

## IN BRIEF A Summary of the Evidence

# Drugs for the Management of Rheumatoid Arthritis

### Key Messages

- For rheumatoid arthritis patients with moderate to severe disease in whom treatment with methotrexate has failed or who are intolerant to methotrexate, conventional synthetic disease-modifying antirheumatic drugs (alone or in combination), biologics (including biosimilars), and targeted synthetic disease-modifying antirheumatic drugs appear to be effective for different outcomes.
- It is unclear how the efficacy and safety of the treatments compare with one another.
- The treatment outcomes of most importance to patients are disease remission or low disease activity, with improved fatigue and decreased pain also being of high importance.
- The decision of the next treatment option should be based on a discussion between the clinician and patient that takes into consideration benefits and harms, patient treatment goals and tolerance for side effects, accessibility of treatment (e.g., whether travel is necessary), and affordability.

### Context

Rheumatoid arthritis (RA) is a chronic inflammatory disease that affects joints throughout the body, causing pain, swelling, stiffness, and joint damage. Approximately 300,000 Canadians have RA. Untreated, it can lead to functional limitation and severe disability and, therefore, can have a significant impact on quality of life. Although people who have RA would like to achieve total disease remission before significant damage occurs to their joints, they recognize that this might not be a realistic goal. Those for whom total remission is unrealistic want to have enough control over their disease to allow them to live a life that is as productive and pain-free as possible.

### Technology

The first line of treatment for RA is usually a conventional synthetic disease-modifying antirheumatic drug (csDMARD), such as methotrexate (MTX), to slow the joint destruction caused by the disease. Patients in whom this treatment is ineffective, partially effective, or causes side effects may be switched to a different csDMARD. However, other treatments are available, including biologic disease-modifying antirheumatic drugs (DMARDs) – also known as “biologics” – or their biosimilar versions, and targeted synthetic DMARDs (tsDMARDs).

### Issue

For patients with moderate to severe RA in whom treatment with MTX has failed or who are intolerant to MTX, there is uncertainty about which treatment to try next. A review of the comparative clinical efficacy and safety of biologics (including biosimilars), tsDMARDs, and csDMARD combination therapies will help guide treatment decisions for this patient population.

### Methods

A systematic review of published clinical evidence and a network meta-analysis were conducted. Input from patient groups, clinicians, and other stakeholders was considered and incorporated into the review.

### Results

The systematic review included 91 unique studies that were analyzed using both direct and indirect comparisons. To allow indirect comparisons where there was a lack of head-to-head comparison studies, network meta-analyses were conducted on the outcomes of interest. However, because the included studies did not always report on all of the outcomes of interest, comparisons of benefits or harms across several outcomes were not possible for all treatments.

The analysis came to the following conclusions:

- In general, in the patient population included in the review (i.e., those with an inadequate response to MTX), most treatments appear to be more effective than MTX alone.
- Compared with double-csDMARD therapy, triple-csDMARD therapy appears to be more effective regarding disease response and equally effective for improved function.
- Compared with biologics in combination with MTX, triple-csDMARD therapy appears to be comparable regarding disease response.
- Combining MTX with a biologic, a biosimilar, or a tsDMARD appears to be more effective than biologic or tsDMARD monotherapy.
- The review could not indicate if any one treatment has greater benefits than the others because not all treatments had data available for each of the outcomes and there were often no important differences in the head-to-head comparison results of these treatments.

It should be noted that the results of the review are limited to the shorter term, evidence from observational studies was not included in the review, and the majority of included studies had a high or unclear risk of bias. Results should therefore be interpreted with caution.

## Read more about CADTH and its review of drugs for the management of rheumatoid arthritis at:



[www.cadth.ca/drugs-management-rheumatoid-arthritis](http://www.cadth.ca/drugs-management-rheumatoid-arthritis).

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