

4.04 ETANERCEPT

Injection 50 mg in 1 mL single use auto-injector, 4, Injection 50 mg in 1 mL single use pre-filled syringes, 4, Erelzi[®], Sandoz Pty Ltd

1 Purpose of Application

- 1.1 The minor submission sought listing of a new biosimilar brand of etanercept (Erelzi[®]) for all indications for which the reference brand Enbrel[®] is currently PBS listed.

2 Requested listing

- 2.1 The submission requested listing for 50 mg pre-filled syringe and 50 mg auto-injector forms of Erelzi for the following indications for which the reference brand Enbrel is currently PBS listed:
- Severe active rheumatoid arthritis – S85 General Schedule
 - Severe psoriatic arthritis - S85 General Schedule
 - Ankylosing spondylitis - S85 General Schedule
 - Severe chronic plaque psoriasis - S85 General Schedule
 - Juvenile severe chronic plaque psoriasis - S85 General Schedule
 - Severe active juvenile idiopathic arthritis – S85 General Schedule (patients aged 18 years and over) S100 Highly Specialised Drugs (HSD) Program (patients under 18 years of age)
- 2.2 The submission requested that Erelzi be ‘a’ flagged with Enbrel.
- 2.3 The submission requested listing under the same conditions as the current listings for the Brenzys[®] brand of etanercept for the adult indications, which includes Authority Required (STREAMLINED) listings for subsequent continuing treatment.
- 2.4 There are currently no biosimilar brands listed for the juvenile indications. The submission requested that for the juvenile indications, Erelzi be limited to patients weighing over 62.5kg as etanercept requires weight-based dosing for patients under that weight threshold, and Erelzi is not available in a suitable dose form for patients weighing less than 62.5kg. The submission proposed that biosimilar uptake drivers be applied to listings of Erelzi for the juvenile indications. The submission did not propose full restriction wording for these indications.

For more detail on PBAC's view, see section 7 PBAC outcome.

3 Background

- 3.1 The Erelzi brand of etanercept was TGA registered on 30 November 2017. 25 mg and 50 mg pre-filled syringe forms are available. The sponsor has not requested PBS listing of the 25 mg dose form.
- 3.2 The PBAC has not previously considered an application for this brand of etanercept.
- 3.3 At its August 2017 meeting, the PBAC considered an application from the sponsor of another biosimilar etanercept, Brenzys, which requested a range of biosimilar uptake drivers be applied to the listings for etanercept. The PBAC advised that there would not be clinical or other concerns about appropriate use of medicines if a policy decision were made to lower the authority requirement for only the biosimilar brand of etanercept under certain conditions. These conditions included¹:
- All initial treatment restrictions for etanercept, including those for new patients, patients changing treatment and recommencing treatment, should remain Authority Required (in writing) listings;
 - Continuing restrictions for etanercept could be split into first continuing and subsequent continuing restrictions, with first continuing restrictions to remain Authority required (in writing), retaining response to treatment criteria that currently exist in continuing restrictions, whilst subsequent continuing restrictions be Authority Required (STREAMLINED) listings;
 - The PBAC recommended that subsequent continuing restrictions for etanercept retain the requirement for patients to be responding to treatment, but noted that being an Authority Required (STREAMLINED) listing, no evidence of response would be provided to the Department of Human Services (DHS) at time of prescribing, rather that ongoing treatment response would be documented in the patient's medical notes.
- 3.4 These changes to etanercept listings were implemented on 1 December 2017. As an additional biosimilar brand, the PBAC may wish to consider whether there would be clinical or other concerns about appropriate use of medicines if a policy decision were made to lower the authority requirement for only the biosimilar brand(s) of etanercept for the juvenile indications.

¹ August 2017 PBAC, Etanercept (Brenzys) Public Summary Document. Available at [PBAC PSD website](#)

Brand equivalence and brand substitution at the pharmacist level ('a' flagging)

- 3.5 The Schedule of Pharmaceutical Benefits provide the following definition of brand equivalence:

Extract from the Explanatory Notes to the PBS Schedule²

BRAND EQUIVALENCE

'a' located immediately before brand names of a particular strength of an item indicates that the sponsors of these brands have submitted evidence that they have been demonstrated to be bioequivalent or therapeutically equivalent, or that justification for not needing bioequivalence or therapeutic equivalence data has been provided to and accepted by the Therapeutic Goods Administration. It would thus be expected that these brands may be interchanged without differences in clinical effect.

- 3.6 Many medicines are available on the PBS in different brands. The Schedule of Pharmaceutical Benefits indicates where different brands are considered equivalent for the purposes of substitution at the point of dispensing by using "a" flags.
- 3.7 The ability for prescribers and pharmacists to substitute generic brands for originator brands is an important part of encouraging use of generics in the marketplace and adds to the sustainability of the PBS.
- 3.8 For any individual prescription, a prescriber may choose to not permit brand substitution by indicating 'substitution not permitted' on the prescription. Likewise, when substitution is permitted, a patient may nominate which "a" flagged brand they wish to receive from the pharmacist, except when State or Territory Law prohibits substitution (e.g. for Schedule 8 drugs of dependence). The substitution process allows for patient and prescriber choice and is not automatic.
- 3.9 The *National Health Act 1953* ("The Act") makes it an offence for a pharmacist to supply a pharmaceutical benefit other than the benefit directed to be supplied in a prescription except when, amongst other criteria, the Schedule issued by the Department of Health states that the specified benefit and the substitute benefit are equivalent.
- 3.10 At the March 2018 meeting, the PBAC advised that the following revised considerations will be used to make a recommendation on brand equivalence ('a' flagged) of biosimilars with the reference brand;

² Symbols used in the Schedule - <http://www.pbs.gov.au/info/healthpro/explanatory-notes/section2/section-2-symbols>

- The Therapeutic Goods Administration has determined that the product is a biosimilar of the reference medicine as evidenced by ARTG registration documentation;
 - Availability of supportive data relating to the effects of switching between the reference product and the biosimilar product/s; and
 - Practical considerations relating to substitution by the pharmacist at the point of dispensing. This includes strength of formulation, number of units per pack and maximum quantities between the brands, which may make substitution at the pharmacy level difficult from a practical perspective.
- 3.11 The PBAC considered that where a biosimilar product could not be recommended to be brand equivalent ('a' flagged) at the time of PBS listing, data should be collected to support this consideration at a later point.
- 3.12 After the PBAC provides advice, the decision to apply brand equivalence ('a' flagging) to listings in the Schedule is made by the Minister for Health (or Delegate).

4 Comparator

- 4.1 The minor submission nominated originator brand etanercept (Enbrel) as the comparator, which was appropriate.

For more detail on PBAC's view, see section 7 PBAC outcome.

5 Consideration of the evidence

Sponsor hearing

- 5.1 There was no hearing for this item as it was a minor submission.

Consumer comments

- 5.2 The PBAC noted that no consumer comments were received for this item.

Clinical trials

- 5.3 The sponsor supported its TGA application with bioequivalence and equivalence studies that compared the Erelzi brand to the originator brand, Enbrel. This included four pharmacokinetic studies (in healthy subjects), and one pivotal efficacy trial comparing the Erelzi and Enbrel brands of etanercept in moderate-to-severe chronic plaque psoriasis.

