

5.08 ETANERCEPT, SUBCUTANEOUS INJECTION, 50MG, BRENZYS®, MERCK SHARP & DOHME PTY LTD

1 Purpose of Application

- 1.1 The submission was seeking listing of the biosimilar Brenzys® for all indications for which etanercept (Enbrel®) is currently PBS-listed. These include: rheumatoid arthritis (RA), ankylosing spondylitis (AS), psoriatic arthritis (PsA), plaque psoriasis, juvenile idiopathic arthritis and paediatric plaque psoriasis. All are currently listed as authority required on the PBS general schedule.
- 1.2 The submission requested “a limited “a”-flagging system for Brenzys where substitution is permitted at a pharmacy level for naïve to molecule patients only” (Source: the submission).

2 Requested listing

- 2.1 The submission was seeking listing of Brenzys for all indications for which etanercept is currently PBS-listed. No changes to the wording for any of the indications was requested.

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Dispensed Price for Max. Qty	Proprietary Name and Manufacturer
ETANERCEPT				
Auto-injector, 50mg (4)	1	3	\$1493.64	Brenzys MSD
Prefilled-Syringe, 50mg (4)	1	3	\$1493.64	

Authority required

- 2.2 The submission was seeking listing on a cost-minimisation basis against the reference brand of etanercept (Enbrel).

For more detail on PBAC’s view, see section 7 “PBAC outcome”

3 Background

- 3.1 TGA status at time of PBAC consideration: The submission was made under TGA/PBAC Parallel Process. At the time of PBAC consideration, the Delegate's Overview and Advisory Committee for Prescription Medicines (ACPM) advice were available.
- 3.2 Brenzys has not been previously considered by the PBAC.

Substitution of biosimilars at the pharmacist level (“a” flagging)

- 3.3 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. 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.
- 3.4 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.
- 3.5 The Schedule of Pharmaceutical Benefits provide the following definition of brand equivalence:

Extract from the Explanatory Notes to the PBS Schedule¹

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 At the March 2015 meeting, the PBAC:
- “indicated it would consider the marking of equivalent (i.e. “a” flagging) in the Schedule of Pharmaceutical Benefits (the Schedule) of biosimilar medicines with their reference medicine on a case by case basis, taking into account the evidence presented in each submission to list a biosimilar medicine.”

¹ Symbols used in the Schedule - <http://www.pbs.gov.au/info/healthpro/explanatory-notes/section2/section-2-symbols>

- 3.7 When "a" flagging of biosimilar brands and their reference brands was discussed by the PBAC at its special meeting on 17 April 2015, the PBAC advised that biosimilar products would be recommended for "a" flagging, "where the data are supportive of this conclusion."

"The PBAC advised that the following would be relevant considerations in establishing that a biosimilar product could be "a" flagged with the originator product:

- Absence of data to suggest significant differences in clinical effectiveness or safety compared with the originator product;
- Absence of identified populations where the risks of using the biosimilar product are disproportionately high;
- Availability of data to support switching between the originator product and the biosimilar product;
- Availability of data for treatment-naïve patients initiating on the biosimilar product;
- Whether the Therapeutic Goods Administration has deemed a product to be biosimilar with the originator product.

The PBAC considered that where a biosimilar product could not be "a" flagged at the time of PBS listing, data should be collected to support "a" flagging at a later point.

4 Clinical place for the proposed therapy

- 4.1 Brenzys is a biosimilar to etanercept, a tumour necrosis factor alpha (TNF- α) inhibitor. By competitive inhibition of TNF- α receptors, Brenzys prevents TNF-mediated cellular responses which mediates much of the joint pathology in RA, AS and skin pathology in plaque psoriasis.
- 4.2 Brenzys is an alternative brand to the existing etanercept product (Enbrel) currently listed on the PBS.

5 Comparator

- 5.1 The submission appropriately nominated Enbrel as the comparator.

6 Consideration of the evidence

Sponsor hearing

- 6.1 There was no hearing for this item.

Consumer comments

- 6.2 The PBAC noted and welcomed the input from health care professionals (4) and organisations (1) via the Consumer Comments facility on the PBS website. The comments largely raised concerns about potential 'a' flagging and pharmacy level

substitution due to a perceived lack of evidence regarding switching between originator brand etanercept and biosimilars.

Clinical trials

6.3 The submission is based on one head-to-head trial (SB4-G31-RA) comparing Brenzys to etanercept (n=596) in patients over 18 years of age with RA not responding to methotrexate treatment who have not received treatment with bDMARDs previously.

