

INFLIXIMAB

NOTE:

Any queries concerning the arrangements to prescribe infliximab 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 infliximab 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 www.medicareaustralia.gov.au

NOTE:

TREATMENT OF ADULT PATIENTS WITH ACTIVE ANKYLOSING SPONDYLITIS

The following information applies to the prescribing under the Pharmaceutical Benefits Scheme (PBS) of adalimumab, etanercept and infliximab for adult patients with active ankylosing spondylitis. Where the term 'tumour necrosis factor (TNF) alfa antagonist' appears in the following NOTES and restrictions, it refers to adalimumab, etanercept and infliximab only.

A patient is eligible for PBS-subsidised treatment with only 1 of the 3 TNF-alfa antagonists at any 1 time.

From 1 March 2007, under the PBS, all patients will be able to commence a treatment cycle where they may trial each PBS-subsidised TNF-alfa antagonist without having to experience a disease flare when swapping to the alternate agent. Under these interchangeability arrangements, within a single treatment cycle, a patient may continue to receive long-term treatment with a TNF-alfa antagonist while they continue to show a response to therapy.

A patient who received PBS-subsidised TNF-alfa antagonist treatment prior to 1 March 2007 is considered to be in their first cycle as of 1 March 2007.

Within the same treatment cycle, a patient cannot trial and fail, or cease to respond to, the same PBS-subsidised TNF-alfa antagonist more than once.

A patient who, prior to 1 March 2007, was authorised to receive PBS-subsidised initial treatment for ankylosing spondylitis with the same agent twice, is exempt from this condition in respect of applications approved prior to 1 March 2007.

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 TNF-alfa antagonist therapy before they are eligible to commence the next cycle. The 5-year break is measured from the date of the last approval for PBS-subsidised TNF-alfa antagonist treatment in the most recent cycle to the date of the first application for initial treatment with a TNF-alfa antagonist under the new treatment cycle.

A patient who has failed fewer than 3 TNF-alfa antagonists 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 TNF-alfa antagonists 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.

How to prescribe PBS-subsidised TNF-alfa antagonist therapy after 1 March 2007.

(1) (a) Initial treatment.

Applications for initial treatment should be made where:

- (i) a patient has received no prior PBS-subsidised TNF-alfa antagonist treatment in this treatment cycle and wishes to commence such therapy (Initial 1); or
- (ii) a patient has received prior PBS-subsidised (initial or continuing) TNF-alfa antagonist 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 TNF-alfa antagonist following a break in PBS-subsidised therapy with that agent (Initial 2).

Initial treatment authorisations will be limited to provide for a maximum of 16 weeks of therapy for etanercept and adalimumab and 18 weeks of treatment for infliximab.

From 1 March 2007, a patient must be assessed for response to any course of initial PBS-subsidised treatment 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.

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 TNF-alfa antagonist.

For second and subsequent courses of PBS-subsidised TNF-alfa antagonist 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 posted to Medicare Australia no later than 2 weeks prior to the patient completing their current treatment course.

(1) (b) Continuing treatment.

Following the completion of an initial treatment course with a specific TNF-alfa antagonist, 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 TNF-alfa antagonist 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 TNF-alfa antagonist 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. 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 TNF-alfa antagonist.

(2) Swapping therapy.

Once initial treatment with the first PBS-subsidised TNF-alfa antagonist is approved, a patient may swap to an alternate TNF-alfa antagonist 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 BASDAI), or the prior NSAID therapy and exercise program requirements.

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

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.

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

(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 BASDAI, ESR and/or CRP submitted with the first authority application for a TNF-alfa antagonist. 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.

For a new patient, the BASDAI used to determine the baseline must be measured while the patient is receiving NSAID therapy and completing their exercise program. However, this is not required for any subsequent BASDAI results for these patients, nor for patients who were 'grandfathered' on to TNF-alfa antagonist treatment.

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.

(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 TNF-alfa antagonist 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 NSAID, at an adequate dose, for a minimum of 3 consecutive months immediately prior to the time the BASDAI, ESR and/or CRP levels are measured.

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

From 1 March 2007, a patient who commenced treatment with infliximab for active ankylosing spondylitis prior to 1 March 2004 and who was 'grandfathered' onto PBS-subsidised therapy, and who continues to receive treatment in the same treatment cycle, will have further applications for treatment with infliximab assessed under the continuing treatment restriction.

