Conventional Synthetic Disease-Modifying Antirheumatic Drugs for Adults with Moderate to Severe Rheumatoid Arthritis: Clinical Effectiveness
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Acknowledgments:

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About CADTH: CADTH is an independent, not-for-profit organization responsible for providing Canada’s health care decision-makers with objective evidence to help make informed decisions about the optimal use of drugs, medical devices, diagnostics, and procedures in our health care system.
Research Question
What is the clinical effectiveness of conventional synthetic disease-modifying antirheumatic drugs in adult patients with moderate to severe rheumatoid arthritis?

Key Findings
Five systematic reviews (two with meta-analyses and one with a network meta-analysis) and four randomized controlled trials were identified regarding the clinical effectiveness of conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) in adult patients with moderate to severe rheumatoid arthritis.

Methods
A limited literature search was conducted on key resources including PubMed, Ovid Medline, Ovid Embase, and The Cochrane Library, as well as a focused Internet search. Methodological filters were applied to limit retrieval to health technology assessments, systematic reviews, meta-analyses and network meta-analyses, randomized controlled trials. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2016 and June 6, 2018 for the search limited by randomized controlled trials, and to English language documents published between January 1, 2015 and June 6, 2018 for the search limited by health technology assessments, systematic reviews, meta-analyses and network meta-analyses. Internet links were provided where available.

Selection Criteria
One reviewer screened citations and selected studies based on the inclusion criteria presented in Table 1.
### Table 1: Selection Criteria

<table>
<thead>
<tr>
<th>Population</th>
<th>Adults with moderate to severe, active rheumatoid arthritis (RA) who have failed or are intolerant to methotrexate (inadequate responders)</th>
</tr>
</thead>
</table>
| Interventions | • Triple conventional synthetic disease-modifying antirheumatic drugs (csDMARDs), including a combination of any of the following:  
  o Methotrexate  
  o Sulfasalazine  
  o Hydroxychloroquine  
  o Leflunomide  
  • Double csDMARDs, including a combination of any of the following:  
    o Methotrexate  
    o Sulfasalazine  
    o Hydroxychloroquine  
    o Leflunomide |
| Comparators | • Double csDMARDs (including any combination of methotrexate, sulfasalazine, hydroxychloroquine, leflunomide)  
  • Triple csDMARDs (including any combination of methotrexate, sulfasalazine, hydroxychloroquine, leflunomide)  
  • Biologic DMARDs (tumour necrosis factor [TNF] inhibitors and non-TNF inhibitors) and their biosimilars with or without methotrexate  
  • Targeted synthetic (ts) DMARDS (e.g., tofacitinib, baricitinib)  
  • Placebo |
| Outcomes | Clinical effectiveness and safety |
| Study Designs | Health technology assessments, systematic reviews, meta-analyses, randomized controlled trials |

### Results

Rapid Response reports are organized so that the higher quality evidence is presented first. Therefore, health technology assessment reports, systematic reviews, and meta-analyses are presented first. These are followed by randomized controlled trials.

Five systematic reviews (two with meta-analyses and one with a network meta-analysis) and four randomized controlled trials were identified regarding the clinical effectiveness of csDMARDs in adult patients with moderate to severe rheumatoid arthritis. No relevant health technologies were identified.

Additional references of potential interest are provided in the appendix.

**Health Technology Assessments**

No literature identified.
Systematic Reviews and Meta-analyses

   PubMed: PM28356243


Triple csDMARDs


Randomized Controlled Trials

Double csDMARDs


Triple csDMARDs


Appendix — Further Information

Previous CADTH Reports


Systematic Reviews and Meta-Analyses

DMARD Combinations Unspecified


Systematic Review of Observational Studies


Randomized Controlled Studies - Upcoming Trials

Review Articles
