Rheumatoid arthritis: Quality use of b/tsDMARDs and other medicines

The Australian Rheumatology Association and NPS MedicineWise are working together as part of the national *Targeted Therapies Alliance* to improve the quality use of medicines for the management of rheumatoid arthritis (RA). In this report, the *Targeted Therapies Alliance* provides insights into the prescribing of medicines for patients with RA. These include biological disease-modifying antirheumatic drugs (bDMARDs), targeted synthetic DMARDs (tsDMARDs), conventional synthetic DMARDs (csDMARDs), glucocorticoids and opioids.

You are receiving this report because, as a future or early career rheumatologist, you will be ideally placed to optimise the use of b/tsDMARDs for RA and to support and influence other health professionals to improve patient health outcomes. This PBS Practice Review includes aggregate state and national data about the prescribing of current rheumatologists and immunologists across Australia for patients with RA. The aim is to give you an opportunity to reflect on the prescribing of DMARDs and other medicines for the management of RA. The aggregate data are presented alongside distillations of best practice guidelines and recent evidence.[1–3] For more information on the data as well as further state and national aggregate data, visit our website at: nps.org.au/pbs-bdmards.

What's next?

As part of the *Targeted Therapies Alliance* program, additional resources are available, including:

- An Australian living guideline for the pharmacological management of inflammatory arthritis
- Position Statement on the use of low-dose methotrexate
- Down-titration algorithm
- Down-titration patient decision aid
- Down-titration factsheet
- Low-dose methotrexate for rheumatoid arthritis and psoriatic arthritis patient action plan
- Rheumatoid arthritis roadmap
- Psoriatic arthritis roadmap
- Ankylosing spondylitis roadmap.

For more information, see nps.org.au/bdmards.

We hope this PBS Practice Review will be of value to you and we welcome your feedback on this report. Future PBS Practice Reviews are planned to provide further guidance on the management of RA and other related rheumatological conditions.

Yours sincerely,

Professor Catherine Hill (MBBS, MD MSc (Epi), FRACP)
President, Australian Rheumatology Association

Adjunct Associate Professor Steve Morris
Chief Executive Officer, NPS MedicineWise

National PBS data snapshot

From 1 Jan 2018 to 31 Dec 2019 across Australia, **11243** patients were started on a b/tsDMARD for RA. On average:

- Prescribers had **96** patients who were prescribed a b/tsDMARDs for RA (starting or continuation of treatment).
- Prescribers started **25** patients on b/tsDMARD treatment. See page 7 for definition of starting treatment.

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Helping consumers and health professionals make safe and wise therapeutic decisions about biological disease-modifying antirheumatic drugs (bDMARDs) and other specialised medicines. Funded by the Australian Government Department of Health through the Value in Prescribing bDMARDs Program Grant.

Use of csDMARDs before starting b/tsDMARD treatment

Optimise csDMARD use by considering subcutaneous methotrexate (MTX) before starting a b/tsDMARD.

Points for reflection

- MTX remains the first-line DMARD for RA.[1–3] Optimise use by rapidly escalating to required dose.[4,5] If patients are not sufficiently responding to or are intolerant of oral MTX, always consider subcutaneous MTX.
- Subcutaneous MTX is more efficacious and generally better tolerated than oral MTX, with significantly fewer associated gastrointestinal adverse effects (eg, nausea and diarrhoea).[6]
- Switching from oral to subcutaneous MTX is highly effective; in one study, 72% of patients who switched remained on subcutaneous MTX for the duration of the 5-year observational period without the addition of a biologic.
- Subcutaneous MTX prefilled syringes were listed on the PBS in April 2018 for patients with RA for whom an oral form of MTX is unsuitable, for example where improved tolerance and/or bioavailability is needed.[8]

Box 1 – Optimising adherence to MTX

- Establish realistic expectations with patients about MTX treatment, which takes 6–12 weeks to achieve maximal effect.[2]
- Ensure patients receive folic acid supplementation to reduce the risk of gastrointestinal and hepatic adverse effects associated with MTX.[9]

Fig. 1 – Types of csDMARD[a,b] dispensed before starting b/tsDMARD treatment for RA