Where pre-TNF-alfa antagonist treatment baselines were not provided, the following criteria must be met to demonstrate a response to treatment:

The BASDAI score must be either:

- (i) no more than 20% greater than the score included in the initial application for PBS-subsidised treatment; or
- (ii) no greater than 2. AND

One of the following:

- (a) an ESR measurement no greater than 25 mm per hour; or
- (b) a CRP measurement no greater than 10 mg per L.

'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 apply to a new patient. See 'Re-commencement of treatment after a 5-year break in PBS-subsidised therapy' above for further details.

Public hospital authority required

Initial 1 (new patients)

First course of PBS-subsidised treatment with infliximab, by a rheumatologist, of an adult with active ankylosing spondylitis who has radiographically (plain X-ray) confirmed Grade II bilateral sacroiliitis or Grade III unilateral sacroiliitis and who has not received any PBS-

subsidised treatment with either adalimumab, etanercept or infliximab in this treatment cycle;
AND

(a) who has at least 2 of the following:

(i) low back pain and stiffness for 3 or more months that is relieved by exercise but not by rest; or

(ii) limitation of motion of the lumbar spine in the sagittal and the frontal planes as determined by a score of at least 1 on each of the lumbar flexion and lumbar side flexion measurements of the Bath Ankylosing Spondylitis Metrology Index (BASMI) [for further information on the BASMI please refer to the Medicare Australia website at www.medicareaustralia.gov.au]; or

(iii) limitation of chest expansion relative to normal values for age and gender [for chest expansion normal values please refer to the Medicare Australia website at

www.medicareaustralia.gov.au]; AND

(b) who has failed to achieve an adequate response following treatment with at least 2 non-steroidal anti-inflammatory drugs (NSAIDs), whilst completing an appropriate exercise program, for a total period of 3 months.

The application must include details of the NSAIDs trialled, their doses and duration of treatment. If the NSAID dose is less than the maximum recommended dose in the relevant TGA-approved Product Information, the application must include the reason a higher dose cannot be used.

If treatment with NSAIDs is contraindicated according to the relevant TGA-approved Product Information, the application must provide details of the contraindication.

If intolerance to NSAID treatment develops during the relevant period of use which is of a severity to necessitate permanent treatment withdrawal, the application must provide details of the nature and severity of this intolerance. Details of the toxicities, including severity, which will be accepted for the purposes of administering this restriction can be found on the Medicare Australia website [www.medicareaustralia.gov.au].

For details on the appropriate minimum exercise program that will be accepted for the purposes of administering this restriction, please refer to the Medicare Australia website at www.medicareaustralia.gov.au.

The following criteria indicate failure to achieve an adequate response and must be demonstrated at the time of the initial application:

(a) a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) of at least 4 on a 0-10 scale; AND

(b) an elevated erythrocyte sedimentation rate (ESR) greater than 25 mm per hour or a C-reactive protein (CRP) level greater than 10 mg per L.

The BASDAI must be determined at the completion of the 3 month NSAID and exercise trial, but prior to ceasing NSAID treatment. The BASDAI must be no more than 1 month old at the time of initial application.

Both ESR and CRP measures should be provided with the initial treatment application and both must be no more than 1 month old. If the above requirement to demonstrate an elevated ESR or CRP cannot be met, the application must state the reason this criterion cannot be satisfied.

Authority applications must be made in writing and must include:

(a) a completed authority prescription form; and

(b) a completed Ankylosing Spondylitis PBS Authority Application - Supporting Information Form [www.medicareaustralia.gov.au] which must include the following:

(i) a copy of the radiological report confirming Grade II bilateral sacroiliitis or Grade III unilateral sacroiliitis; and

(ii) a completed BASDAI Assessment Form [www.medicareaustralia.gov.au]; and

(iii) a completed Exercise Program Self Certification Form included in the supporting information form; and

(iv) a signed patient acknowledgment form. Completion of this form declares that the patient understands and acknowledges that PBS-subsidised treatment with the TNF-alfa antagonists (adalimumab, etanercept or infliximab) for ankylosing spondylitis will cease if they do not demonstrate the response to treatment required to support continuation of PBS-subsidised treatment at any assessment where a response must be demonstrated.

The assessment of the patient's response to the initial course of treatment must be made following a minimum of 12 weeks of treatment and submitted to Medicare Australia no later than 4 weeks from the cessation of that treatment course. If the response assessment is not submitted within these timeframes, the patient will be deemed to have failed this course of treatment.

A maximum of 18 weeks of treatment with infliximab will be approved under this criterion. At the time of the authority application, the doctor should request the appropriate number of vials, based on the weight of the patient, to provide for a single infusion at a dose of 5 mg per kg. Up to a maximum of 3 repeats will be authorised. Where fewer than 3 repeats are initially requested with the authority prescription, authority approvals for sufficient repeats to complete a maximum of 18 weeks of treatment may be requested by telephone.