6.4 Details of the trial presented in the submission are provided in Table 1.

Table 1: Trials and associated reports presented in the submission

Trial	Protocol title/ Publication title	Publication citation
Direct randomised trial(s)		
SB4-G31-RA	A Randomised, Double-blind, Parallel Group, Multicentre Clinical Study to Evaluate the Efficacy, Safety, Pharmacokinetics and Immunogenicity of SB4 Compared to Enbrel® in Subjects with Moderate to Severe Rheumatoid Arthritis despite Methotrexate Therapy. P Emery, J Vencovsky, A Sylwestrzak, P Leszczynski, W Porawska, A Baranauskaite, V Tseluyko, V M Zhdan, B Stasiuk, R Milasiene, A A B Rodriguez, S Y Cheong, J Ghil. A phase III randomised, double-blind, parallel-group study comparing SB4 with etanercept reference product in patients with active rheumatoid arthritis despite methotrexate therapy. NCT01895309 A Randomised, Double-blind, Parallel Group, Multicentre Clinical Study to Evaluate the Efficacy, Safety, Pharmacokinetics and Immunogenicity of SB4 Compared to Enbrel® in Subjects With Moderate to Severe Rheumatoid Arthritis Despite Methotrexate Therapy	Clinical Study Report Annals of the Rheumatic Diseases 2015. 6 July. Published online: Ann Rheum Dis doi:10.1136/annrheumdis-2015-207588 NA

Source: p35 and Table B.2-3, p36of the submission

6.5 The key features of Trial SB4-G31-RA are summarised in Table 2.

Table 2: Key features of the included evidence

Trial	N	Design/ duration	Risk of bias	Patient population	Outcome(s)	Use in modelled evaluation
SB4 vs etanercept						
SB4-G31-RA	596	R, DB 52 weeks	Low	RA, bDMARD treatment naive	ACR20, ACR50, ACR70, DAS28	NA

DB=double blind; R=randomised; RA = Rheumatoid arthritis, bDMARD = biological disease modifying anti-rheumatoid drugs, ACR20 = American College of Rheumatology 20% improvement criteria; ACR50 = American College of Rheumatology 50% improvement criteria; ACR70 = American College of Rheumatology 70% improvement criteria, DAS28 = Disease Activity Score for 28 joints.

Source: compiled during the evaluation

- 6.6 The submission presented only clinical evidence for Brenzys in patients with RA and implicitly assumed that the evidence can be extrapolated to patients with other conditions.
- 6.7 The SB4-G31-RA open label extension study presented an additional 52 weeks of data, including a group that switched from Enbrel to Brenzys. The key features from the SB4-G31-RA extension are summarised in Table 3.

Table 3: Key features of the included evidence

Trial	N	N (Brenzys-> Brenzys)	N (Enbrel-> Brenzys)	Design/ duration	Patient population	Outcome(s)	Use in modelled evaluation
Brenzys -> Brenzys vs. Enbrel -> Brenzys at transition to extension study							
SB4-G31-RA Extension	245	126	119	OL 52 weeks	RA, enrolled in SB4-G31-RA	ACR20, ACR50, ACR70 DAS28	NA

OL=open label; RA = Rheumatoid arthritis, ACR20 = American College of Rheumatology 20% improvement criteria; ACR50 = American College of Rheumatology 50% improvement criteria; ACR70 = American College of Rheumatology 70% improvement criteria, DAS28 = Disease Activity Score for 28 joints.

Source: Compiled by PBAC Secretariat

Comparative effectiveness

- 6.8 The key results from SB4-G31-RA are summarised in Table 4.

Table 4: Results of ACR20, ACR50 and ACR70 in the per protocol population in SB4-G31-RA

Outcome	Brenzys n/N (%)	Enbrel n/N (%)	Adjusted Difference (95%CI) ¹	Difference (95% CI) ²	OR (95%CI) ²
24 weeks					
ACR20	193/247 (78.1)	190/236 (80.5)	-2.37% (-9.54, 4.80)	-2.4% (-9.6,4.9)	0.87 (0.54, 1.38)
ACR50	114/247 (46.2)	100/236 (42.4)	4.36% (-4.33, 13.05)	3.8% (-5.1, 12.6)	1.17 (0.80, 1.70)
ACR70	63/247 (25.5)	53/236 (22.5)	3.29% (-4.18, 10.76)	3.0% (-4.6, 10.7)	1.18 (0.76, 1.84)
52 weeks					
ACR20	181/224 (80.8)	176/216 (81.5)	-0.74% (-8.03,6.56)	-0.7% (-8.0,6.7)	0.96 (0.58, 1.59)
ACR50	131/224 (58.5)	115/216 (53.2)	4.50% (-4.67, 13.67)	5.2% (-4.0,14.4)	1.24 (0.83, 1.84)
ACR70	84/224 (37.5)	67/216 (31.0)	7.02%(-1.69,15.74)	6.5% (-2.4,15.3)	1.33 (0.88, 2.02)