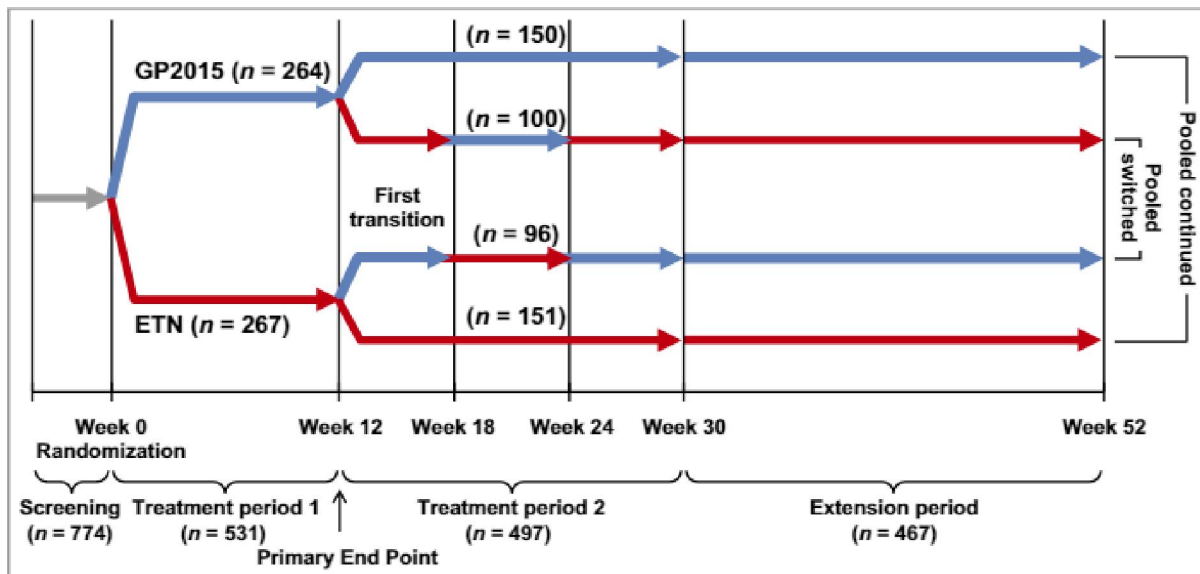
Table 1: Trials and associated reports presented in the submission

Trial ID/First Author	Protocol title/ Publication title	Publication citation
Direct randomised trial(s)		
GP15-302 (EGALITY)	Study to Demonstrate Equivalent Efficacy and to Compare Safety of Biosimilar Etanercept (GP2015-302) and Enbrel (EGALITY) The EGALITY study: a confirmatory, randomized, double-blind study comparing the efficacy, safety and immunogenicity of GP2015, a proposed etanercept biosimilar, vs. the originator product in patients with moderate-to-severe chronic plaque-type psoriasis	British Journal of Dermatology. 1 March 2017, pp 928-938. Published Online: Br J Dermatol Doi: doi:10.1111/bjd.15152

Source: Submission (main body); Publication not included with submission, available online at British Journal of Dermatology.

- 5.4 The minor submission did not present the results of the study in a summarised form; however summaries of clinical efficacy and safety from the Clinical Study Report (CSR) were included as attachments to the submission.
- 5.5 The EGALITY study recruited 531 patients, of which 264 were randomised to Erelzi and 267 were randomised to Enbrel. The study included multiple switches between starting and alternative therapy. The first switch occurred at week 12 (following the primary endpoint) with additional switches at weeks 18, 24 and 30 as shown in Figure 1 below.

Figure 1: Patient allocation and treatment switches over 52 weeks of etanercept treatment



Source: CEM Griffiths, et al. The EGALITY study: a confirmatory, randomized, double-blind study comparing the efficacy, safety and immunogenicity of GP2015, a proposed etanercept biosimilar, vs. the originator product in patients with moderate-to-severe chronic plaque-type psoriasis. British Journal of Dermatology. 1 March 2017, p 930.

Comparative effectiveness

5.6 The TGA Delegate and ACM considered the comparative effectiveness of the Erelzi brand of etanercept as part of its application for Australian Registration.

5.7 With respect to the comparative effectiveness of Erelzi, the ACM considered the following³:

- The ACM noted one Phase 3 Study (GP15-302) in adults with plaque psoriasis to evaluate the efficacy and safety of Erelzi compared with the innovator (Enbrel). Clinical equivalence was demonstrated within the definition of the study including an equivalence margin of 18% used to test the primary variable (proportion of Psoriasis Area and Severity Index [PASI] responders at Week 12) and a margin of 15% used for the secondary variable (PASI percentage improvement from baseline to Week 12).
- The ACM noted the lack of any clinical data from the paediatric population. The ACM also noted previous discussions about the evaluation of biosimilar products and discussed the application of the most recent TGA and EMA guidelines (2015) on biosimilar products to the consideration of this application. The ACM recommended that the indications (i) polyarticular juvenile idiopathic arthritis (children and adolescents 2 to 17 years); and (ii) paediatric plaque psoriasis (children and adolescents 4 to 17 years) be removed. This was due, in part, to the lack of a dose form of Erelzi proposed to be made available for patients weighing less than 62.5kg who require weight-based dosing.
- The ACM agreed that the efficacy for plaque psoriasis had been demonstrated, and noted the trial design was strong and the standard outcome of PASI75 at 12 weeks was not statistically significantly different between the two arms of the study. The ACM noted that in the context of similar decisions made in relation to biosimilars, Erelzi is non-inferior to Enbrel for the plaque psoriasis indication.
- The ACM considered the principle of extrapolation has been established for other biosimilars and that there was sufficient evidence to support extrapolation of the data in patients with plaque psoriasis to the other indications.

Comparative harms

5.8 The TGA Delegate and ACM considered the comparative safety of the Erelzi brand of etanercept as part of its application for Australian Registration.

5.9 With respect to the comparative safety of Erelzi, the ACM considered the following⁴:

³ Therapeutic Goods Administration (2017). Advisory Committee on Medicines (ACM) Ratified minute of meeting 5, 5-6 October 2017 (unpublished).

- The ACM noted the safety profiles from the Phase 3 study and from other data in the application for adults do not demonstrate any clear toxicity difference between the two products, including the short two-way switching phase in the study. However, the ACM also noted that the overall frequency of adverse effects was higher with Erelzi compared to Enbrel and that the pattern of some adverse events appeared slightly different between treatment groups. It was noted, however, that the sample size was small and safety issues in larger numbers and in the longer term are unknown. The ACM also noted the lack of any safety data from the paediatric population.

5.10 Treatment-emergent adverse events (TEAEs), serious adverse events (SAEs), treatment-related TEAEs and discontinuations due to adverse events were similar between the continued and switched Erelzi and Enbrel groups were similar as shown in the table below.

Table 2: Summary of treatment emergent adverse events (TEAE) up to week 52 for continued and switched groups

Treatment group	Continued Erelzi N = 164 n (%)	Continued Enbrel N = 171 n (%)	Switched Erelzi N = 100 n (%)	Switched Enbrel N = 96 n (%)
Any TEAE	98 (59.8)	98 (57.3)	61 (61)	57 (59.4)
Any SAE	7 (4.3)	7 (4.1)	6 (6.0)	6 (6.3)
Any treatment-related TEAE	34 (20.7)	33 (19.3)	22 (22.0)	20 (20.8)
Discontinuation due to TEAE	11 (6.7)	8 (4.7)	2 (2.0)	5 (5.2)

Source: CEM Griffiths, et al. The EGALITY study: a confirmatory, randomized, double-blind study comparing the efficacy, safety and immunogenicity of GP2015, a proposed etanercept biosimilar, vs. the originator product in patients with moderate-to-severe chronic plaque-type psoriasis. *British Journal of Dermatology*. 1 March 2017, p 935.

5.11 The study found five patients (1.9) in the Enbrel group had confirmed non-neutralising anti-drug antibodies (ADAs) during the early weeks of the trial, and one patient in the subsequent switched Enbrel group showed confirmed non-neutralising anti-drug antibodies at week 36. No ADAs were found in the Erelzi group.

Clinical claim

5.12 The submission described Erelzi as a biosimilar etanercept, and equivalent in terms of comparative effectiveness and equivalent in terms of comparative safety to Enbrel.

⁴ Therapeutic Goods Administration (2017). Advisory Committee on Medicines (ACM) Ratified minute of meeting 5, 5-6 October 2017 (unpublished)

- 5.13 The ACM considered the principle of extrapolation has been established for other biosimilars and that there was sufficient evidence to support extrapolation of the data in patients with plaque psoriasis to the other adult indications for which Erelzi was seeking TGA registration, including rheumatoid arthritis, psoriatic arthritis, plaque psoriasis, ankylosing spondylitis and non-radiographic axial spondyloarthritis.
- 5.14 The ACM noted the lack of clinical data from paediatric populations and recommended that Erelzi not be registered for juvenile idiopathic arthritis or paediatric plaque psoriasis. The Delegate, however, decided to grant registration to Erelzi for the paediatric indications, with restrictions in the approved PI noting that patients weighing less than 62.5kg should be accurately dosed on a mg/kg basis with other etanercept products.
- 5.15 The PBAC noted the ACM had declared the Erelzi brand of etanercept to be a biosimilar of the reference brand, Enbrel, and considered the claim of non-inferior comparative efficacy and safety was therefore adequately supported.

