

## 5.20 ETANERCEPT

**50 mg in 1 mL pre-filled syringe,**

**Rymti<sup>®</sup>,**

**Alphapharm Pty Ltd**

### 1 Purpose of Submission

- 1.1 The Category 3 submission sought Section 85 and Section 100 Highly Specialised Drug Program (HSD) listings of a new brand of biosimilar brand of etanercept in the form of 50 mg in 1 mL pre-filled syringe (PFS; herein referred to as Rymti PFS) under the same circumstances as the PBS-listed reference biologic Enbrel<sup>®</sup>.

### 2 Background

#### **Registration status**

- 2.1 Rymti PFS was TGA registered on 1 October 2020 as a biosimilar medicine to Enbrel. The wording of the indications for Rymti is not identical to the wording of the indications for Enbrel. The clinical evaluator recommended approval of Rymti for all the approved indications of the reference product Enbrel, with the proposed dosing instructions that direct the prescriber to other etanercept products for patients weighing less than 62.5 kg (p30, Australian Public Assessment Report for Etanercept).
- 2.2 The submission also sought Section 85 and Section 100 HSD listings of etanercept in the form of 50 mg in 1 mL pre-filled auto-injector. The submission also requested a brand name change from Rymti to Nepexto. The submission noted an application for these requests were submitted to the TGA, however, no TGA decision outcome was available at the time of the November 2021 PBAC meeting. Therefore, these requests were not considered in this submission because the required TGA documentation were not available at the time of lodging the Category 3 submission and the November 2021 PBAC meeting.

#### **Previous PBAC consideration**

- 2.3 Rymti has not previously been considered by the PBAC.
- 2.4 Enbrel (reference brand) and Brenzys (biosimilar brand) are currently listed on the PBS. Brenzys was listed on 1 April 2017. The PBAC recommended Brenzys<sup>®</sup>, noting it was a biosimilar of originator brand Enbrel, on a cost minimisation basis with Enbrel for all adult indications at its July 2016 meeting.
- 2.5 The PBAC recommended a second etanercept biosimilar, Erelzi<sup>®</sup>, at its March 2018 meeting. The PBAC recommended Erelzi be listed for adult and juvenile indications.

For more detail on PBAC's view, see section 6 PBAC outcome.

### 3 Requested listing

3.1 The submission proposed identical listings for all indications for which the reference brand Enbrel in the form of etanercept 50 mg in 1 mL PFS is currently PBS listed:

- Severe active rheumatoid arthritis
- Severe psoriatic arthritis
- Ankylosing spondylitis
- Severe chronic plaque psoriasis
- Juvenile idiopathic arthritis

The submission noted that only the Enbrel brand is listed for severe chronic plaque psoriasis (under 18 years; PBS item 1963H). The TGA approval for Rymti PFS states that children and adolescents weighing less than 62.5 kg should not receive Rymti and that these patients should be accurately dosed on a mg/kg basis with other etanercept products. At its July 2016 meeting, the PBAC noted similar advice from the TGA delegate regarding Brenzys where they did not intend to approve Brenzys for registration for juvenile plaque psoriasis or juvenile idiopathic arthritis because it was not available in a dose form that would enable weight based dosing for children weighing less than 62.5 kg. As such the PBAC recommended that Brenzys should also not be subsidised for these indications (paragraph 7.3, etanercept (Brenzys), Public Summary Document, July 2016 PBAC meeting). Therefore, it would be appropriate for Rymti to be have an identical listing as Brenzys for the same form and strength.

3.2 The PBAC advised biosimilar uptake drivers which currently apply to Brenzys, including the differential treatment in authority requirements for subsequent continuing treatment with the reference and biosimilar brands, would also apply to Rymti PFS.

3.3 The submission requested Rymti PFS to be 'a'-flagged against Enbrel of the same strength and form. The PBAC previously advised that, under Section 101(4AACD) of the *National Health Act 1953* (the Act), in the Schedule of Pharmaceutical Benefits, the same form and strength for the brands Brenzys and Enbrel should be treated as equivalent ('a' flagged) to each other for the purpose of substitution. The PBAC advised, under Section 101(4AACD) of the Act, in the Schedule of Pharmaceutical Benefits the same form and strength of Brenzys, Enbrel and Rymti PFS should be treated as equivalent ('a'-flagged) to each other for the purpose of substitution.