- 6.9 The results presented were based on a per-protocol set (PPS) rather than the full ITT set (referred to as the Full Analysis Set in the submission). The submission defined the primary population (PPS1, the population in which the primary outcome is measured) as all patients who completed their randomised treatment up to week 24 (i.e. not withdrawn or discontinued) with adherence between 80-120% without any major protocol deviations.
- 6.10 An equivalence margin of 15% was proposed for the primary outcome of ACR20 at 24 weeks. That is, if the 95% confidence interval of the difference in proportion of patients who satisfied the ACR20 response at 24 weeks between patients treated with Brenzys and Enbrel was between -15% and 15%, then a conclusion that

treatment with Brenzys and Enbrel are equivalent could be made. No justification for the selection of the value of 15% was presented. However the margin of 15% for equivalence is identical to the margin used in the infliximab biosimilar submission for patients with RA in Study 3.1 (p12, Infliximab PSD July 2015).

- 6.11 The submission also presented the change in DAS28 score from baseline at week 24 and week 52. There was no statistically significant difference between the score for patients treated with Brenzys compared to patients treated with Enbrel, and the results appear to support equivalence of Brenzys with Enbrel as the 95% CI for the difference in change from baseline of DAS28 between Enbrel and Brenzys is within the nominated margin of 0.6.
- 6.12 The results of the SB4-G31-RA extension study for ACR 20, ACR50 and ACR70 at initiation (week 52), week 76 and week 100 showed that response rates for all ACR outcomes were comparable between the Brenzys -> Brenzys (BR/BR) and Enbrel -> Brenzys (EN/BR) groups. The key results from the SB4-G31-RA extension trial are summarised in table 5.

Table 5: Results of ACR20, ACR50 and ACR70 from the SB4-G31-RA extension

ACR Response	Time point	Treatment group	
		Brenzys -> Brenzys (BR/BR) N=126 n/n' (%)	Enbrel -> Brenzys (EN/BR) N = 119 n/n' (%)
ACR20	Week 52 (start)	99/125 (79.2)	98/119 (82.4)
	Week 76	102/125 (81.6)	90/117 (76.9)
	Week 100	95/122 (77.9)	91/115 (79.1)
ACR50	Week 52 (start)	65/125 (52.0)	64/119 (53.8)
	Week 76	74/125 (59.2)	62/117 (53.0)
	Week 100	73/122 (59.8)	70/115 (60.9)
ACR70	Week 52 (start)	48/125 (38.4)	39/119 (32.8)
	Week 76	49/125 (39.2)	44/117 (37.6)
	Week 100	52/122 (42.6)	48/115 (41.7)

n' = number of subjects with available assessment results at each time point, ACR20 = American College of Rheumatology 20% improvement criteria; ACR50 = American College of Rheumatology 50% improvement criteria; ACR70 = American College of Rheumatology 70% improvement criteria

Source: SB4-G31-RA 100 week Extension Clinical Study Report

- 6.13 The mean change in DAS28 score from baseline at Week 76 was 2.9066 in the BR/BR treatment group and 2.9188 in the EN/BR treatment group. The mean change in DAS28 score from baseline at Week 100 was 2.8548 in the BR/BR treatment group and 3.0005 in the EN/BR treatment group.

Comparative harms

- 6.14 Overall, with the exception of injection site erythema (RR=0.18, 95% CI: 0.08, 0.41; favouring Brenzys), the rate of adverse events reported in patients treated with Brenzys was comparable to patients treated with etanercept in Trial SB4-G31-RA.
- 6.15 The SB4-G31-RA extension study found that the incidences of serious adverse events (SAEs) and treatment-emergent adverse events (TEAEs) were comparable

between the BR/BR and EN/BR groups. The study also reported that the overall incidence of anti-drug antibodies and neutralising antibodies to etanercept was low (fewer than 5 patients at week 100) in the BR/BR and EN/BR groups. No antibodies were found to be neutralising during the open-label, extension period.

