

5.11 ETANERCEPT, Injection 50 mg in 1 mL single use auto-injector, 4, Nepexto[®], Alphapharm Pty Ltd

1 Purpose of Submission

- 1.1 The Category 3 submission sought General Schedule (Section 85) and Section 100 Highly Specialised Drug Program (HSD) listings of a biosimilar brand of etanercept (Nepexto[®]) in the form of Injection 50 mg in 1 mL single use auto-injector under the same conditions as its reference biologic Enbrel[®], 50 mg in 1 mL single use auto-injector.

2 Background

Registration status

- 2.1 Nepexto was Therapeutic Goods Administration (TGA) registered on 14 September 2022 as a biosimilar product to Enbrel.

Previous PBAC consideration

- 2.2 Nepexto single use auto-injector has not been considered by the Pharmaceutical Benefits Advisory Committee (PBAC) previously.
- 2.3 Enbrel (reference brand) and Brenzys[®] (biosimilar brand) are currently listed on the Pharmaceutical Benefits Scheme (PBS) in the following forms:
- Enbrel: pre-filled syringe (PFS) 50 mg/mL, single use auto-injector 50 mg/mL, cartridges single dose auto-injector reusable 50 mg/mL, single dose vial 25 mg
 - Brenzys: PFS 50 mg/mL, single use auto-injector 50 mg/mL
- 2.4 Rymti[®] 50 mg in 1 mL PFS (biosimilar brand) by the same sponsor as Nepexto single use auto-injector was recommended at the November 2021 PBAC meeting. Rymti 50 mg in 1 mL PFS was not yet PBS-listed at the time of the November 2022 PBAC meeting.

3 Requested listing

- 3.1 The submission requested Nepexto single use auto-injector be listed for all indications for which the reference brand Enbrel is currently PBS listed:
- Severe psoriatic arthritis
 - Ankylosing spondylitis
 - Severe active rheumatoid arthritis

- Severe chronic plaque psoriasis
 - Severe active juvenile idiopathic arthritis
- 3.2 The PBAC noted the TGA approved Product Information for Nepexto states that children and adolescents weighing less than 62.5 kg should not receive Nepexto and that these patients should be accurately dosed on a mg/kg basis with other etanercept products, which is the same dosage directions as that for Rymti on the ARTG Public Summary. The PBAC recalled that at its November 2021 meeting, the PBAC recommended Rymti PFS to be PBS-listed for the same indications as Enbrel as noted above (paragraph 7.1, etanercept (Rymti), Public Summary Document (PSD), November 2021 PBAC meeting). Therefore, the PBAC maintained its previous view from November 2021 and advised that the following caution be added to the restriction for Nepexto: ‘This formulation of etanercept is intended for use in children and adolescents weighing 62.5 kg or more’ and be flowed on to relevant indications/products for Enbrel (paragraph 7.2, etanercept (Rymti), PSD, November 2021 PBAC meeting).
- 3.3 The sponsor requested Nepexto be listed under the same PBS item codes and for the same indications as Enbrel 50 mg in 1 mL single use auto-injector, including the maximum quantity, packs and number of repeats to match that already listed for Enbrel for the indications above.
- 3.4 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, should also apply to Nepexto.
- 3.5 The PBAC advised that the following Administrative note for relevant PBS-listings of etanercept 50 mg in 1 mL are updated as follows: “Prescribing of the biosimilar brands Brenzys and Nepexto 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).”
- 3.6 The submission requested Nepexto 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 strengths of etanercept dose-dispenser cartridge, etanercept PFS and etanercept single use auto-injector should be considered equivalent at the pharmacy level (‘a’ flagged) for the purpose of substitution (paragraph 6.5, etanercept (Enbrel), PSD, July 2021 PBAC meeting). The PBAC considered this to be appropriate for Nepexto.
- 3.7 As the applicant requested no changes to the restrictions compared to Enbrel, the restrictions have not been reproduced, however an example has been included below

(for ‘Severe psoriatic arthritis’, treatment phase: Initial treatment - Initial 1 (new patient)).

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
ETANERCEPT					
Etanercept 50mg/mL injection, 4 x 1 mL pen devices	9457R	1	1	3	Enbrel ^a Brenzys ^a Nepexto ^a

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

4 Comparator

- 4.1 The submission nominated Enbrel 50 mg in 1.0 mL solution for PFS and single use auto-injector as the main comparator. The PBAC considered this was appropriate and noted that Brenzys is 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 no consumer comments were received for this item.

Clinical trials

- 5.3 The submission presented the following clinical study reports. The clinical trials presented in the submission were evaluated by the TGA to register Nepexto as a biosimilar to Enbrel. The PBAC previously reviewed these clinical trials when recommending Rymti PFS at its November 2021 meeting.