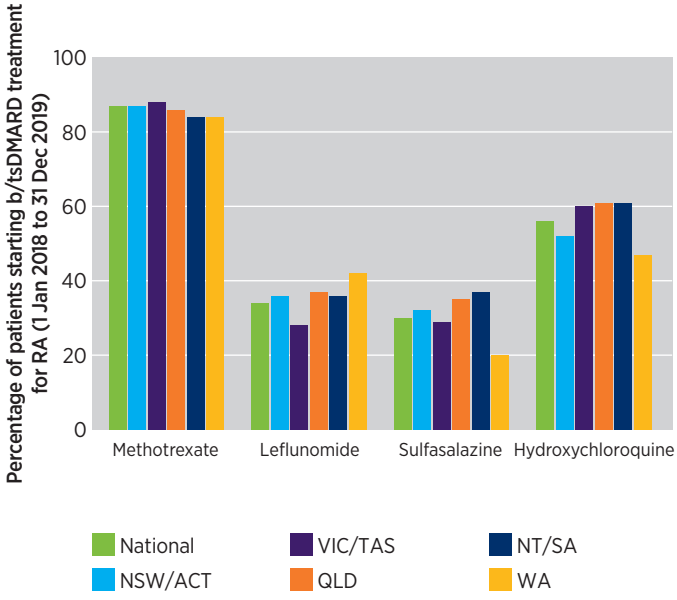
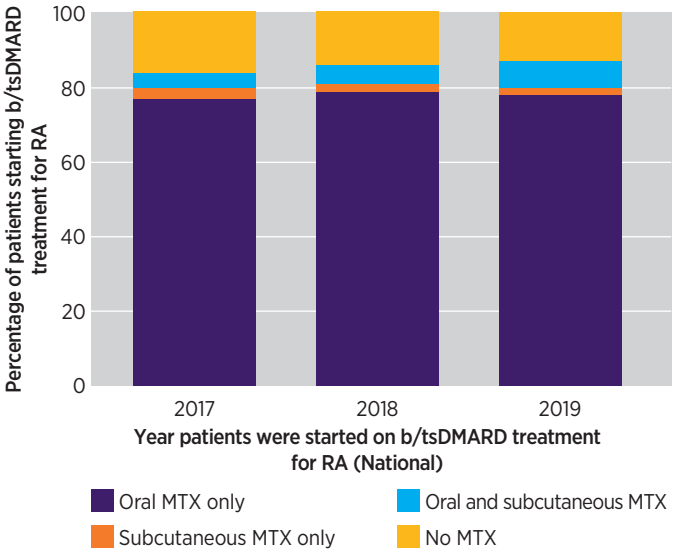


Fig. 2 – Types of MTX[a,b] dispensed before starting b/tsDMARD for RA across Australia



Questions for reflection

- How does the national data on the prescribing of csDMARDs compare with guidelines? Is this consistent with your expectations?
- What are some barriers that might prevent the use of subcutaneous MTX?
- How could you encourage patients to try subcutaneous MTX?
- How could you assess and promote adherence to MTX for patients?

[a] The indication for csDMARD prescribing cannot be determined from PBS data except for leflunomide. Leflunomide prescribing in this report is known to be indicated for RA.