Clinical claim

- 6.16 The submission described Brenzys as equivalent in terms of comparative effectiveness and equivalent in terms of comparative safety to Enbrel.
- 6.17 The ACPM considered that the clinical data and justifications by the sponsor were acceptable to support extrapolation to the other adult indications requested for Brenzys, including ankylosing spondylitis, psoriatic arthritis and plaque psoriasis. The ACPM noted that Enbrel is also approved for two paediatric conditions, juvenile idiopathic arthritis and juvenile plaque psoriasis. The ACPM advised that Brenzys is not indicated for use in children less than 18 years of age as a 25 mg dose form will not be made available and the recommended dose of etanercept for paediatric patients is 0.8 mg/kg given once weekly.
- 6.18 The PBAC considered that the claim of non-inferior comparative effectiveness was reasonable.
- 6.19 The PBAC considered that the claim of non-inferior comparative safety was reasonable.

Economic analysis

- 6.20 The economic analysis presented was a cost minimisation analysis.
- 6.21 Brenzys 50 mg and Enbrel 50 mg, both given as subcutaneous injections, were proposed to be equi-effective. The submission acknowledged that etanercept is subject to special pricing arrangements and is willing to work on the pricing of Brenzys with the department of health following a positive recommendation. The Department advised that special pricing arrangements are not ordinarily agreed for multi-branded drugs in the F2 formulary.

Drug cost/patient/year: \$19,417.32

- 6.22 Based on 52 weekly injections of Brenzys 50 mg, with each pack of 4 injections costed at a DPMQ of \$1,493.64 (13 packs over 52 weeks). The DPMQ of Brenzys and Enbrel is expected to be identical, and thus the drug cost/patient/year is also expected to be identical.

Estimated PBS usage & financial implications

6.23 This submission was not considered by DUSC. The submission used a market share approach to estimate the financial impact of listing Brenzys on the PBS, see Table 6.

Table 6: Estimated extent of use and financial impact of Brenzys

	2017	2018	2019	2020	2021
Estimated etanercept 50 mg packs	115,759	124,065	132,371	140,677	148,983
Uptake/substitution rate of Brenzys	12%	24%	26%	24%	22%
Estimated Enbrel 50 mg packs after Brenzys listing	101,868	94,289	97,955	106,915	116,207
Estimated Brenzys packs	13,891	29,776	34,416	33,762	32,776
Total cost of Brenzys in submission ¹	\$20,448,385	\$43,832,059	\$50,662,417	\$49,699,690	\$48,248,239
Total co-payment ²	\$299,768	\$642,566	\$742,697	\$728,584	\$707,306
Net cost of Brenzys scripts	\$20,448,385	\$43,832,059	\$50,662,417	\$49,699,690	\$48,248,239
Cost offset from switching from Enbrel 50 mg ¹	\$20,448,385	\$43,832,059	\$50,662,417	\$49,699,690	\$48,248,239
Total cost from switching in submission¹	\$0	\$0	\$0	\$0	\$0
Total cost of Brenzys based on reduced Enbrel price from 1 April 2016 ³	\$19,763,837	\$42,364,697	\$48,966,396	\$48,035,898	\$46,633,037
Total co-payment ²	\$299,768	\$642,566	\$742,697	\$728,584	\$707,306
Net cost of Brenzys scripts	\$19,464,069	\$41,722,131	\$48,223,699	\$47,307,314	\$45,925,731
Cost offset from switching from Enbrel 50 mg ³	\$19,464,069	\$41,722,131	\$48,223,699	\$47,307,314	\$45,925,731
Total cost from switching with current price³	\$0	\$0	\$0	\$0	\$0
Estimated net cost of Enbrel 50 mg with no Brenzys listing in submission ⁴	\$201,651,020	\$216,119,989	\$230,588,958	\$245,057,927	\$259,526,896
Estimated net cost of Enbrel 50 mg plus Brenzys if Brenzys listed ⁵	\$170,404,194	\$182,631,124	\$194,858,054	\$207,084,985	\$219,311,915
Difference to net cost before and after Brenzys listing	-\$31,246,827	-\$33,488,865	-\$35,730,904	-\$37,972,943	-\$40,214,981
Estimated net cost of Enbrel 50 mg with no Brenzys listing with current cost ⁶	\$191,886,749	\$205,655,107	\$219,423,464	\$233,191,822	\$246,960,180
Estimated net cost of Enbrel 50 mg plus Brenzys if Brenzys listed with current costs ⁷	\$162,201,511	\$173,839,878	\$185,478,245	\$197,116,612	\$208,754,980
Difference to net cost before and after Brenzys listing	-\$29,685,238	-\$31,815,229	-\$33,945,219	-\$36,075,210	-\$38,205,201

¹ Assume a DPMQ for Brenzys and Enbrel 50 mg of \$1,493.64

² Assume an average co-payment of \$21.58 per script

³ Assume a DPMQ for Brenzys and Enbrel 50 mg of \$1422.78

⁴ Assume DPMQ for Enbrel 50 mg of \$1,763.57 and submission's estimate Enbrel 50 mg packs, minus co-payment. Lower than submission estimates in table E.3-6, p65 of the submission but unclear how submission's estimates are derived.