Estimated PBS usage & financial implications

- 5.16 As an additional brand of etanercept, the submission requested Erelzi be priced at the same amount as existing listings for other brands of etanercept.
- 5.17 The minor submission estimated there to be no financial implications to the PBS/changes in PBS usage as the submission expects Erelzi to only substitute for other brands of etanercept. As such, a full breakdown of expected utilisation and financial implications was not included as part of the submission and has not been presented.

For more detail on PBAC's view, see section 7 PBAC outcome.

6 PBAC Outcome

- 6.1 The PBAC recommended the listing of the Erelzi brand of etanercept for the same indications as the reference brand Enbrel, including juvenile idiopathic arthritis (JIA) and juvenile plaque psoriasis (JPP). In making this recommendation, the PBAC noted the TGA Advisory Committee for Medicines (ACM) has declared Erelzi to be a biosimilar of the reference brand, Enbrel.
- 6.2 The PBAC advised the Minister that, under Section 101(4AACD) of the National Health Act, 1953 the Erelzi, Brenzys and Enbrel brands of etanercept could be marked as equivalent in the Schedule of Pharmaceutical Benefits.
- 6.3 The PBAC noted the equi-effective doses for the biosimilar and reference brands were 50 mg Erelzi = 50 mg Enbrel.
- 6.4 The PBAC was also of a mind to recommend the 25 mg pre-filled syringe form of

Erelzi had that form been part of the application, and noted that this form was TGA registered and some patients may benefit from the availability of an alternative 25 mg form of etanercept, and considered it may be appropriate to explore the potential PBS listing of this form with the sponsor.

- 6.5 The PBAC considered it was appropriate for biosimilar uptake drivers to be applied to this brand of etanercept and the listings for Erelzi should align with the current listings for the Brenzys brand of etanercept for the adult indications (rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis and plaque psoriasis), and include a streamlined authority listing for subsequent continuing prescribing and include a note in the restriction regarding biosimilar uptake.
- 6.6 With regards to the juvenile indications (JIA and JPP), the PBAC noted the Brenzys brand was not listed for these indications. The PBAC noted the Erelzi brand was TGA registered for these indications and recommended that similar to the adult indications, the restrictions for JIA and JPP be remodelled to facilitate the application of biosimilar uptake drivers to Erelzi listings for these indications under the following parameters:
- For JIA, Authority Required listings for initial and first continuing restrictions, and Authority Required (STREAMLINED) listings for subsequent continuing prescribing, similar to the current structure of etanercept listings for the adult indications, including for the JIA listings in Section 100 (Highly Specialised Drugs Program – Public and Private Hospital);
 - For JPP, the PBAC noted the restrictions are structured differently to the other indications, with no continuing restrictions, and patients are able to access an initial supply for etanercept for induction of remission, and are later able to access re-treatment cycles as required. Given the difference in restriction structure, the PBAC considered it was appropriate to retain the Authority Required restriction for JPP for initial treatment, and to lower the authority level for re-treatment restrictions to a streamlined authority listing;
 - Similar to existing Enbrel listings for juvenile indications, a note regarding patient weight does not need to be included in the PBS restrictions as weight-based dosing protocols are documented in the approved Product Information (PI).
 - The PBAC noted at present there is a difference in the maximum number of repeats between the General Schedule and Section 100 listings for JIA and considered the number of repeats for the Section 100 listings could be aligned with the General Schedule listings; and

- A note encouraging prescribing of the biosimilar to treatment naïve patients, similar to existing Brenzys listings, would be appropriate for the juvenile indications.
- 6.7 The PBAC noted the pivotal trial (EGALITY) was a randomised, double-blind trial of 531 patients in moderate-to-severe plaque psoriasis with a 52 week duration and included groups with multiple switches between reference and biosimilar brands. The PBAC noted there were no clear differences in toxicity between Erelzi and Enbrel, however noted the trial was likely too small to detect large differences in adverse events between groups. The PBAC also noted no safety data from the paediatric population was available.
- 6.8 The PBAC agreed with the submission claim that Erelzi would only substitute for other etanercept brands was appropriate and considered the listing of an additional biosimilar would not grow the overall market for etanercept or the overall biologic market.
- 6.9 The PBAC recommended that the Early Supply Rule should apply, and considered this should be flowed onto existing etanercept listings for the juvenile indications, including those in Section 100 (Highly Specialised Drugs Program – Public and Private Hospital).
- 6.10 The PBAC noted the restrictions for the juvenile indications would require substantial remodelling to facilitate the implementation of biosimilar uptake drivers.
- 6.11 The PBAC noted the submission is not eligible for an Independent Review as it received a positive recommendation.

Outcome:

Recommended

7 Recommended listing

7.1 Add new item:

Etanercept, Injection 50 mg in 1 mL single use auto-injector, 4; Injection 50 mg in 1 mL single use pre-filled syringes, 4

Restrictions same as Brenzys brand of etanercept for adult indications.

Adult indications:

Severe active rheumatoid arthritis – S85 General Schedule

Severe psoriatic arthritis - S85 General Schedule

Ankylosing spondylitis - S85 General Schedule

Severe chronic plaque psoriasis - S85 General Schedule

Amend the note regarding biosimilar policy as below:

Note

Biosimilar prescribing policy: Prescribing of the biosimilar brands Brenzys or Erelzi are encouraged for treatment naive patients.

Encouraging biosimilar prescribing for treatment naive patients is Government policy. A viable biosimilar market is expected to result in reduced costs for biological medicines, allowing the Government to reinvest in new treatments. Further information can be found on the Biosimilar Awareness Initiative webpage (www.health.gov.au/biosimilars).

Restrictions for juvenile indications are to be finalised.

Juvenile indications:

Juvenile severe chronic plaque psoriasis - S85 General Schedule

Severe active juvenile idiopathic arthritis – S85 General Schedule (patients aged 18 years and over) S100 Highly Specialised Drugs (HSD) Program (patients under 18 years of age)

Appendix A: Juvenile Idiopathic Arthritis Secretariat Proposed Restrictions

The Secretariat proposes the following remodelled restrictions for juvenile idiopathic arthritis to align the listings for this indication with the recently remodelled adult indications for etanercept.

Table 3: S85 - Initial 1 and 2 Restrictions

Name, Restriction, Manner of administration and form	Max. Qty	№.of Rpts	Proprietary Manufacturer	Name and
ETANERCEPT				
Injection 50 mg in 1 mL single use auto-injector, 4	1	3	Enbrel®	Pfizer Australia Pty Ltd
Injection 50 mg in 1 mL single use pre-filled syringe, 4	1	3	Erelzi®	Sandoz Pty Ltd

Category / Program	GENERAL – General Schedule (Code GE)
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
PBS Indication:	Severe active juvenile idiopathic arthritis