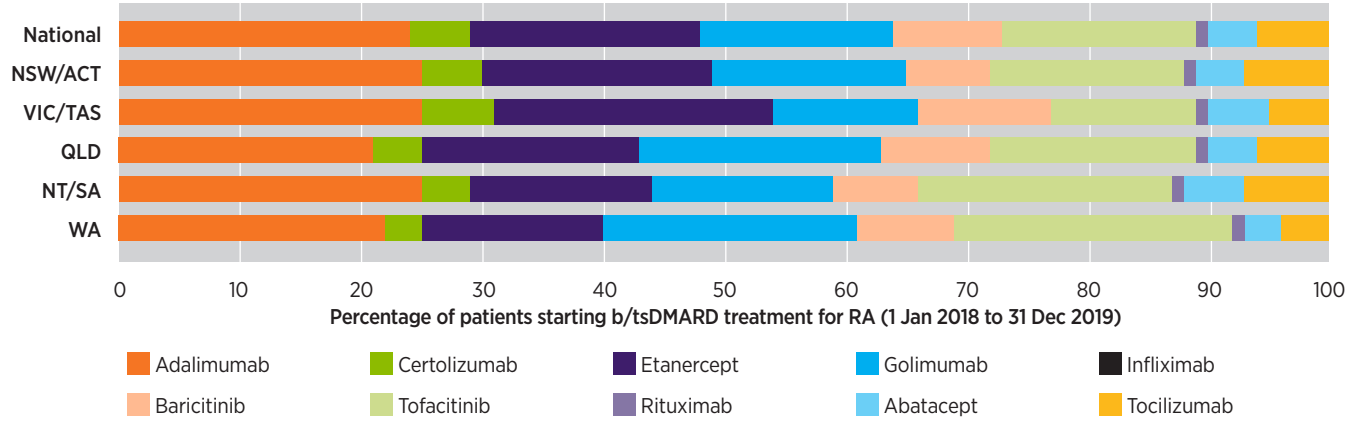
[b] csDMARDs prescribed by any prescriber and dispensed between mid-2015 and Dec 2019 are considered here.

b/tsDMARD prescribing – initiation

Points for reflection (Figs. 3, 4a, 4b)

- b/tsDMARDs are generally considered to have comparable efficacy for RA.[1,2] Individualise the choice of b/tsDMARD (see Box 2).
- Combination csDMARD and b/tsDMARD therapy is more effective than b/tsDMARD monotherapy.[1]
- For patients for whom MTX is contraindicated, consider tocilizumab or a tsDMARD, as these may have some advantages as monotherapy, compared to other bDMARDs.[1,10]
- Consider stepwise reduction in the dose of b/tsDMARDs for patients who have had sustained low disease activity or been in remission for at least 6 months but do not stop b/tsDMARDs suddenly.[11] A b/tsDMARD down-titration algorithm that takes patient perspectives into account is available at nps.org.au/bdmards/rheumatology-conditions.

Fig. 3 – Choice of first-line b/tsDMARD treatment for patients with RA



Box 2 – Individualised choice of b/tsDMARD should be informed by factors such as:

