

RITUXIMAB

NOTE:

Any queries concerning the arrangements to prescribe rituximab may be directed to Medicare Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday).

Written applications for authority to prescribe rituximab should be forwarded to:

Medicare Australia
Prior Written Approval of Specialised Drugs
Reply Paid 9826
GPO Box 9826
HOBART TAS 7001

Further prescribing information is on the Medicare Australia website at <http://www.medicare.gov.au/provider/pbs/drugs/index.shtml>

TREATMENT OF ADULT PATIENTS WITH SEVERE ACTIVE RHEUMATOID ARTHRITIS

The following information applies to the prescribing under the Pharmaceutical Benefits Scheme (PBS) of the biological disease modifying anti-rheumatic drugs (bDMARDs) for adults with severe active rheumatoid arthritis. Where the term bDMARD appears in the following notes and restrictions it refers to the tumour necrosis factor (TNF) alfa antagonists (adalimumab, etanercept, infliximab), the chimeric anti-CD20 monoclonal antibody (rituximab) and the interleukin-1 inhibitor (anakinra) and the T-cell co-stimulation modulator (abatacept).

Patients are eligible for PBS-subsidised treatment with only 1 of the above biological disease modifying anti-rheumatic drugs at any 1 time.

PBS-subsidised infliximab, anakinra and rituximab must be used in combination with methotrexate at a dose of at least 7.5 mg weekly. Where a patient cannot tolerate 7.5 mg of methotrexate weekly, they are only eligible to receive PBS-subsidised etanercept and adalimumab.

In order to be eligible to receive PBS-subsidised treatment with rituximab, a patient must have already failed to demonstrate a response to at least 1 course of treatment with a PBS-subsidised TNF-alfa antagonist.

From 1 March 2008, under the PBS, all patients will be able to commence a Treatment Cycle where they may trial PBS-subsidised bDMARD agents without having to experience a disease flare when swapping to an alternate agent. Under these interchangeability arrangements, within a single Treatment Cycle, a patient may continue to receive long-term treatment with a bDMARD while they continue to show a response to therapy.

A patient who received PBS-subsidised bDMARD treatment prior to 1 March 2008 is considered to be in their first Cycle as of 1 March 2008.

Within the same Treatment Cycle, a patient cannot trial and fail, or cease to respond to, the same PBS-subsidised bDMARD more than once.

Once a patient has either failed or ceased to respond to treatment 3 times, they are deemed to have completed a Treatment Cycle and they must have, at a minimum, a 5-year break in PBS-subsidised bDMARD therapy before they are eligible to commence the next Cycle.

For patients who have failed PBS-subsidised treatment with 3 bDMARDs prior to 1 March 2008 please contact Medicare Australia on 1800 700 270.

The 5-year break is measured from the date of the last approval for PBS-subsidised bDMARD treatment in the most recent Cycle to the date of the first application for initial treatment with a bDMARD under the new Treatment Cycle.

A patient who has failed fewer than 3 bDMARDs in a Treatment Cycle and who has a break in therapy of less than 5 years, may commence a further course of treatment within the same Treatment Cycle.

A patient who has failed fewer than 3 bDMARDs in a Treatment Cycle and who has a break in therapy of more than 5 years, may commence a new Treatment Cycle.

There is no limit to the number of Treatment Cycles a patient may undertake in their lifetime.

If patients fail to respond to a particular bDMARD within a single Treatment Cycle, they are not eligible to receive further PBS-subsidised treatment with that drug until they commence the next Cycle.

(1) How to prescribe PBS-subsidised bDMARD therapy after 1 March 2008.

(a) Initial treatment.

Applications for initial treatment should be made where:

- (i) a patient has received no prior PBS-subsidised bDMARD treatment in this Treatment Cycle and wishes to commence such therapy, excluding rituximab (Initial 1); or
- (ii) a patient has received prior PBS-subsidised (initial or continuing) bDMARD therapy and wishes to trial an alternate agent (Initial 2) [further details are under 'Swapping therapy' below]; or
- (iii) a patient wishes to re-commence treatment with a specific bDMARD following a break in PBS-subsidised therapy with that agent (Initial 2).