<p>Restriction Level / Method:</p>	<p><input type="checkbox"/> Restricted benefit <input checked="" type="checkbox"/> Authority Required - In Writing <input type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required – Emergency <input type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined</p>
<p>Administrative Advice (Note) (all treatment phases):</p>	<p>TREATMENT OF ADULT PATIENTS WITH A HISTORY OF JUVENILE IDIOPATHIC ARTHRITIS</p> <p>The following information applies to the prescribing under the Pharmaceutical Benefits Scheme (PBS) of adalimumab, etanercept and tocilizumab for a patient over 18 years who has a history of juvenile idiopathic arthritis with onset prior to the age of 18 years. Where the term bDMARD appears in notes and restrictions, it refers to adalimumab, etanercept and tocilizumab only.</p> <p>A patient is eligible for PBS-subsidised treatment with only 1 of the 3 bDMARDs at any one time.</p> <p>From 1 April 2014, a patient receiving PBS-subsidised bDMARD therapy is considered to be in a treatment cycle where they may swap to an alternate bDMARD without having to experience a disease flare. Under these interchangeability arrangements, within a single treatment cycle, a patient may:</p> <p>(i) continue to receive long-term treatment with a PBS-subsidised bDMARD while they continue to show a response to therapy; and</p> <p>(ii) fail to respond or to sustain a response to each PBS-subsidised bDMARD once only.</p> <p>Once a patient has either failed or ceased to respond to PBS-subsidised bDMARD treatment 3 times, they are deemed to have completed a single treatment cycle and they must have, at a minimum, a 5 year break in PBS-subsidised bDMARD therapy before they are eligible to receive further PBS-subsidised bDMARD therapy. The length of a treatment break is measured from the date of the last approval for PBS-subsidised bDMARD therapy in the last treatment cycle to the date of the first application for initial treatment with a bDMARD under the new treatment cycle.</p> <p>A patient who was receiving PBS-subsidised bDMARD treatment immediately prior to 1 April 2014 is considered to be in their first cycle as of 1 April 2014. A patient who has had a break in bDMARD treatment of at least 24 months immediately prior to making a new application, on or after 1 April 2014, will commence a new treatment cycle.</p> <p>A patient who has failed fewer than 3 trials of a bDMARD in a treatment cycle and who has a break in therapy of less than 24 months may commence a further course of treatment within the same treatment cycle.</p> <p>A patient who has failed fewer than 3 trials of a bDMARD in a treatment cycle and who has a break in therapy of more than 24 months must commence a new treatment cycle. The length of the break in therapy is measured from the date the most recent treatment with PBS-subsidised bDMARD treatment was stopped to the date of the first application for initial treatment with a bDMARD under the new treatment cycle.</p> <p>There is no limit to the number of treatment cycles a patient may undertake.</p> <p>(1) How to prescribe PBS-subsidised bDMARD therapy after 1 April 2014.</p>

(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 (Initial 1); or
 - (ii) a patient wishes to re-commence treatment with a bDMARD following a break in PBS-subsidised therapy of more than 24 months (Initial 1); or
 - (iii) 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
- (iv) a patient wishes to re-commence treatment with a specific bDMARD following a break of less than 24 months 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.

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 the Department of Human Services no later than 4 weeks from the date that course was ceased.

Where a response assessment is not submitted to the Department of Human Services 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, it is recommended that a patient is reviewed in the 4 weeks prior to completing their current course of treatment and that an application is posted to the Department of Human Services no later than 2 weeks prior to the patient completing their current treatment course.

(b) Continuing treatment.

Following the completion of an initial treatment course with a specific bDMARD, 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.

A 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 the Department of Human Services no later than 4 weeks from the date that course was ceased.

	<p>Where a response assessment is not submitted to the Department of Human Services within these timeframes, the patient will be deemed to have failed to respond to treatment with that bDMARD.</p> <p>(2) Swapping therapy. Once initial treatment with the first PBS-subsidised bDMARD is approved, a patient may swap to an alternate bDMARD without having to requalify with respect to the indices of disease severity (joint count and ESR/CRP) or the prior non-bDMARD therapy requirements, except if the patient has had a break in therapy of more than 24 months. 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 current 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 bDMARD should be accompanied by the approved authority prescription or remaining repeats for the bDMARD the patient is ceasing.</p> <p>(3) Baseline measurements to determine response. The Department of Human Services will determine whether a response to treatment has been demonstrated based on the baseline measurements of the joint count submitted with the first authority application for a bDMARD. However, prescribers may provide a new baseline measurement any time that an initial treatment authority application is submitted within a treatment cycle and the Department of Human Services will assess response according to the revised baseline measurement.</p> <p>(4) Re-commencement of treatment after a 24 month break in PBS-subsidised therapy. A patient who wishes to start a second or subsequent treatment cycle following a break in PBS-subsidised bDMARD therapy of at least 24 months, must requalify for treatment under the Initial 1 treatment restriction. No increase in the maximum quantity or number of units may be authorised. No increase in the maximum number of repeats may be authorised.</p>
Treatment phase:	Initial 1 (new patient or patient recommencing treatment after a break of more than 24 months)
Treatment criteria:	<ul style="list-style-type: none"> • Must be treated by a rheumatologist; OR • Must be treated by a clinical immunologist with expertise in the management of rheumatoid arthritis.

<p>Clinical criteria:</p>	<ul style="list-style-type: none"> • Patient must have a documented history of severe active juvenile idiopathic arthritis with onset prior to the age of 18 years; AND • Patient must have received no PBS-subsidised treatment with a biological disease modifying anti-rheumatic drug (bDMARD) for this condition in the previous 24 months; OR • Patient must have received no PBS-subsidised bDMARD treatment for at least 5 years if they failed or ceased to respond to PBS-subsidised bDMARD treatment 3 times (once with each agent) in their last treatment cycle; AND • Patient must have failed, in the 24 months immediately prior to the date of the application, to achieve an adequate response to a trial of at least 6 months of intensive treatment with disease modifying anti-rheumatic drugs (DMARDs) which must include at least 3 months continuous treatment with each of at least 2 DMARDs, one of which must be methotrexate at a dose of at least 20 mg weekly and one of which must be: (i) hydroxychloroquine at a dose of at least 200 mg daily; or (ii) leflunomide at a dose of at least 10 mg daily; or (iii) sulfasalazine at a dose of at least 2 g daily; OR • Patient must have failed, in the 24 months immediately prior to the date of the application, to achieve an adequate response to a trial of at least 6 months of intensive treatment with DMARDs which, if methotrexate is contraindicated according to the Therapeutic Goods Administration (TGA)-approved Product Information or cannot be tolerated at a 20 mg weekly dose, must include at least 3 months continuous treatment with each of at least 2 of the following DMARDs: (i) hydroxychloroquine at a dose of at least 200 mg daily; and/or (ii) leflunomide at a dose of at least 10 mg daily; and/or (iii) sulfasalazine at a dose of at least 2 g daily; OR • Patient must have failed, in the 24 months immediately prior to the date of the application, to achieve an adequate response to a trial of at least 6 months of intensive treatment with DMARDs which, if 3 or more of methotrexate, hydroxychloroquine, leflunomide and sulfasalazine are contraindicated according to the relevant TGA-approved Product Information or cannot be tolerated at the doses specified above, must include at least 3 months continuous treatment with each of at least 2 DMARDs, with one or more of the following DMARDs being used in place of the DMARDs which are contraindicated or not tolerated: (i) azathioprine at a dose of at least 1 mg/kg per day; and/or (ii) cyclosporin at a dose of at least 2 mg/kg/day; and/or (iii) sodium aurothiomalate at a dose of 50 mg weekly; AND • Patient must not receive more than 16 weeks of treatment under this restriction.
<p>Population criteria:</p>	<ul style="list-style-type: none"> • Patient must be aged 18 years or older.