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: Nepexto main body of submission, p12

Clinical claim

- 5.4 The submission claimed that Nepexto was a biosimilar medicine to Enbrel which was accepted by the PBAC.
- 5.5 The PBAC considered that the claims of non-inferior comparative effectiveness and safety were reasonable.

Economic analysis

- 5.6 The submission did not present an economic analysis as it was a Category 3 submission. The submission proposed Nepexto to have the same approved ex-manufacturer price (AEMP) as Enbrel.
- 5.7 Equi-effective doses were not presented in the submission. The equi-effective doses should be: Nepexto 50 mg = Enbrel 50 mg = Brenzys 50 mg.

Estimated PBS utilisation and financial implications

- 5.8 The submission stated that if Nepexto is listed it is not expected to increase the overall market utilisation. This was appropriate as it is expected that Nepexto single use auto-injector would substitute for Brenzys and Enbrel.

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 (Nepexto®) in the form of injection 50 mg in 1 mL single use auto-injector as a biosimilar brand of Enbrel® on the General Schedule (Section 85) and Section 100 Highly Specialised Drug Program. The PBAC's recommendation for listing was based on, among other matters, its assessment that the cost-effectiveness of Nepexto would be acceptable if it were cost-minimised to Enbrel for the following indications:
- Severe psoriatic arthritis
 - Ankylosing spondylitis
 - Severe active rheumatoid arthritis
 - Severe chronic plaque psoriasis
 - Severe active juvenile idiopathic arthritis
- 6.2 The PBAC recommended Nepexto be listed for the same indications as Enbrel 50 mg in 1 mL single use auto-injector (as listed above), with the same maximum quantity, packs and number of repeats as that already listed for Enbrel for the specific indications.
- 6.3 The PBAC advised the equi-effective doses are Nepexto 50 mg = Enbrel 50 mg = Brenzys 50 mg.

- 6.4 The PBAC considered that biosimilar uptake drivers should apply to Nepexto consistent with the current PBS listings for etanercept biosimilar Brenzys, including:
- Written/digital submission listing of Enbrel, Brenzys and Nepexto for initial treatment restrictions, first and subsequent continuing treatment restrictions.
 - A separate Authority Required (Streamlined) listing of Brenzys and Nepexto for subsequent continuing treatment restrictions.
 - The inclusion of Nepexto in the following Administrative note for relevant PBS-listings of etanercept 50 mg in 1 mL:
“Prescribing of the biosimilar brand Brenzys *and* Nepexto 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).”
- 6.5 The PBAC noted the TGA approved Product Information for Nepexto states that children and adolescents weighing less than 62.5 kg should not receive Nepexto and that these patients should be accurately dosed on a mg/kg basis with other etanercept products. Therefore, the PBAC advised that the following caution be added to the restriction for Nepexto: ‘This formulation of etanercept is intended for use in children and adolescents weighing 62.5 kg or more’ and be flowed on to relevant indications/products for Enbrel.
- 6.6 The PBAC advised that, under Section 101 (4AACD) of the *National Health Act*, that the same strengths of Nepexto single use auto-injector; Enbrel single use auto-injector, pre-filled syringe (PFS) and cartridges single dose auto-injector reusable; Brenzys single use auto-injector and PFS; and Rymti PFS, if listed, should be considered equivalent for the purposes of substitution (i.e., ‘a’ flagged in the Schedule with a NOTE stating pharmaceutical benefits of the different forms in the same strength are equivalent for the purposes of substitution).
- 6.7 The PBAC noted that the listing of Nepexto is expected to have no change in the overall net cost to the government.
- 6.8 The PBAC noted that its recommendation was on a cost-minimisation basis and advised that, because Nepexto 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 2022* for Pricing Pathway A were not met.
- 6.9 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 (Nepexto) with schedule equivalence ('a' flagged) for the same indications as Enbrel as noted in paragraph 6.1 of the minutes.

7.2 Amend existing/recommended listing as noted in paragraph 6.4 and 6.5 as follows:

- Written/digital submission listing of Enbrel, Brenzys and Nepexto for initial treatment restrictions, first and subsequent continuing treatment restrictions.
- A separate Authority Required (Streamlined) listing of Brenzys and Nepexto for subsequent continuing treatment restrictions.
- The inclusion of Nepexto in the Biosimilar prescribing policy in the following Administrative note for relevant PBS-listings of etanercept 50 mg in 1 mL: "Prescribing of the biosimilar brand Brenzys or Nepexto 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).

- Add the following caution to Nepexto and flow on the restriction to relevant indications/products for Enbrel: 'This formulation of etanercept is intended for use in children and adolescents weighing 62.5 kg or more'.

MEDICINAL PRODUCT medicinal product pack	Proprietary Name, Manufacturer
ETANERCEPT etanercept 50 mg/mL injection, 4 x 1 mL pen devices	Nepexto, Alphapharm Pty Ltd

This restriction is yet to be finalised and 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.