™) compared to branded and other adalimumab biosimilar products, sites procuring TNFIs are encouraged to frequently reevaluate whether increasing utilization of adalimumab-bwwd (Hadlima™) would be preferential as a cost-mitigation strategy. Furthermore, recent actions by the FDA demonstrate a commitment to increasing approval and availability of biosimilars. Multiple etanercept biosimilars are anticipated to be available in 2029.[8,9,10]

If you have any questions regarding this document, please contact the NPTC at IHSNPTC1@ihs.gov . For more information about the NPTC, please visit the NPTC website.

References:

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