<p>Prescriber Instructions:</p>	<p>For the purposes of this restriction 'biological disease modifying anti-rheumatic drug' and 'bDMARD' mean adalimumab, etanercept or tocilizumab.</p> <p>If methotrexate is contraindicated according to the TGA-approved Product Information or cannot be tolerated at a 20 mg weekly dose, the application must include details of the contraindication or intolerance to methotrexate. The maximum tolerated dose of methotrexate must be documented in the application, if applicable.</p> <p>The application must include details of the DMARDs trialled, their doses and duration of treatment, and all relevant contraindications and/or intolerances.</p> <p>The requirement to trial at least 2 DMARDs for periods of at least 3 months each can be met using single agents sequentially or by using one or more combinations of DMARDs.</p> <p>If the requirement to trial 6 months of intensive DMARD therapy with at least 2 DMARDs cannot be met because of contraindications and/or intolerances of a severity necessitating permanent treatment withdrawal to all of the DMARDs specified above, details of the contraindication or intolerance and dose for each DMARD must be provided in the authority application.</p> <p>The following criteria indicate failure to achieve an adequate response and must be demonstrated in all patients at the time of the initial application:</p> <p>an elevated erythrocyte sedimentation rate (ESR) greater than 25 mm per hour or a C-reactive protein (CRP) level greater than 15 mg per L; AND either</p> <p>(a) an active joint count of at least 20 active (swollen and tender) joints; or</p> <p>(b) at least 4 active joints from the following list:</p> <p>(i) elbow, wrist, knee and/or ankle (assessed as swollen and tender); and/or</p> <p>(ii) shoulder, cervical spine 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).</p> <p>The joint count and ESR and/or CRP must be determined at the completion of the 6 month intensive DMARD trial, but prior to ceasing DMARD therapy. All measures must be no more than one month old at the time of initial application.</p> <p>If the above requirement to demonstrate an elevated ESR or CRP cannot be met, the application must state the reasons why this criterion cannot be satisfied.</p> <p>The authority application must be made in writing and must include:</p> <p>(1) a completed authority prescription form; and</p> <p>(2) a completed Juvenile Idiopathic Arthritis PBS Authority Application - Supporting Information Form; and</p> <p>(3) a signed patient acknowledgement.</p> <p>If a patient fails to respond to PBS-subsidised bDMARD treatment 3 times (once with each agent) they will not be eligible to receive further PBS-subsidised bDMARD therapy in this treatment cycle. A patient may re-trial etanercept after a minimum of 5 years have elapsed between the date of the last approval for PBS-subsidised bDMARD therapy in the last treatment cycle and the date of the first application under a new treatment cycle.</p>
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<p>Administrative Advice:</p>	<p>The Department of Human Services website (www.humanservices.gov.au) has details of the toxicities, including severity, which will be accepted for the following purposes:</p> <p>(a) exempting a patient from the requirement to undertake a minimum 3 month trial of methotrexate at a 20 mg weekly dose;</p> <p>(b) substituting azathioprine, cyclosporin or sodium aurothiomalate for another DMARD as part of the 6 month intensive DMARD trial;</p> <p>(c) exempting a patient from the requirement for a 6 month trial of intensive DMARD therapy.</p> <p>Biosimilar prescribing policy <i>Prescribing of the biosimilar brands Brenzys or Erelzi is encouraged for treatment naive patients.</i></p> <p><i>Encouraging biosimilar prescribing for treatment naive patients is Government policy. A viable biosimilar market is expected to result in reduced costs for biological medicines, allowing the Government to reinvest in new treatments. Further information can be found on the Biosimilar Awareness Initiative webpage (www.health.gov.au/biosimilars).</i></p> <p>Any queries concerning the arrangements to prescribe may be directed to the Department of Human Services on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday). Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Department of Human Services website at www.humanservices.gov.au</p> <p>Applications for authority to prescribe should be forwarded to:</p> <p>Department of Human Services Complex Drugs Reply Paid 9826 HOBART TAS 7001</p>
<p>Treatment phase:</p>	<p>Initial 2 (change or recommencement of treatment after break of less than 24 months)</p>
<p>Treatment criteria:</p>	<ul style="list-style-type: none"> • Must be treated by a rheumatologist; <li style="padding-left: 20px;">OR • Must be treated by a clinical immunologist with expertise in the management of rheumatoid arthritis.
<p>Clinical criteria:</p>	<ul style="list-style-type: none"> • Patient must have a documented history of severe active juvenile idiopathic arthritis with onset prior to the age of 18 years, <li style="padding-left: 20px;">AND • Patient must have received prior PBS-subsidised treatment with adalimumab, etanercept or tocilizumab for this condition in this treatment cycle, <li style="padding-left: 20px;">AND • Patient must not have failed PBS-subsidised therapy with etanercept for this condition in the current treatment cycle, <li style="padding-left: 20px;">AND • Patient must not receive more than 16 weeks of treatment under this restriction.
<p>Population criteria:</p>	<ul style="list-style-type: none"> • Patient must be aged 18 years or older.

<p>Prescriber Instructions:</p>	<p>For the purposes of this restriction 'biological disease modifying anti-rheumatic drug' and 'bDMARD' mean adalimumab, etanercept or tocilizumab.</p> <p>The authority application must be made in writing and must include:</p> <p>(1) a completed authority prescription form; and</p> <p>(2) a completed Juvenile Idiopathic Arthritis PBS Authority Application - Supporting Information Form.</p> <p>Applications for a patient who has received PBS-subsidised treatment with etanercept in this treatment cycle and who wishes to recommence therapy with this drug, must be accompanied by evidence of a response to the patient's most recent course of PBS-subsidised etanercept treatment, within the timeframes specified below.</p> <p>Where the most recent course of PBS-subsidised etanercept treatment was approved under either of the Initial 1 or 2 treatment restrictions, the patient must have been assessed for response following a minimum of 12 weeks of therapy. This assessment must be submitted no later than 4 weeks from the date that course was ceased.</p> <p>Where the most recent course of PBS-subsidised etanercept treatment was approved under the continuing treatment criteria, the patient must have been assessed for response, and the assessment must be submitted no later than 4 weeks from the date that course was ceased.</p> <p>Where a response assessment is not undertaken and submitted within these timeframes, the patient will be deemed to have failed to respond to treatment with etanercept.</p> <p>If a patient fails to respond to PBS-subsidised biological disease modifying anti-rheumatic drug (bDMARD) treatment 3 times (once with each agent) they will not be eligible to receive further PBS-subsidised bDMARD therapy in this treatment cycle.</p> <p>An adequate response to treatment is defined as:</p> <p>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;</p> <p>AND either of the following:</p> <p>(a) an active joint count of fewer than 10 active (swollen and tender) joints; or</p> <p>(b) a reduction in the active (swollen and tender) joint count by at least 50% from baseline; or</p> <p>(c) a reduction in the number of the following active joints, from at least 4, by at least 50%:</p> <p>(i) elbow, wrist, knee and/or ankle (assessed as swollen and tender); and/or</p> <p>(ii) shoulder, cervical spine 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).</p>
<p>Administrative advice:</p>	<p>Any queries concerning the arrangements to prescribe may be directed to the Department of Human Services on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday). Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Department of Human Services website at www.humanservices.gov.au</p> <p>Applications for authority to prescribe should be forwarded to:</p> <p>Department of Human Services Complex Drugs Reply Paid 9826 HOBART TAS 7001</p>
<p>Treatment phase:</p>	<p>Initial 1 (new patient or patient recommencing treatment after a break of more than 24 months) or Initial 2 (change or recommencement of treatment after break of less than 24 months) – balance of supply</p>

Treatment criteria:	<ul style="list-style-type: none"> • Must be treated by a rheumatologist; OR • Must be treated by a clinical immunologist with expertise in the management of rheumatoid arthritis.
Clinical criteria:	<ul style="list-style-type: none"> • Must be treated by a rheumatologist; OR • Must be treated by a clinical immunologist with expertise in the management of rheumatoid arthritis. AND • The treatment must provide no more than the balance of up to 16 weeks treatment available under above restrictions.
Administrative advice:	<p>Authority approval for sufficient therapy to complete a maximum of 16 weeks of treatment may be requested by telephone by contacting the Department of Human Services on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday).</p> <p>Written application for authority approval for sufficient therapy to complete a maximum of 16 weeks of treatment should be forwarded to:</p> <p>Department of Human Services Complex Drugs Reply Paid 9826 HOBART TAS 7001</p>

Table 4: S85 - 1st Continuing Restrictions

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Name and Manufacturer
ETANERCEPT Injection 50 mg in 1 mL single use auto-injector, 4	1	5	Enbrel® Pfizer Australia Pty Ltd
Injection 50 mg in 1 mL single use pre-filled syringe, 4	1	5	Erelzi® Sandoz Pty Ltd

Category / Program	GENERAL – General Schedule (Code GE)
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
PBS Indication:	Severe active juvenile idiopathic arthritis
Restriction Level / Method:	<input type="checkbox"/> Restricted benefit <input checked="" type="checkbox"/> Authority Required - In Writing <input type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required – Emergency <input type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined