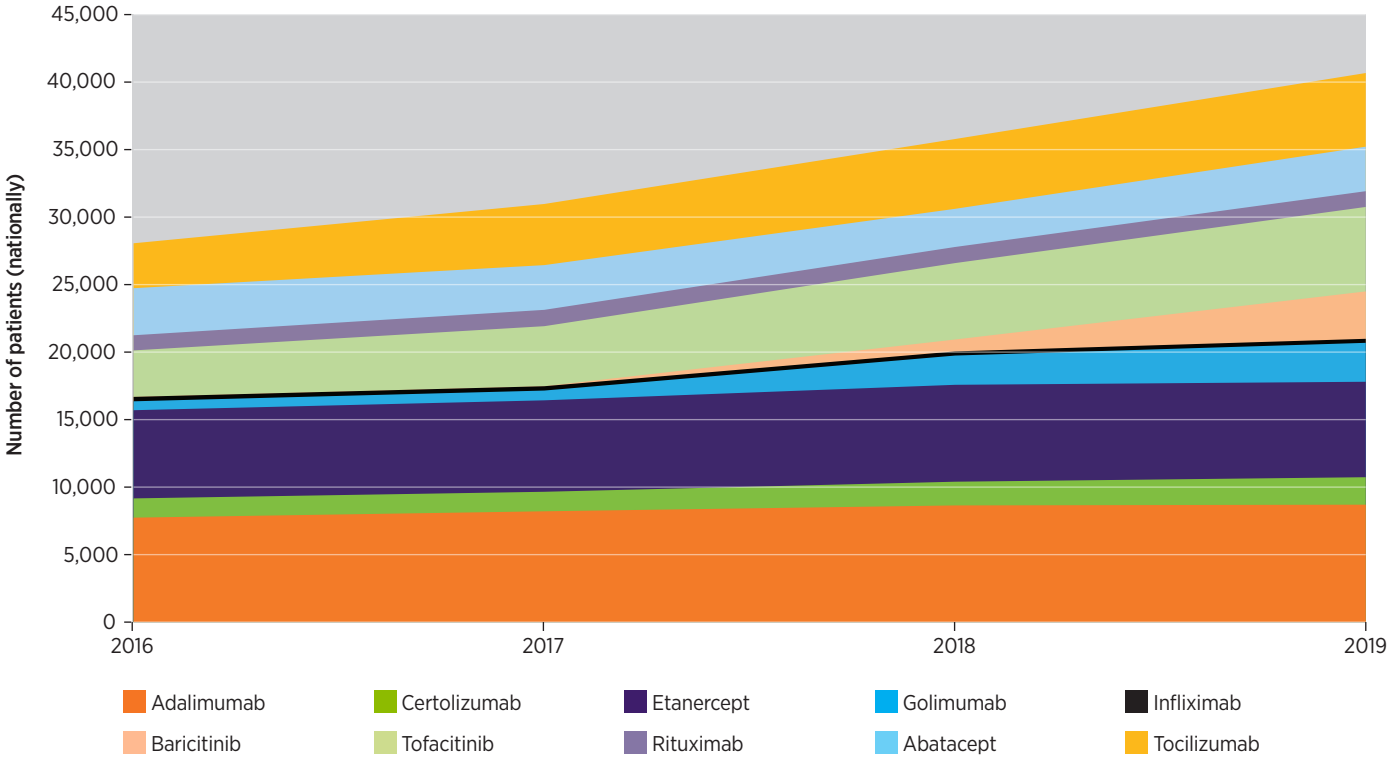
- patient preferences[1,2]
- patient comorbidities[1,12] eg, previous serious infections (abatacept is associated with lower risk),[12] congestive heart failure[3] and multiple sclerosis (avoid TNF inhibitors (TNFi)),[12] high risk of thromboembolism (avoid Janus Kinase (JAK) inhibitors),[1] history of malignancy (rituximab may be preferred)[12,13]
- disease characteristics eg, seropositive RA is a positive predictor of response to rituximab[14] and abatacept[15]
- previous response to treatment (including adverse effects). Changing to an agent with a different mechanism of action may be beneficial following inadequate response to a b/tsDMARD, although a second TNFi may be effective after failure of first TNFi[1]
- planned pregnancy (consider certolizumab due to lack of placental transfer)[16,17]
- cost to patient and/or government.

Choice of b/tsDMARDs for patients with RA over the years

Fig. 4a – Number of unique patients dispensed prescriptions for b/tsDMARDs for RA (Australia-wide, 2016 to 2019)

Class	b/tsDMARD	2016	2017	2018	2019
TNF inhibitors	Adalimumab	7681	8149	8580	8640
	Certolizumab	1416	1435	1744	2021
	Etanercept	6484	6723	7125	7020
	Golimumab	657	719	2152	2864
	Infliximab	325	318	305	296
JAK inhibitors	Baricitinib	0	0	875	3486
	Tofacitinib	3420	4415	5619	6213
B lymphocyte modulator	Rituximab	1114	1204	1184	1158
T lymphocyte modulator	Abatacept	3463	3291	2806	3274
IL-6 inhibitor	Tocilizumab	3302	4494	5132	5419
Total		**27856**	**30745**	**35521**	**40375**

Fig. 4b – Number of unique patients dispensed prescriptions for b/tsDMARDs for RA (Australia-wide, 2016 to 2019)



Questions for reflection (Figs. 3, 4a, 4b)

- What factors influence prescribing choices for b/tsDMARDs?
- How can b/tsDMARD choice be optimised and individualised for patients? Were any factors listed in Box 2 new to you?
- Do patients continue csDMARDs after starting b/tsDMARD treatment?

Glucocorticoid use

Reduce patient use of glucocorticoids beyond 3 months and clearly communicate to GPs how to manage glucocorticoids for your patients.

Points for reflection

- If a glucocorticoid is considered necessary, guidelines recommend short-term use to control flare-ups and limiting use to ≤ 3 months for bridging therapy when starting or changing DMARDs.[1,2]
- Harms associated with long-term glucocorticoid use can occur even at low doses. However, these harms are dose-dependent with elevated risk at doses > 10 mg/day. Reduce risk of harms for patients unable to stop glucocorticoid treatment, by aiming for a dose ≤ 5 mg/day.[18]
- Provide clear guidance to GPs on the quality use of glucocorticoids and advice on how to reduce the dose.