Initial treatment authorisations will be limited to provide a maximum of 16 weeks of therapy for etanercept, adalimumab and anakinra, 22 weeks of therapy for infliximab and 2 infusions of rituximab.

From 1 March 2008, a patient must be assessed for response to any course of initial PBS-subsidised treatment (excluding rituximab) following a minimum of 12 weeks of therapy and this assessment must be submitted to Medicare Australia no later than 4 weeks from the date that course was ceased.

Rituximab patients must be assessed following a minimum of 12 weeks after the first infusion, and this assessment must be submitted to Medicare Australia within 4 weeks.

Where a response assessment is not submitted to Medicare Australia within these timeframes, the patient will be deemed to have failed to respond to treatment with that bDMARD.

For second and subsequent courses of PBS-subsidised bDMARD (excluding rituximab) treatment it is recommended that a patient is reviewed in the month prior to completing their current course of treatment and that an application is submitted to Medicare Australia no later than 2 weeks prior to the patient completing their current treatment course.

Rituximab patients:

A further application may be submitted to Medicare Australia 24 weeks after the first infusion. New baselines may be submitted with this application if appropriate.

(b) Continuing treatment.

Following the completion of an initial treatment course with a specific bDMARD (excluding rituximab), a patient may qualify to receive up to 24 weeks of continuing treatment with that drug providing they have demonstrated an adequate response to treatment. The patient remains eligible to receive continuing bDMARD treatment with the same drug in courses of up to 24 weeks providing they continue to sustain the response.

It is recommended that a patient be reviewed in the month prior to completing their current course of treatment to ensure uninterrupted bDMARD supply.

Assessments of response to a course of PBS-subsidised therapy must be submitted to Medicare Australia no later than 4 weeks from the date that course was ceased.

Rituximab patients:

A patient may qualify to receive a further course of treatment (every 24 weeks) with this agent providing they have demonstrated an adequate response to treatment following a minimum of 12 weeks after the first infusion of their most recent treatment with rituximab. The patient remains eligible to receive a course of rituximab every 24 weeks providing they continue to demonstrate a response as specified in the restriction.

Where a response assessment is not submitted to Medicare Australia within these time frames, the patient will be deemed to have failed to respond to treatment with that bDMARD.

(2) Swapping therapy.

Once initial treatment with the first PBS-subsidised bDMARD is approved, a patient may swap to an alternate bDMARD within the same Treatment Cycle without having to requalify with respect to the indices of disease severity (i.e. the erythrocyte sedimentation rate (ESR), the C-reactive protein (CRP) levels and the joint count) or the prior non-bDMARD therapy requirements. However the requirement for concomitant treatment with methotrexate, where it applies, must be met for each bDMARD trialled.

Patients who are not able to complete a minimum of 12 weeks of an initial treatment course will be deemed to have failed treatment with that agent.

A patient may trial an alternate bDMARD at any time, regardless of whether they are receiving therapy (initial or continuing) with a bDMARD at the time of the application. However, they cannot swap to a particular bDMARD if they have failed to respond to prior treatment with that drug within the same Treatment Cycle.

In order to trial rituximab, a patient must have trialled and failed to demonstrate a response to at least 1 PBS-subsidised TNF-alfa antagonist treatment.

To ensure a patient receives the maximum treatment opportunities allowed under the interchangeability arrangements, it is important that they are assessed for response to every course of treatment approved, within the timeframes specified in the relevant restriction.

PBS subsidy does not allow for patients to receive treatment with another PBS-subsidised biological agent during the required treatment-free period applying to patients who have demonstrated a response to their most recent course of rituximab. This means that patients who have demonstrated a response to a course of rituximab must have a PBS-subsidised biological therapy treatment-free period of at least 22 weeks, immediately following the second infusion, before swapping to an alternate bDMARD. Patients who fail to respond to rituximab and who qualify and wish to trial a course of an alternate bDMARD may do so without having to have any treatment-free period.

To avoid confusion, an application for a patient who wishes to swap to an alternate bDMARD should be accompanied by the approved authority prescription or remaining repeats for the bDMARD the patient is ceasing.

Note:

(3) Baseline measurements to determine response.

Medicare Australia will determine whether a response to treatment has been demonstrated based on the baseline measurements of the joint count, ESR and/or CRP submitted with the first authority application for a bDMARD. However, prescribers may provide new baseline measurements any time that an initial treatment authority application is submitted within a Treatment Cycle and Medicare Australia will assess response according to these revised baseline measurements.