Administrative Advice (Note) (all treatment phases):	<p>TREATMENT OF ADULT PATIENTS WITH A HISTORY OF JUVENILE IDIOPATHIC ARTHRITIS</p> <p>The following information applies to the prescribing under the Pharmaceutical Benefits Scheme (PBS) of adalimumab, etanercept and tocilizumab for a patient over 18 years who has a history of juvenile idiopathic arthritis with onset prior to the age of 18 years. Where the term bDMARD appears in notes and restrictions, it refers to adalimumab, etanercept and tocilizumab only.</p> <p>A patient is eligible for PBS-subsidised treatment with only 1 of the 3 bDMARDs at any one time.</p> <p>From 1 April 2014, a patient receiving PBS-subsidised bDMARD therapy is considered to be in a treatment cycle where they may swap to an alternate bDMARD without having to experience a disease flare. Under these interchangeability arrangements, within a single treatment cycle, a patient may:</p> <ul style="list-style-type: none">(i) continue to receive long-term treatment with a PBS-subsidised bDMARD while they continue to show a response to therapy; and(ii) fail to respond or to sustain a response to each PBS-subsidised bDMARD once only. <p>Once a patient has either failed or ceased to respond to PBS-subsidised bDMARD treatment 3 times, they are deemed to have completed a single treatment cycle and they must have, at a minimum, a 5 year break in PBS-subsidised bDMARD therapy before they are eligible to receive further PBS-subsidised bDMARD therapy. The length of a treatment break is measured from the date of the last approval for PBS-subsidised bDMARD therapy in the last treatment cycle to the date of the first application for initial treatment with a bDMARD under the new treatment cycle.</p> <p>A patient who was receiving PBS-subsidised bDMARD treatment immediately prior to 1 April 2014 is considered to be in their first cycle as of 1 April 2014. A patient who has had a break in bDMARD treatment of at least 24 months immediately prior to making a new application, on or after 1 April 2014, will commence a new treatment cycle.</p> <p>A patient who has failed fewer than 3 trials of a bDMARD in a treatment cycle and who has a break in therapy of less than 24 months may commence a further course of treatment within the same treatment cycle.</p> <p>A patient who has failed fewer than 3 trials of a bDMARD in a treatment cycle and who has a break in therapy of more than 24 months must commence a new treatment cycle. The length of the break in therapy is measured from the date the most recent treatment with PBS-subsidised bDMARD treatment was stopped to the date of the first application for initial treatment with a bDMARD under the new treatment cycle.</p> <p>There is no limit to the number of treatment cycles a patient may undertake.</p> <p>(1) How to prescribe PBS-subsidised bDMARD therapy after 1 April 2014.</p>
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(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 (Initial 1); or
- (ii) a patient wishes to re-commence treatment with a bDMARD following a break in PBS-subsidised therapy of more than 24 months (Initial 1); or
- (iii) 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
- (iv) a patient wishes to re-commence treatment with a specific bDMARD following a break of less than 24 months 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.

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 the Department of Human Services no later than 4 weeks from the date that course was ceased.

Where a response assessment is not submitted to the Department of Human Services 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, it is recommended that a patient is reviewed in the 4 weeks prior to completing their current course of treatment and that an application is posted to the Department of Human Services no later than 2 weeks prior to the patient completing their current treatment course.

(b) Continuing treatment.

Following the completion of an initial treatment course with a specific bDMARD, 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.

A 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 the Department of Human Services no later than 4 weeks from the date that course was ceased.

	<p>Where a response assessment is not submitted to the Department of Human Services within these timeframes, the patient will be deemed to have failed to respond to treatment with that bDMARD.</p> <p>(2) Swapping therapy. Once initial treatment with the first PBS-subsidised bDMARD is approved, a patient may swap to an alternate bDMARD without having to requalify with respect to the indices of disease severity (joint count and ESR/CRP) or the prior non-bDMARD therapy requirements, except if the patient has had a break in therapy of more than 24 months. 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 current 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 bDMARD should be accompanied by the approved authority prescription or remaining repeats for the bDMARD the patient is ceasing.</p> <p>(3) Baseline measurements to determine response. The Department of Human Services will determine whether a response to treatment has been demonstrated based on the baseline measurements of the joint count submitted with the first authority application for a bDMARD. However, prescribers may provide a new baseline measurement any time that an initial treatment authority application is submitted within a treatment cycle and the Department of Human Services will assess response according to the revised baseline measurement.</p> <p>(4) Re-commencement of treatment after a 24 month break in PBS-subsidised therapy. A patient who wishes to start a second or subsequent treatment cycle following a break in PBS-subsidised bDMARD therapy of at least 24 months, must requalify for treatment under the Initial 1 treatment restriction. No increase in the maximum quantity or number of units may be authorised. No increase in the maximum number of repeats may be authorised.</p>
Treatment phase:	First continuing treatment
Treatment criteria:	<ul style="list-style-type: none"> • Must be treated by a rheumatologist; OR • Must be treated by a clinical immunologist with expertise in the management of rheumatoid arthritis.
Clinical criteria:	<ul style="list-style-type: none"> • Patient must have a documented history of severe active juvenile idiopathic arthritis with onset prior to the age of 18 years, AND • Patient must have demonstrated an adequate response to treatment with etanercept, AND • Patient must have received etanercept as their most recent course of PBS-subsidised biological disease modifying anti-rheumatic drug (bDMARD) treatment in this treatment cycle, AND • Patient must not receive more than 24 weeks of treatment per continuing treatment course authorised under this restriction.

Population criteria:	<ul style="list-style-type: none"> • Patient must be aged 18 years or older.
Prescriber Instructions:	<p>For the purposes of this restriction 'biological disease modifying anti-rheumatic drug' and 'bDMARD' mean adalimumab, etanercept or tocilizumab.</p> <p>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: (a) an active joint count of fewer than 10 active (swollen and tender) joints; or (b) a reduction in the active (swollen and tender) joint count by at least 50% from baseline; or (c) a reduction in the number of the following active joints, from at least 4, by at least 50%: (i) elbow, wrist, knee and/or ankle (assessed as swollen and tender); and/or (ii) shoulder, cervical spine 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).</p> <p>Where the baseline active joint count is based on total active joints (i.e. more than 20 active joints), response will be determined according to the 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. If only an ESR or CRP level is provided with the initial application, the same marker will be used to determine response.</p> <p>The authority application must be made in writing and must include: (1) a completed authority prescription form; and (2) a completed Juvenile Idiopathic Arthritis PBS Authority Application - Supporting Information Form.</p> <p>All applications for continuing treatment with etanercept must include a measurement of response to the prior course of therapy. This assessment must be submitted no later than 4 weeks from the cessation of that treatment course. If the application is the first application for continuing treatment with etanercept, it must be accompanied by an assessment of response to a minimum of 12 weeks of treatment with an initial treatment course.</p> <p>Where a response assessment is not undertaken and submitted within these timeframes, the patient will be deemed to have failed to respond to treatment with etanercept.</p> <p>If a patient fails to respond to PBS-subsidised bDMARD treatment 3 times (once with each agent) they will not be eligible to receive further PBS-subsidised bDMARD therapy in this treatment cycle.</p>
Administrative Advice:	<p>Any queries concerning the arrangements to prescribe may be directed to the Department of Human Services on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday). Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Department of Human Services website at www.humanservices.gov.au</p> <p>Applications for authority to prescribe should be forwarded to: Department of Human Services Complex Drugs Reply Paid 9826 HOBART TAS 7001</p>
Treatment phase:	Continuing treatment – balance of supply

Public Summary Document – March 2018 PBAC Meeting

Treatment criteria:	<ul style="list-style-type: none"> • Must be treated by a rheumatologist; OR • Must be treated by a clinical immunologist with expertise in the management of rheumatoid arthritis.
Clinical criteria:	<ul style="list-style-type: none"> • Patient must have received insufficient etanercept therapy under the Continuing treatment restriction to complete 24 weeks treatment, AND • The treatment must provide no more than the balance of up to 24 weeks treatment available under the above restriction.
Population criteria	<ul style="list-style-type: none"> • Patient must be aged 18 years or older.
Administrative advice:	<p>Authority approval for sufficient therapy to complete a maximum of 24 weeks of treatment may be requested by telephone by contacting the Department of Human Services on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday).</p> <p>Written application for authority approval for sufficient therapy to complete a maximum of 24 weeks of treatment should be forwarded to:</p> <p>Department of Human Services Complex Drugs Reply Paid 9826 HOBART TAS 7001</p>

Table 5: S85 - Subsequent Continuing Restrictions

Name, Restriction, Manner of administration and form	Max. Qty	№.of Rpts	Proprietary Name and Manufacturer
ETANERCEPT			
Injection 50 mg in 1 mL single use auto-injector, 4	1	5	Erelzi® Sandoz Pty Ltd
Injection 50 mg in 1 mL single use pre-filled syringe, 4	1	5	