3.4 The requested restrictions are complex due to the number of items and indications required for the listing. If recommended by the PBAC, implementation of these listings may occur across separate stages. As the applicant requested no changes to the restrictions compared to Enbrel, the restrictions have not been reproduced.

For more detail on PBAC’s view, see section 6 PBAC outcome.

## 4 Comparator

- 4.1 The submission nominated the reference brand of etanercept, Enbrel, as the main comparator. The PBAC considered this was appropriate and advised that Brenzys was also an appropriate comparator.

For more detail on PBAC’s view, see section 6 PBAC outcome.

## 5 Consideration of the evidence

### Sponsor hearing

- 5.1 There was no hearing for this item.

### Consumer comments

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

### Clinical trials

- 5.3 The submission presented the following clinical study reports. As a Category 3 submission, no evaluation of the clinical evidence was undertaken.

**Table 1. Studies presented in the submission**

Trial ID	Protocol/Publication Title	Publication Citation
LBC-14-155	A phase 1 :An Open Label, Balanced, Randomized, Single-Dose, Two-Treatment, Two-Sequence, Two-Period, Crossover, Comparative Pharmacokinetics-Pharmacodynamics Study of Etanercept Lupin 50 mg Solution for Injection for Subcutaneous Injection Manufactured by Lupin Limited, India and Enbrel (Etanercept 50 mg) Solution for Injection for Subcutaneous Injection Manufactured by John Wyeth and Brother Ltd., UK in Healthy, Adult, Human Male Subjects	Clinical Study Report 8/2014 – 11/2014
YLB113-001	A Phase 1: comparative pharmacokinetic and safety study of Etanercept Lupin vs Enbrel 25 mg solution for SC injection in healthy, adult, human male subjects.	Clinical Study Report 7/2014 – 10/2014
YLB113-002	A phase 3: A Comparative Study to Assess the Efficacy, Safety and Immunogenicity of Etanercept Lupin and Enbrel for the Treatment of Rheumatoid Arthritis	Clinical Study Report date 07/2015-06/2017

Source: Rymti main body of submission, p13

- 5.4 The clinical trials presented in the submission were evaluated by the TGA to register Rymti PFS as a biosimilar to Enbrel.

### Clinical claim

- 5.5 The submission claimed that Rymti PFS was biosimilar to Enbrel.
- 5.6 The PBAC considered that Rymti PFS was biosimilar to Enbrel based on the TGA approval.

### **Economic analysis**

5.7 The submission did not present an economic analysis as it was a Category 3 submission. The submission proposed Rymti PFS to have the same AEMP as Enbrel.

5.8 Equi-effective doses were not presented in the submission.

### **Estimated PBS utilisation and financial implications**

5.9 The submission noted it is expected that the listing of Rymti PFS will not increase the overall market utilisation. This was appropriate as it is expected that Rymti PFS would substitute for Brenzys PFS and Enbrel PFS.

*For more detail on PBAC's view, see section 6 PBAC outcome.*

## **6 PBAC Outcome**

6.1 The PBAC recommended the Authority Required listing of etanercept (Rymti PFS) in the form of 50 mg in 1 mL PFS as a biosimilar brand of Enbrel on the General Schedule (Section 85) and S100 HSD. The PBAC's recommendation for listing was based on, among other matters, its assessment that the cost-effectiveness of Rymti PFS would be acceptable if it were cost-minimised to Enbrel for the following indications:

- Severe active rheumatoid arthritis
- Severe psoriatic arthritis
- Ankylosing spondylitis
- Severe chronic plaque psoriasis
- Juvenile idiopathic arthritis.