To ensure consistency in determining response, the same indices of disease severity used to establish baseline at the commencement of treatment with each initial treatment application must be provided for all subsequent continuing treatment applications. Therefore, where only an ESR or CRP level is provided at baseline, an ESR or CRP level respectively must be provided to determine response. Similarly, where the baseline active joint count is based on total active joints (ie: more than 20 active joints), response will be determined according to a reduction in the total number of active joints. Where the baseline is determined on total number of major joints, the response must be demonstrated on the total number of major joints.

The baseline joint and blood counts should be performed whilst the patient is still on treatment or within one month of ceasing prior treatment.

(4) Re-commencement of treatment after a 5-year break in PBS-subsidised therapy.

A patient who wishes to trial a second or subsequent Treatment Cycle following a break in PBS-subsidised bDMARD therapy of at least 5 years, must requalify for initial treatment with respect to the indices of disease severity. Patients must have received treatment with at least 1 non-biological DMARD, at an adequate dose, for a minimum of 3 months at the time the ESR and/or CRP levels and the active joint count are measured.

(5) Patients 'grandfathered' onto PBS-subsidised treatment with rituximab.

From 1 March 2008, a patient who commenced treatment with rituximab for severe rheumatoid arthritis prior to 7 March 2007 and who was 'grandfathered' on to PBS-subsidised therapy, and who continues to receive treatment in the same Treatment Cycle, will have further applications for treatment with rituximab assessed under the continuing treatment restriction.

A patient may only qualify for PBS subsidised treatment under this criterion once. A maximum of 24 weeks of treatment with abatacept will be authorised under this criterion.

'Grandfather' arrangements will only apply for the first Treatment Cycle. For the second and subsequent Cycles, a 'grandfather' patient must requalify for initial treatment under the criteria that applies to a new patient. See 'Re-commencement of treatment after a 5-year break in PBS-subsidised therapy' above for further details.

Initial 2 (change or re-commencement)

Application for an initial course of PBS-subsidised treatment with rituximab, in combination with methotrexate at a dose of at least 7.5 mg weekly, by a rheumatologist or clinical immunologist with expertise in the management of rheumatoid arthritis, of an adult who:

(a) has a documented history of severe active rheumatoid arthritis; and

- (b) has failed to respond to at least 1 PBS-subsidised TNF-alfa antagonist in this Treatment Cycle; and
- (c) has not previously failed to respond to PBS-subsidised rituximab in the current Treatment Cycle.

Applications for patients who have demonstrated a response to PBS-subsidised rituximab treatment within this Treatment Cycle and who wish to re-commence rituximab treatment within the same Cycle following a break in therapy, will only be approved where evidence of a response to the patient's most recent course of PBS-subsidised rituximab treatment has been submitted to Medicare Australia.

A patient may qualify to receive a further course of treatment (1 infusion at week 0 and 1 infusion at week 2) every 24 weeks with this agent providing they have demonstrated an adequate response to treatment following a minimum of 12 weeks after the first infusion of their most recent treatment with rituximab. The patient remains eligible to receive a course of rituximab every 24 weeks providing they continue to demonstrate a response as specified in the restriction. The demonstration of response must be submitted to Medicare Australia within 4 weeks of assessment.

The same indices of disease severity used to establish baseline at the commencement of treatment with each initial application must be used for assessment of all continuing applications..

The authority application must be made in writing and must include:

- (1) a completed authority prescription form; and
- (2) a completed Rheumatoid Arthritis PBS Authority Application - Supporting Information Form [<http://www.medicare.gov.au/provider/pbs/drugs/index.shtml>].

Patients who fail to demonstrate a response to treatment with rituximab under this restriction will not be eligible to receive further PBS-subsidised treatment with this drug, in this Treatment Cycle. Patients may re-trial rituximab after a minimum of 5 years have elapsed between the date the last prescription for a PBS-subsidised bDMARD was approved in this Cycle and the date of the first application under the new Cycle.

Patients who fail to demonstrate a response to rituximab treatment and who qualify to trial an alternate bDMARD according to the interchangeability arrangements for bDMARDs for the treatment of severe rheumatoid arthritis, may do so without having to have a 22 week treatment-free period.