Category / Program	GENERAL – General Schedule (Code GE)
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
PBS Indication:	Severe active juvenile idiopathic arthritis
Restriction Level / Method:	<input type="checkbox"/> Restricted benefit <input type="checkbox"/> Authority Required - In Writing <input type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required – Emergency <input type="checkbox"/> Authority Required - Electronic <input checked="" type="checkbox"/> Streamlined

Administrative Advice (Note) (all treatment phases):	<p>TREATMENT OF ADULT PATIENTS WITH A HISTORY OF JUVENILE IDIOPATHIC ARTHRITIS</p> <p>The following information applies to the prescribing under the Pharmaceutical Benefits Scheme (PBS) of adalimumab, etanercept and tocilizumab for a patient over 18 years who has a history of juvenile idiopathic arthritis with onset prior to the age of 18 years. Where the term bDMARD appears in notes and restrictions, it refers to adalimumab, etanercept and tocilizumab only.</p> <p>A patient is eligible for PBS-subsidised treatment with only 1 of the 3 bDMARDs at any one time.</p> <p>From 1 April 2014, a patient receiving PBS-subsidised bDMARD therapy is considered to be in a treatment cycle where they may swap to an alternate bDMARD without having to experience a disease flare. Under these interchangeability arrangements, within a single treatment cycle, a patient may:</p> <ul style="list-style-type: none">(i) continue to receive long-term treatment with a PBS-subsidised bDMARD while they continue to show a response to therapy; and(ii) fail to respond or to sustain a response to each PBS-subsidised bDMARD once only. <p>Once a patient has either failed or ceased to respond to PBS-subsidised bDMARD treatment 3 times, they are deemed to have completed a single treatment cycle and they must have, at a minimum, a 5 year break in PBS-subsidised bDMARD therapy before they are eligible to receive further PBS-subsidised bDMARD therapy. The length of a treatment break is measured from the date of the last approval for PBS-subsidised bDMARD therapy in the last treatment cycle to the date of the first application for initial treatment with a bDMARD under the new treatment cycle.</p> <p>A patient who was receiving PBS-subsidised bDMARD treatment immediately prior to 1 April 2014 is considered to be in their first cycle as of 1 April 2014. A patient who has had a break in bDMARD treatment of at least 24 months immediately prior to making a new application, on or after 1 April 2014, will commence a new treatment cycle.</p> <p>A patient who has failed fewer than 3 trials of a bDMARD in a treatment cycle and who has a break in therapy of less than 24 months may commence a further course of treatment within the same treatment cycle.</p> <p>A patient who has failed fewer than 3 trials of a bDMARD in a treatment cycle and who has a break in therapy of more than 24 months must commence a new treatment cycle. The length of the break in therapy is measured from the date the most recent treatment with PBS-subsidised bDMARD treatment was stopped to the date of the first application for initial treatment with a bDMARD under the new treatment cycle.</p> <p>There is no limit to the number of treatment cycles a patient may undertake.</p> <p>(1) How to prescribe PBS-subsidised bDMARD therapy after 1 April 2014.</p>
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(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 (Initial 1); or
- (ii) a patient wishes to re-commence treatment with a bDMARD following a break in PBS-subsidised therapy of more than 24 months (Initial 1); or
- (iii) 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
- (iv) a patient wishes to re-commence treatment with a specific bDMARD following a break of less than 24 months 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.

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 the Department of Human Services no later than 4 weeks from the date that course was ceased.

Where a response assessment is not submitted to the Department of Human Services 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, it is recommended that a patient is reviewed in the 4 weeks prior to completing their current course of treatment and that an application is posted to the Department of Human Services no later than 2 weeks prior to the patient completing their current treatment course.

(b) Continuing treatment.

Following the completion of an initial treatment course with a specific bDMARD, 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.

A 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 the Department of Human Services no later than 4 weeks from the date that course was ceased.

	<p>Where a response assessment is not submitted to the Department of Human Services within these timeframes, the patient will be deemed to have failed to respond to treatment with that bDMARD.</p> <p>(2) Swapping therapy. Once initial treatment with the first PBS-subsidised bDMARD is approved, a patient may swap to an alternate bDMARD without having to requalify with respect to the indices of disease severity (joint count and ESR/CRP) or the prior non-bDMARD therapy requirements, except if the patient has had a break in therapy of more than 24 months. 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 current 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 bDMARD should be accompanied by the approved authority prescription or remaining repeats for the bDMARD the patient is ceasing.</p> <p>(3) Baseline measurements to determine response. The Department of Human Services will determine whether a response to treatment has been demonstrated based on the baseline measurements of the joint count submitted with the first authority application for a bDMARD. However, prescribers may provide a new baseline measurement any time that an initial treatment authority application is submitted within a treatment cycle and the Department of Human Services will assess response according to the revised baseline measurement.</p> <p>(4) Re-commencement of treatment after a 24 month break in PBS-subsidised therapy. A patient who wishes to start a second or subsequent treatment cycle following a break in PBS-subsidised bDMARD therapy of at least 24 months, must requalify for treatment under the Initial 1 treatment restriction. No increase in the maximum quantity or number of units may be authorised. No increase in the maximum number of repeats may be authorised.</p>
Treatment phase:	Subsequent continuing treatment
Treatment criteria:	<ul style="list-style-type: none"> • Must be treated by a rheumatologist; OR • Must be treated by a clinical immunologist with expertise in the management of rheumatoid arthritis.
Clinical criteria:	<ul style="list-style-type: none"> • Patient must have received this drug as their most recent course of PBS-subsidised biological agent treatment for this condition in this treatment cycle, AND • Patient must have demonstrated an adequate response to treatment with this drug, AND • Patient must not receive more than 24 weeks of treatment per continuing treatment course under this restriction.
Population criteria:	<ul style="list-style-type: none"> • Patient must be aged 18 years or older.

Prescriber Instructions:	<p>For the purposes of this restriction 'biological disease modifying anti-rheumatic drug' and 'bDMARD' mean adalimumab, etanercept or tocilizumab.</p> <p>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: (a) an active joint count of fewer than 10 active (swollen and tender) joints; or (b) a reduction in the active (swollen and tender) joint count by at least 50% from baseline; or (c) a reduction in the number of the following active joints, from at least 4, by at least 50%: (i) elbow, wrist, knee and/or ankle (assessed as swollen and tender); and/or (ii) shoulder, cervical spine 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).</p> <p>Where the baseline active joint count is based on total active joints (i.e. more than 20 active joints), response will be determined according to the 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. If only an ESR or CRP level is provided with the initial application, the same marker will be used to determine response.</p> <p><i>The measurement of response to the prior course of therapy must be documented in the patient's medical notes.</i></p> <p><i>Patients who fail to demonstrate a response to treatment with this drug under this restriction will not be eligible to receive further PBS-subsidised treatment with this drug in this treatment cycle. Patients may re-trial this drug after a minimum 24 months have elapsed between the date the last prescription for a PBS-subsidised biological agent was issued in this cycle and the date of the first application under a new cycle.</i></p>
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Table 6: S85 - Subsequent continuing restrictions (Enbrel)

Name, Restriction, Manner of administration and form	Max. Qty	Nº. of Rpts	Proprietary Name and Manufacturer
ETANERCEPT			
Injection 50 mg in 1 mL single use auto-injector, 4	1	5	Enbrel® Pfizer Australia Pty Ltd
Injection 50 mg in 1 mL single use pre-filled syringe, 4	1	5	

Category / Program	GENERAL – General Schedule (Code GE)
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
PBS Indication:	Severe active juvenile idiopathic arthritis