Public hospital authority required

Initial 2 (change or re-commencement for all patients)

Initial course of PBS-subsidised treatment with infliximab, by a rheumatologist, of an adult with a documented history of active ankylosing spondylitis who, in this treatment cycle, has received prior PBS-subsidised treatment with either adalimumab, etanercept or infliximab for this condition and has not failed PBS-subsidised therapy with infliximab.

To demonstrate a response to treatment the application must be accompanied by the results of the most recent course of TNF-alfa antagonist therapy within the timeframes specified in the relevant restriction.

Where the most recent course of PBS-subsidised TNF-alfa antagonist treatment was approved under an initial treatment restriction after 1 March 2007, the patient must have been assessed for response to that course following a minimum of 12 weeks of treatment. Where the most recent course of PBS-subsidised TNF-alfa antagonist treatment was approved under an initial treatment restriction prior to 1 March 2007, the patient must have been assessed for response to that course following at least 4 weeks of treatment. These assessments must be provided to Medicare Australia no later than 4 weeks from the date the course was ceased.

If the response assessment to the previous course of TNF-alfa antagonist treatment is not submitted as detailed above, the patient will be deemed to have failed therapy with that particular course of TNF-alfa antagonist.

Authority applications must be made in writing and must include:

- (a) a completed authority prescription form; and
- (b) a completed Ankylosing Spondylitis PBS Authority Application - Supporting Information Form [www.medicareaustralia.gov.au] which includes a completed BASDAI Assessment Form with certification by the prescriber and the patient that the patient did not have access to their baseline BASDAI at the time of their assessment.

A maximum of 18 weeks of treatment with infliximab will be approved under this criterion. At the time of the authority application, the doctor should request the appropriate number of vials, based on the weight of the patient, to provide for a single infusion at a dose of 5 mg per kg. Up to a maximum of 3 repeats will be authorised. Where fewer than 3 repeats are initially requested with the authority prescription, authority approvals for sufficient repeats to complete a maximum of 18 weeks of treatment may be requested by telephone.

Public hospital authority required

Continuing treatment for all patients

Continuing PBS-subsidised treatment, by a rheumatologist, of an adult with a documented history of active ankylosing spondylitis who:

- (a) has demonstrated a response to treatment with infliximab; and
- (b) whose most recent course of PBS-subsidised therapy in this treatment cycle was with infliximab.

Response is defined as an improvement from baseline of at least 2 of the BASDAI and 1 of the following:

- (a) an ESR measurement no greater than 25 mm per hour; or
- (b) a CRP measurement no greater than 10 mg per L; or
- (c) an ESR or CRP measurement reduced by at least 20% from baseline.

For a 'grandfather' patient who does not have baselines prior to commencing treatment with a TNF-alfa antagonist, see Note 5 for a definition of response to treatment.

Where only 1 acute phase reactant measurement is supplied in the first application for PBS-subsidised treatment, that same marker must be measured and supplied in all subsequent continuing treatment applications.

Where the most recent course of PBS-subsidised TNF-alfa antagonist treatment was approved under an initial treatment restriction after 1 March 2007, the patient must have been assessed for response to that course following a minimum of 12 weeks of treatment. Where the most recent course of PBS-subsidised TNF-alfa antagonist treatment was approved under an initial treatment restriction prior to 1 March 2007, the patient must have been assessed for response to that course following at least 4 weeks of treatment.

Applications for continuing treatment must be made in writing and should be posted to Medicare Australia no less than 2 weeks prior to the completion of the current treatment course.

Written applications for authorisation must include:

- (a) a completed authority prescription form; and
- (b) a completed Ankylosing Spondylitis PBS Authority Application - Supporting Information Form [www.medicareaustralia.gov.au] which includes a completed BASDAI Assessment Form with certification by the prescriber and the patient that the patient did not have access to their baseline BASDAI at the time of their continuing treatment assessment.

All measurements provided must be no more than 1 month old at the time of application.

A maximum of 24 weeks of treatment with infliximab will be authorised under this criterion.

At the time of the authority application, the doctor should request the appropriate number of vials, based on the weight of the patient, to provide for a single infusion at a dose of 5 mg per kg. Up to a maximum of 3 repeats will be authorised.

Where fewer than 3 repeats are initially requested with the authority prescription, authority approvals for sufficient repeats to complete a maximum of 24 weeks of treatment may be requested by telephone.

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