



Facilitating the translation of evidence into best practice: Optimising the pharmacological management of inflammatory arthritis

Summary of key recommendations

1. Rheumatology departments should develop and implement local protocols (and supporting materials for prescribers and consumers) that facilitate down-titration of biological/targeted synthetic disease-modifying antirheumatic drugs (b/tsDMARDs) for rheumatoid arthritis and axial spondyloarthritis.
2. Health service organisations should develop and implement local programs to optimise opioid therapy for the treatment of pain in inflammatory arthritis.
3. Rheumatology departments should develop and implement local programs to optimise use of glucocorticoids for the treatment of rheumatoid arthritis.
4. Rheumatologists should use a treat-to-target approach for all patients with RA, irrespective of the choice of initial treatment regimen.
5. Health service organisations should develop and implement local guidance for the perioperative use of DMARDs in people with inflammatory arthritis

Background

Living guidelines present up-to-date and state-of-the-art knowledge and guidance to practitioners. They use continuous evidence surveillance and rapid response pathways to incorporate new relevant evidence into systematic reviews and clinical practice guideline recommendations as soon as it becomes available.⁽¹⁾ For further information on living evidence see <https://livingevidence.org.au/about-living-evidence>.

As part of the ViP bDMARDs Program, the 'Australian Living Guideline for the Pharmacological Management of Inflammatory Arthritis' (mskguidelines.org) was developed to present the best available, current scientific evidence for pharmacological management of the most common forms of inflammatory arthritis, namely rheumatoid arthritis (RA), psoriatic arthritis (PsA) and axial spondyloarthritis (SpA), including choice of disease-modifying antirheumatic drug (DMARD), switching, combination therapy and down-titration of treatment.

Purpose

CATAG has developed this document to facilitate and support the translation of best available evidence into practice for the management of inflammatory arthritis. This will assist good governance and

decision-making for health service organisations, medicines governance committees¹ and health professionals.

These recommendations will be updated as further recommendations from the Australian Living Guidelines are released.

Scope

This guidance applies to the care of those patients who have been diagnosed with rheumatoid arthritis (RA), psoriatic arthritis (PsA) and axial spondyloarthritis (SpA) and adapts the Living Guidelines for consideration by medicines governance committees. It can be used in conjunction with formulary decisions and recommendations.

RECOMMENDATIONS

1. Rheumatology departments should develop and implement local protocols (and supporting materials for prescribers and consumers) that facilitate down-titration of b/tsDMARDs for rheumatoid arthritis and axial spondyloarthritis, where appropriate.

The decision to down-titrate bDMARDs is a shared decision between the patient and treating clinician.

The aim for treatment of people with inflammatory arthritis conditions is to achieve either disease remission or low disease activity using the lowest possible dose of biological/targeted synthetic disease-modifying antirheumatic drugs (b/tsDMARDs). Benefits of reducing the dose include fewer injections or infusions, the convenience of taking less medicines and reduced cost. Limited data from clinical trials suggest there is little difference in safety or tolerability of b/tsDMARDs if the dose is reduced.(2) These benefits must be weighed against the risk of losing disease control, experiencing more pain, inflammation and joint damage, experiencing a flare or being unable to undertake usual daily activities. Nevertheless, most people are able to regain good control by returning to the previous dose.(2)

The Australian Living Guideline for the Pharmacological Management of Inflammatory Arthritis recommends:

- In people with RA or SpA who have been in sustained low disease activity or remission for at least 6 months, consider stepwise reduction in the dose of b/tsDMARD. Continue dose reduction until cessation is achieved or the lowest effective b/tsDMARD dose is identified, as long as the treatment target is maintained.
- Do not routinely reduce the dose of b/tsDMARDs in patients with psoriatic arthritis who are in low disease activity or remission.
- Abrupt cessation of b/tsDMARDs is not recommended for patients with RA, SpA or PsA.

Resources

- [b/tsDMARDs down-titration algorithm for rheumatoid arthritis](#)
- [bDMARDs down-titration strategies used in clinical trials](#)
- [bDMARDs down-titration patient decision aid](#)

¹ Examples of medicines governance committees include drug and therapeutics committees, medicines advisory committees or equivalent, medication safety committees

- [Down-titration factsheet](#)

2. Health service organisations should develop and implement local programs to optimise opioid therapy for the treatment of pain in inflammatory arthritis

Pain, for both people with inflammatory arthritis and their clinicians is a significant issue, with pain management a high priority.(3) The pain is often due to inflammation, but may also be as a result of joint damage or destruction and peripheral and central sensitization.(4) This pain may not be controlled by DMARDs and non-steroidal anti-inflammatory drugs (NSAIDs) and additional pain relief may be required. The use of opioids may provide short-term improvement in pain, however, there is potential for significant adverse effects, such as risk of dependence, misuse or overdose. There is no data on the benefits of long-term use of opioids, but the potential for long-term harms of opioid use for chronic non-cancer pain is widely accepted. Any decision to initiate the use of opioids should take place within a clear shared decision-making framework, tailored to the individual's circumstances (including comorbidities and concomitant medications).(2)

The Australian Living Guideline for the Pharmacological Management of Inflammatory Arthritis recommends:

- Do not routinely use opioids for the treatment of pain in RA, SpA or PsA.
- A brief course of a short-acting opioid may be considered for severe pain associated with RA only, and only when other analgesic options have failed.