Patients who fail to demonstrate a response to treatment with 3 bDMARDs are deemed to have completed this Treatment Cycle and must cease PBS-subsidised therapy. These patients may re-commence a new bDMARD Treatment Cycle after a minimum of 5 years has elapsed between the date the last prescription for a PBS-subsidised bDMARD was approved in this Cycle and the date of the first application under the new Cycle.

Public hospital authority required

Initial 3 ('grandfather' patients)

Initial PBS-subsidised supply for continuing treatment with rituximab, in combination with methotrexate at a dose of at least 7.5 mg weekly, by a rheumatologist or clinical immunologist with expertise in the management of rheumatoid arthritis, of an adult who:

- (a) has a documented history of severe active rheumatoid arthritis; and
- (b) was receiving treatment with rituximab prior to 7 March 2007; and
- (c) has demonstrated a response as specified in the criteria for continuing PBS-subsidised treatment with rituximab.

The authority application must be made in writing and must include:

- (1) a completed authority prescription form; and
- (2) a completed Rheumatoid Arthritis PBS Authority Application - Supporting Information

Form [<http://www.medicare.gov.au/provider/pbs/drugs/index.shtml>] which includes the signed patient acknowledgement form.

The same indices of disease severity used to establish baseline at the commencement of treatment with a bDMARD must be used for assessment of all continuing applications.

Patients who fail to demonstrate a response to treatment with 3 bDMARDs are deemed to have completed this Treatment Cycle and must cease PBS-subsidised therapy. These patients may re-commence a new bDMARD Treatment Cycle after a minimum of 5 years has elapsed between the date the last prescription for a PBS-subsidised bDMARD was approved in this Cycle and the date of the first application under the new Cycle.

Patients can qualify for PBS-subsidised treatment under this criteria once only.

Public hospital authority required

Continuing treatment

Continuing PBS-subsidised treatment with rituximab, in combination with methotrexate at a dose of at least 7.5 mg weekly, by a rheumatologist or clinical immunologist with expertise in the management of rheumatoid arthritis, of an adult:

- (a) who has a documented history of severe active rheumatoid arthritis; and
- (b) who has demonstrated an adequate response to treatment with rituximab; and
- (c) whose most recent course of PBS-subsidised bDMARD treatment in this Treatment Cycle was with rituximab..

An adequate response to treatment is defined as:

an ESR no greater than 25 mm per hour or a CRP level no greater than 15 mg per L or either marker reduced by at least 20% from baseline;

AND either of the following:

- (i) a reduction in the total active (swollen and tender) joint count by at least 50% from baseline, where baseline is at least 20 active joints; or
- (ii) a reduction in the number of the following major active joints, from at least 4, by at least 50%:
 - elbow, wrist, knee and/or ankle (assessed as swollen and tender); and/or
 - shoulder and/or hip (assessed as pain in passive movement and restriction of passive movement, where pain and limitation of movement are due to active disease and not irreversible damage such as joint destruction or bony overgrowth)..

The authority application must be made in writing and must include:

- (1) a completed authority prescription form; and
- (2) a completed Rheumatoid Arthritis PBS Authority Application - Supporting Information Form [<http://www.medicare.gov.au/provider/pbs/drugs/index.shtml>].

Patients may qualify to receive a further course of treatment (every 24 weeks) with this agent providing they have demonstrated an adequate response to treatment following a minimum of 12 weeks after the first infusion of their most recent treatment with rituximab. The patient remains eligible to receive a course of rituximab every 24 weeks providing they continue to demonstrate a response as specified in the restriction. The demonstration of response must be submitted to Medicare Australia within 4 weeks of assessment.

The same indices of disease severity used to establish baseline at the commencement of treatment with each initial application must be used for assessment of all continuing applications.

Patients who fail to demonstrate a response to treatment with 3 bDMARDs are deemed to have completed this Treatment Cycle and must cease PBS-subsidised therapy. These patients may re-commence a new bDMARD Treatment Cycle after a minimum of 5 years has elapsed between the date the last prescription for a PBS-subsidised bDMARD was approved in this Cycle and the date of the first application under the new Cycle.