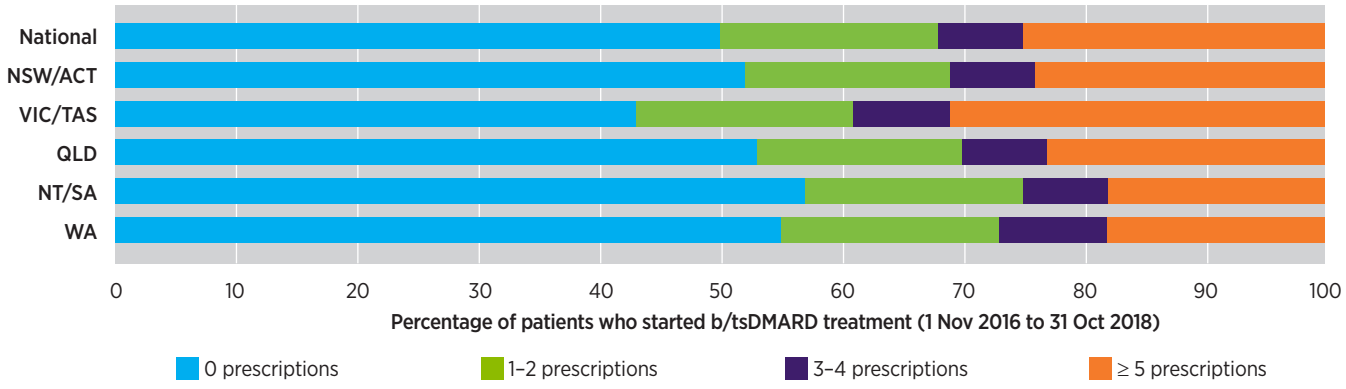
In the 2 years from 01/11/16 to 31/10/18, **9682** patients with RA were commenced on a b/tsDMARD across Australia.

As guidelines recommend withdrawing glucocorticoids after b/tsDMARD initiation, 6 months of bridging therapy was considered when extracting the data.

In the subsequent 12 months to this 6-month withdrawal window:

- **27% (2572)** of these patients were dispensed glucocorticoids prescribed by the rheumatologist/immunologist who initiated the b/tsDMARD
- **50% (4825)** of these patients were dispensed glucocorticoids prescribed by any prescriber (see Fig. 5).

Fig. 5 – Prescribing of glucocorticoids[c] ≥ 6 months after starting b/tsDMARD treatment for RA



Questions for reflection

- Do patients who start on b/tsDMARDs for RA have a plan to reduce or stop glucocorticoid use after 3 months?
- How is guidance provided to GPs on the use of glucocorticoids, including when and how to reduce the dose?

[c] Glucocorticoid prescriptions include all oral (tablet and liquid) preparations of prednisone and prednisolone. Prescribing of glucocorticoids by any prescriber is included.

Opioid use

Discuss the limited role of opioids for patients with RA and identify patients who would benefit from opioid tapering.