Resources

- [NPS MedicineWise opioids program](#)
- [NSW TAG Preventing and managing problems with opioid prescribing for chronic non-cancer pain](#)

3. Rheumatology departments should develop and implement local programs to optimise use of glucocorticoids for the treatment of rheumatoid arthritis.

Glucocorticoids (most commonly prednisone or prednisolone) play a role in the treatment of rheumatoid arthritis, with approximately 50% of patients estimated to receive glucocorticoids in varying doses, for varying durations, at varying stages of their disease(5), however it has been identified that they have the potential for adverse effects, particularly with high doses or long-term use. These include osteoporotic fractures, infection, skin thinning, easy bruising, weight gain, diabetes, hypertension and cataracts(6).

For management of disease flares (i.e. loss of low disease activity state, or increase in disease activity) in patients with recent onset or established disease, short-term glucocorticoid treatment is a common strategy to rapidly decrease inflammation and alleviate symptoms.(2)

Long term use of low-dose glucocorticoids has been used in patients with established disease, who have not been able to reach low-disease activity or remission with DMARDs. The evidence suggests that any potential benefits of long-term glucocorticoids in RA are likely to be of negligible clinical importance.

shared decision-making framework that takes into account all of these factors is of paramount importance.(2)

The use of glucocorticoids in RA should aim for the lowest dose and shortest duration that achieves the individual patient's treatment goals, and should include a plan to monitor for and attempt to mitigate long-term harmful effects.(2)

The Australian Living Guideline for the Pharmacological Management of Inflammatory Arthritis recommends:

- Consider using short-term glucocorticoids for the treatment of rheumatoid arthritis flare in people with previously well-controlled disease, via either a systemic (oral, intramuscular or intravenous) or intra-articular route, in the lowest possible dose for the shortest possible time. Any flare should prompt consideration of the need for adjustment of the DMARD regimen.
- Do not routinely use glucocorticoids as a long-term (>6 months) adjunct to DMARDs for the treatment of rheumatoid arthritis.

Resources

- [NPS Practice review -Rheumatoid arthritis](#)
- [Webinar recording: Corticosteroids: Indications guide optimal use](#)
- [Podcast: The contemporary role of methotrexate and glucocorticoids in RA](#)

4. Rheumatologists should use a treat-to-target approach for all patients with RA, irrespective of the choice of initial treatment regimen.

Methotrexate is considered first line therapy for rheumatoid arthritis. The Living Guideline panel considered the choice of methotrexate (MTX) monotherapy versus MTX combination therapy as the initial choice of treatment in people with RA who have not previously received any DMARDs.

A network meta-analysis that compared MTX monotherapy to MTX-based combination therapies was used as the primary evidence source for this recommendation(7) and two subsequent RCTs of MTX monotherapy versus MTX in combination with JAK inhibitors were used. (8, 9) Based on data from the network meta-analysis, the probability of achieving an ACR50 response with MTX monotherapy is about 41%; this increases to 56-67% with the use of initial combination therapy (either triple therapy or MTX plus most b/tsDMARDs). Triple therapy is defined as methotrexate plus sulfasalazine plus hydroxychloroquine. Combination therapy was also shown to have similar tolerability and safety compared to MTX monotherapy and consumers in general were not averse to combination therapy. It did not show a difference in efficacy between 'triple therapy' (MTX, sulfasalazine and hydroxychloroquine) and any b/tsDMARD in combination with MTX. It is important to note that b/tsDMARDs are more expensive and are not subsidised for initial therapy in Australia.

It is important that any decision regarding the choice of disease-modifying therapy should be made within a shared decision-making framework following a clear discussion of potential benefits and harms, tailored to the individual's circumstances.

The Australian Living Guideline for the Pharmacological Management of Inflammatory Arthritis recommends:

- Consider using methotrexate in combination with other DMARDs as initial therapy in people with rheumatoid arthritis. For most people this implies triple therapy (methotrexate + sulfasalazine + hydroxychloroquine). While the combination of methotrexate and most b/tsDMARDs is also effective, this is currently not a feasible option for most people.