6.2 The PBAC advised the equi-effective doses are Rymti PFS 50 mg = Enbrel 50 mg = Brenzys 50 mg.

6.3 The PBAC considered that the biosimilar uptake drivers should be applied to Rymti PFS consistent with the current PBS listings for etanercept biosimilar brands, including:

- Authority Required (Written/digital submission) listing of Rymti PFS for initial treatment restrictions, first and subsequent continuing treatment restrictions.
- A separate Authority Required (Streamlined) listing of Rymti for subsequent continuing treatment restriction.
- The application of the 'Biosimilar prescribing policy' administrative note encouraging the use of biosimilar brands for treatment naïve patients (this note will need to be updated for the other biosimilar brands of Etanercept to include Rymti PFS in the list):

*Prescribing of the biosimilar brand, Rymti PFS, is encouraged for treatment naïve patients.*

*Encouraging biosimilar prescribing for treatment naïve 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](http://www.health.gov.au/biosimilars))*

- 6.4 The PBAC noted that the Product Information of Rymti indicates that children and adolescents weighing less than 62.5 kg should not receive Rymti and that these patients should be accurately dosed on a mg/kg basis with other etanercept products. The PBAC advised that it is appropriate to include a caution ‘This formulation of etanercept is intended for use in children and adolescents weighting 62.5kg or more’. The PBAC also advised the caution flowed onto relevant indications/products for Enbrel.
- 6.5 The PBAC advised that, under Section 101(4AACD) of the Act, in the Schedule of Pharmaceutical Benefits, the same form and strength of Brenzys<sup>®</sup>, Enbrel<sup>®</sup> and Rymti<sup>®</sup> should be treated as equivalent (‘a’-flagged) to each other for the purpose of substitution.
- 6.6 The PBAC noted that the listing of Rymti PFS is expected to have no change in the overall net cost to the government.
- 6.7 The PBAC noted that its recommendation was on a cost-minimisation basis and advised that, because Rymti PFS is not expected to provide a substantial and clinically relevant improvement in efficacy, or reduction of toxicity over Enbrel, or not expected to address a high and urgent unmet clinical need given the presence of an alternative therapy, the criteria prescribed by the *National Health (Pharmaceuticals and Vaccines – Cost Recovery) Regulations 2009* for Pricing Pathway A were not met.
- 6.8 The PBAC noted that this submission is not eligible for an Independent Review as it received a positive recommendation.

**Outcome:**

Recommended

## **7 Recommended listing**

- 7.1 Add new etanercept brand (Rymti) with schedule equivalence (‘a’ flag) for the same indications as Enbrel as noted in Section 3.
- 7.2 Add Caution: ‘This formulation of etanercept is intended for use in children and adolescents weighting 62.5kg or more’ and flowed onto relevant indications/products for Enbrel.

7.3 Amend existing/recommended listing as follows:

- Authority Required (Written/digital submission) listing of Rymti for initial treatment restrictions, first and subsequent continuing treatment restrictions.
- A separate Authority Required (Streamlined) listing of Rymti for subsequent continuing treatment restriction.
- The application of the ‘Biosimilar prescribing policy’ administrative note encouraging the use of biosimilar brands for treatment naïve patients (this note will need to be updated for the other biosimilar brands of etanercept to include Rymti in the list):

*Prescribing of the biosimilar brand, Rymti, is encouraged for treatment naïve patients.*

*Encouraging biosimilar prescribing for treatment naïve 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](http://www.health.gov.au/biosimilars))*

MEDICINAL PRODUCT medicinal product pack	Proprietary Name, Manufacturer
ETANERCEPT etanercept 50 mg in 1 mL pre-filled syringe	Rymti, Alphapharm Pty Ltd

***This restriction may be subject to further review. Should there be any changes made to the restriction the Sponsor will be informed.***

## 8 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised through the Pharmaceutical Benefits Scheme (PBS) in Australia. It considers applications regarding the listing of medicines on the PBS and provides advice about other matters relating to the operation of the PBS in this context. A PBAC decision in relation to PBS listings does not necessarily represent a final PBAC view about the merits of the medicine or the circumstances in which it should be made available through the PBS. The PBAC welcomes applications containing new information at any time.

## 9 Sponsor’s Comment

The sponsor had no comment.