<p>Restriction Level / Method:</p>	<p><input type="checkbox"/> Restricted benefit <input checked="" type="checkbox"/> Authority Required - In Writing <input type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required – Emergency <input type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined</p>
<p>Administrative Advice (Note) (all treatment phases):</p>	<p>TREATMENT OF ADULT PATIENTS WITH A HISTORY OF JUVENILE IDIOPATHIC ARTHRITIS</p> <p>The following information applies to the prescribing under the Pharmaceutical Benefits Scheme (PBS) of adalimumab, etanercept and tocilizumab for a patient over 18 years who has a history of juvenile idiopathic arthritis with onset prior to the age of 18 years. Where the term bDMARD appears in notes and restrictions, it refers to adalimumab, etanercept and tocilizumab only.</p> <p>A patient is eligible for PBS-subsidised treatment with only 1 of the 3 bDMARDs at any one time.</p> <p>From 1 April 2014, a patient receiving PBS-subsidised bDMARD therapy is considered to be in a treatment cycle where they may swap to an alternate bDMARD without having to experience a disease flare. Under these interchangeability arrangements, within a single treatment cycle, a patient may:</p> <p>(i) continue to receive long-term treatment with a PBS-subsidised bDMARD while they continue to show a response to therapy; and</p> <p>(ii) fail to respond or to sustain a response to each PBS-subsidised bDMARD once only.</p> <p>Once a patient has either failed or ceased to respond to PBS-subsidised bDMARD treatment 3 times, they are deemed to have completed a single treatment cycle and they must have, at a minimum, a 5 year break in PBS-subsidised bDMARD therapy before they are eligible to receive further PBS-subsidised bDMARD therapy. The length of a treatment break is measured from the date of the last approval for PBS-subsidised bDMARD therapy in the last treatment cycle to the date of the first application for initial treatment with a bDMARD under the new treatment cycle.</p> <p>A patient who was receiving PBS-subsidised bDMARD treatment immediately prior to 1 April 2014 is considered to be in their first cycle as of 1 April 2014. A patient who has had a break in bDMARD treatment of at least 24 months immediately prior to making a new application, on or after 1 April 2014, will commence a new treatment cycle.</p> <p>A patient who has failed fewer than 3 trials of a bDMARD in a treatment cycle and who has a break in therapy of less than 24 months may commence a further course of treatment within the same treatment cycle.</p> <p>A patient who has failed fewer than 3 trials of a bDMARD in a treatment cycle and who has a break in therapy of more than 24 months must commence a new treatment cycle. The length of the break in therapy is measured from the date the most recent treatment with PBS-subsidised bDMARD treatment was stopped to the date of the first application for initial treatment with a bDMARD under the new treatment cycle.</p> <p>There is no limit to the number of treatment cycles a patient may undertake.</p> <p>(1) How to prescribe PBS-subsidised bDMARD therapy after 1 April 2014.</p>

(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 (Initial 1); or
- (ii) a patient wishes to re-commence treatment with a bDMARD following a break in PBS-subsidised therapy of more than 24 months (Initial 1); or
- (iii) 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
- (iv) a patient wishes to re-commence treatment with a specific bDMARD following a break of less than 24 months 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.

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 the Department of Human Services no later than 4 weeks from the date that course was ceased.

Where a response assessment is not submitted to the Department of Human Services 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, it is recommended that a patient is reviewed in the 4 weeks prior to completing their current course of treatment and that an application is posted to the Department of Human Services no later than 2 weeks prior to the patient completing their current treatment course.

(b) Continuing treatment.

Following the completion of an initial treatment course with a specific bDMARD, 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.

A 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 the Department of Human Services no later than 4 weeks from the date that course was ceased.

	<p>Where a response assessment is not submitted to the Department of Human Services within these timeframes, the patient will be deemed to have failed to respond to treatment with that bDMARD.</p> <p>(2) Swapping therapy. Once initial treatment with the first PBS-subsidised bDMARD is approved, a patient may swap to an alternate bDMARD without having to requalify with respect to the indices of disease severity (joint count and ESR/CRP) or the prior non-bDMARD therapy requirements, except if the patient has had a break in therapy of more than 24 months. 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 current 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 bDMARD should be accompanied by the approved authority prescription or remaining repeats for the bDMARD the patient is ceasing.</p> <p>(3) Baseline measurements to determine response. The Department of Human Services will determine whether a response to treatment has been demonstrated based on the baseline measurements of the joint count submitted with the first authority application for a bDMARD. However, prescribers may provide a new baseline measurement any time that an initial treatment authority application is submitted within a treatment cycle and the Department of Human Services will assess response according to the revised baseline measurement.</p> <p>(4) Re-commencement of treatment after a 24 month break in PBS-subsidised therapy. A patient who wishes to start a second or subsequent treatment cycle following a break in PBS-subsidised bDMARD therapy of at least 24 months, must requalify for treatment under the Initial 1 treatment restriction. No increase in the maximum quantity or number of units may be authorised. No increase in the maximum number of repeats may be authorised.</p>
Treatment phase:	Subsequent continuing treatment
Treatment criteria:	<ul style="list-style-type: none"> • Must be treated by a rheumatologist; OR • Must be treated by a clinical immunologist with expertise in the management of rheumatoid arthritis.
Clinical criteria:	<ul style="list-style-type: none"> • Patient must have a documented history of severe active juvenile idiopathic arthritis with onset prior to the age of 18 years, AND • Patient must have demonstrated an adequate response to treatment with etanercept, AND • Patient must have received etanercept as their most recent course of PBS-subsidised biological disease modifying anti-rheumatic drug (bDMARD) treatment in this treatment cycle, AND • Patient must not receive more than 24 weeks of treatment per continuing treatment course authorised under this restriction.

Population criteria:	<ul style="list-style-type: none"> • Patient must be aged 18 years or older.
Prescriber Instructions:	<p>For the purposes of this restriction 'biological disease modifying anti-rheumatic drug' and 'bDMARD' mean adalimumab, etanercept or tocilizumab.</p> <p>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: (a) an active joint count of fewer than 10 active (swollen and tender) joints; or (b) a reduction in the active (swollen and tender) joint count by at least 50% from baseline; or (c) a reduction in the number of the following active joints, from at least 4, by at least 50%: (i) elbow, wrist, knee and/or ankle (assessed as swollen and tender); and/or (ii) shoulder, cervical spine 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).</p> <p>Where the baseline active joint count is based on total active joints (i.e. more than 20 active joints), response will be determined according to the 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. If only an ESR or CRP level is provided with the initial application, the same marker will be used to determine response.</p> <p>The authority application must be made in writing and must include: (1) a completed authority prescription form; and (2) a completed Juvenile Idiopathic Arthritis PBS Authority Application - Supporting Information Form.</p> <p>All applications for continuing treatment with etanercept must include a measurement of response to the prior course of therapy. This assessment must be submitted no later than 4 weeks from the cessation of that treatment course. If the application is the first application for continuing treatment with etanercept, it must be accompanied by an assessment of response to a minimum of 12 weeks of treatment with an initial treatment course.</p> <p>Where a response assessment is not undertaken and submitted within these timeframes, the patient will be deemed to have failed to respond to treatment with etanercept.</p> <p>If a patient fails to respond to PBS-subsidised bDMARD treatment 3 times (once with each agent) they will not be eligible to receive further PBS-subsidised bDMARD therapy in this treatment cycle.</p>
Administrative Advice:	<p>Any queries concerning the arrangements to prescribe may be directed to the Department of Human Services on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday). Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Department of Human Services website at www.humanservices.gov.au</p> <p>Applications for authority to prescribe should be forwarded to: Department of Human Services Complex Drugs Reply Paid 9826 HOBART TAS 7001</p>
Treatment phase:	Continuing treatment – balance of supply

Treatment criteria:	<ul style="list-style-type: none"> • Must be treated by a rheumatologist; OR • Must be treated by a clinical immunologist with expertise in the management of rheumatoid arthritis.
Clinical criteria:	<ul style="list-style-type: none"> • Patient must have received insufficient etanercept therapy under the Continuing treatment restriction to complete 24 weeks treatment, AND • The treatment must provide no more than the balance of up to 24 weeks treatment available under the above restriction.
Population criteria	<ul style="list-style-type: none"> • Patient must be aged 18 years or older.
Administrative advice:	<p>Authority approval for sufficient therapy to complete a maximum of 24 weeks of treatment may be requested by telephone by contacting the Department of Human Services on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday).</p> <p>Written application for authority approval for sufficient therapy to complete a maximum of 24 weeks of treatment should be forwarded to:</p> <p>Department of Human Services Complex Drugs Reply Paid 9826 HOBART TAS 7001</p>

8 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised in Australia. It considers submissions in this context. A PBAC decision not to recommend listing or not to recommend changing a listing does not represent a final PBAC view about the merits of the medicine. A company can resubmit to the PBAC or seek independent review of the PBAC decision.

9 Sponsor's Comment

The sponsor had no comment.