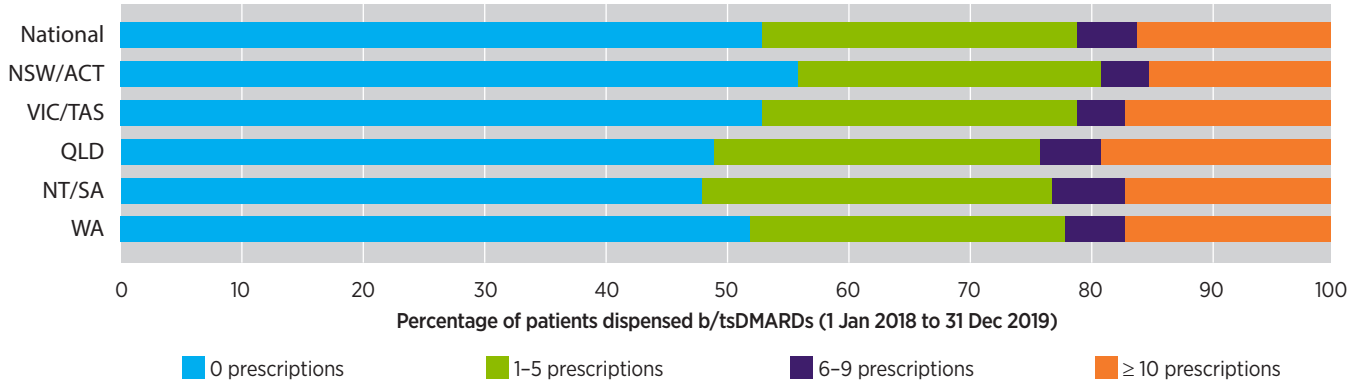
Points for reflection

- There is insufficient evidence to support the long-term use of opioids for pain management for patients with RA.[19,20]
- Any benefits of opioids can usually be determined within a 2–4 week trial of opioid treatment.[21] Short-term use (< 6 weeks) of weak opioids may provide some analgesia, but adverse effects and the risk of harms (including increased risk of serious infection[22] and risk of overdose) limit their use.[19]
- Pain management in RA should focus on an increase in function of joints, rather than on the removal of pain. If pain is related to inflammatory arthritis, a short course of oral glucocorticoids or intra-articular injections is an appropriate treatment option in conjunction with a review of current treatment.
- Develop a pain management plan in collaboration with the patient and their GP. Include agreed treatment goals (eg, improving pain control, function and quality of life), criteria for success and when the opioid will be tapered.[21]

Between 1 Jan 2018 and 31 Dec 2019 across Australia, **43169** patients were prescribed a b/tsDMARD for RA. Of these:

- **3448 (8%)** of patients were also prescribed opioids[d,e] by the same bDMARD prescriber.
- **20675 (48%)** of patients were also prescribed opioids[d,e] by any prescriber (see Fig. 6).

Fig. 6 – Prescribing of opioids[d,e] for patients also prescribed b/tsDMARDs for RA



CPD: Questions for reflection

- How do you approach the management of pain for patients on long-term opioids where the opioids may have been started by another prescriber?
- How can you optimally involve multidisciplinary services when developing pain management plans with patients and their GPs?

[d] To focus on opioid use likely to be for chronic non-cancer pain, PBS codes related to medicines indicated for opioid dependence, palliative care and cancer pain are not included.

[e] To be included, both the opioid and the b/tsDMARD prescriptions must have been dispensed between 1 Jan 2018 and 31 Dec 2019 AND the opioid prescription must have been dispensed after the earliest b/tsDMARD.

About the data

PBS dispensing data

The data provided in this report are from Services Australia and include the following medicines that were dispensed on the PBS:

- csDMARDs: MTX, sulfasalazine, hydroxychloroquine for any indication, leflunomide for RA
- b/tsDMARDs for RA: abatacept, adalimumab, baricitinib, certolizumab, etanercept, golimumab, infliximab, rituximab, tocilizumab, tofacitinib
- glucocorticoids for any indication
- opioids for chronic non-cancer pain. For the full list of opioid medicines included in this report see nps.org.au/pbs-bdmards.

Prescriptions for medicines both above and below co-payment are included. Data reflect the date the prescription was dispensed, and do not reflect the duration of use of the medicine by the patient.

Indication for use of medicines

The indication for prescribing of b/tsDMARDs and leflunomide is known to be for RA (based on PBS authority item codes). The indication for prescribing of MTX, sulfasalazine, hydroxychloroquine, glucocorticoids and opioids cannot be determined from PBS data, **however this report only looks at the use of these medicines for patients who also went on to use, or had previously used b/tsDMARDs for RA**.

Starting b/tsDMARD treatment

This refers to patients who were started a b/tsDMARD medicine for the treatment of RA in the time period specified. Between September 2015 and this time, these patients had not had another prescription dispensed for a b/tsDMARD for RA from any other prescriber.

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This PBS Practice Review has been developed in collaboration with:

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Australian Rheumatology Association

Cochrane Musculoskeletal

University of South Australia

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ABN 61 082 034 393

NPS MedicineWise
PO Box 1147
Strawberry Hills NSW 2012

P: 02 8217 8700
E: info@nps.org.au
nps.org.au

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