5. Health service organisations should develop and implement local guidance for the perioperative use of DMARDs in people with inflammatory arthritis

A large proportion of people with inflammatory arthritis will undergo orthopaedic surgery over the course of their illness, and it is estimated that over 80% of such patients take conventional or biologic DMARDs at the time of their orthopaedic surgery.⁽¹⁰⁾ Two options exist with regards to stopping these medicines- stopping therapy, which increases the risk for post-operative disease flare or continuing therapy, which carries a risk of infection.

The evidence regarding csDMARDs was sufficient to warrant a conditional recommendation in favour of continuing these drugs without interruption in most individuals undergoing elective surgery, although some patients may elect to hold treatment based on an individual assessment of risks and benefits.

bDMARDs are potent immunomodulators that are associated with an increased risk of infection in general, and therefore the lowest-risk approach may be to temporarily discontinue these drugs in the perioperative period. However it was also noted that the current body of observational evidence does not suggest that continuation of therapy is associated with an important risk of infection, and it remains unknown whether interruption of treatment for an arbitrary period either reduces the risk of infection or has a net beneficial effect versus the risk of disease flare. It is thought that disease flare in the perioperative period is unlikely to be benign, particularly if there is an impact on rehabilitation from surgery or if it results in rescue therapy with glucocorticoids.

There is a current lack of evidence for tsDMARDs, the potential impact on the risk of infection and other perioperative complications (including the possibility of blunting of the acute phase response in the setting of infection and a theoretical increase in the risk of thrombosis), the panel agreed on a conditional recommendation to temporarily discontinue tsDMARDs perioperatively.

The Australian Living Guideline for the Pharmacological Management of Inflammatory Arthritis recommends:

- Do not routinely discontinue csDMARDs in the perioperative period.
- Do not routinely discontinue bDMARDs in the perioperative period; consider temporary discontinuation in individuals with a high risk of infection or where the impact of infection would be severe.
- Consider temporary discontinuation of tsDMARDs in the perioperative period.

The Australian Living Guideline for the Pharmacological Management of Inflammatory Arthritis recommend the following practical information.

Consideration of the potential risks and benefits of temporary discontinuation of DMARDs in the perioperative period based on the following factors:

- Type and urgency of surgery
- Risk factors for infection
- Potential impact of infection or flare
- Other risk factors for infection
- The patient's preferences and goals .

For patients planning to withhold DMARDs perioperatively, consider the following schedule as a guide:

- For most bDMARDs, withhold for one dosing cycle prior to surgery
 - i.e., plan surgery at approximately the time of the subsequent dose (e.g., for a monthly injection, aim for surgery in the 5th week after the last injection)
- For rituximab, aim for surgery at least 3 months after the most recent dose
- For JAK inhibitors, stop treatment approximately 7 days before surgery
- For methotrexate, withhold for one dosing cycle prior to surgery (i.e. plan surgery 1-2 weeks after the most recent dose)
- For leflunomide, stop treatment approximately 7 days before surgery

Aim to recommence DMARDs when surgical sutures have been removed, adequate wound healing has occurred and there are no other symptoms or signs of infection

Be aware that some b/tsDMARDs (e.g., tocilizumab and JAK inhibitors) may diminish or eliminate the acute phase response, particularly if the drug is discontinued or recommenced close to the time of surgery, and therefore the practitioner should be vigilant for the possibility of infection even in those with normal inflammatory markers.

Further information

- Australian Living Guideline for the Pharmacological Management of Inflammatory Arthritis mskguidelines.org
- NPS bDMARDS program <https://www.nps.org.au/bdmards>

Appendices

Appendix 1: Glossary

Term	Definition
b/tsDMARD	Biological/targeted synthetic disease-modifying antirheumatic drug
DMARD	disease-modifying antirheumatic drug
Medicines governance committees	the group assigned responsibility for governance of the medication management system, and for ensuring the safe and effective use of medicines in the health service organisation.(11) These may also be known as a medicines advisory committee, pharmacy and therapeutics committee, drug committee, drug and therapeutics advisory committee, formulary committee or quality use of medicines committee.
Down-titration	The stepwise reduction in dose, by either reducing the dose or increasing the dosing interval

Appendix 2: How this guidance was developed

This guidance was developed in consultation with the CATAG member organisations listed below:

- ACT Health
- NSW Therapeutic Advisory Group (NSW TAG)
- Northern Territory Drug and Therapeutics Committee
- Queensland Health Medicines Advisory Committee (QHMAC)
- South Australian Medicines Advisory Committee (SAMAC)
- Tasmanian Medicines Access and Advisory Committee (TMACC)
- Victorian Therapeutics Advisory Group (Vic TAG)
- Western Australian Therapeutics Advisory Group (WATAG)

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This guidance has been developed by CATAG, as part of the ViP bDMARDs program.

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