⁵ Assume DPMQ for Enbrel 50 mg and Brenzys of \$1,493.64 due to 16% price reduction and submission's estimate Enbrel 50 mg packs and Brenzys uptake, minus co-payment. Lower than submission estimates in table E.3-6, p65 of the submission but unclear how submission's estimates are derived.

⁶ Assume DPMQ for Enbrel 50 mg of \$1,679.22 and submission's estimate Enbrel 50 mg packs, minus co-payment

⁷ Assume DPMQ for Enbrel 50 mg of \$1,422.78 due to 16% price reduction and submission's estimate Enbrel

50 mg packs, minus co-payment

Source: Constructed during evaluation using information from Section E Utilisation and Cost Model Spreadsheets_Etanercept Biosimilar.xlsx

- 6.24 Overall, if Brenzys is to be priced identically to Enbrel, it is reasonable to expect that there will be no change in overall cost, and given the statutory 16% price reduction from listing of another brand of etanercept, the estimation of savings based on list price for etanercept is also expected and reasonable.

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

7 PBAC Outcome

- 7.1 The PBAC recommended the listing of etanercept (Brenzys) as a biosimilar of etanercept (Enbrel) on a cost minimisation basis to etanercept (Enbrel). The equivalent doses are 50 mg etanercept (Brenzys) and 50 mg etanercept (Enbrel) administered once weekly. The PBAC recommended that etanercept (Brenzys) be listed for the following indications that are PBS listed for etanercept (Enbrel):
- Severe active rheumatoid arthritis
 - Ankylosing spondylitis
 - Severe psoriatic arthritis
 - Severe chronic plaque psoriasis
- 7.2 The PBAC recommended the restrictions for etanercept (Brenzys) be the same as the restrictions for 50 mg etanercept (Enbrel) for the recommended indications.
- 7.3 The PBAC noted the advice from the TGA delegate that he does not intend to approve etanercept (Brenzys) for registration for juvenile plaque psoriasis or juvenile idiopathic arthritis because it is not available in a dose form that would enable weight based dosing for children weighing less than 62.5 kg (see Enbrel PI). As such the PBAC recommended that etanercept (Brenzys) should also not be subsidised for these indications.
- 7.4 The PBAC considered that a claim of non-inferior comparative effectiveness and non-inferior comparative safety was adequately supported. The PBAC noted that the ACPM was satisfied that the submitted data showed that Brenzys is similar to Enbrel in terms of efficacy and safety, further noting that the ACPM had stated there were sufficient data for it to be satisfied that Brenzys is a biosimilar of Enbrel.
- 7.5 The PBAC advised the Minister that it considered the Enbrel and Brenzys brands of etanercept could be marked as equivalent in the Schedule of Pharmaceutical Benefits ('a' flagged), for the purposes of substitution by the pharmacist at the point of dispensing for all the circumstances (restrictions) that both brands are listed against. The PBAC noted that the substitution process allows for patient and prescriber choice and is not automatic. For any individual prescription, a prescriber may choose to not permit brand substitution. If on the other hand, substitution has been permitted by the prescriber, the patient may choose which brand they wish to receive from the pharmacist.

- 7.6 In forming its view on brand substitution ('a' flagging), the PBAC considered a range of factors including:
- The evidence presented in the SB4-G31-RA trial in treatment-naïve patients initiating on either Enbrel or Brenzys that support a finding that Brenzys has equivalent effectiveness and equivalent safety compared to Enbrel.
 - The key randomised clinical study in rheumatoid arthritis did not indicate differences in efficacy or safety of Brenzys compared with Enbrel.
 - The clinical data provided in the submission did not suggest there were any identified populations where the risks of using the biosimilar product in place of the reference biologic were disproportionately high.
 - In the SB4-G31-RA Phase III extension study, which included 52 weeks of additional data, including from a one-way switch from Enbrel to Brenzys, the clinical evidence suggested no difference in efficacy, safety or immunogenicity between the biosimilar and the reference biologic. The drug, etanercept, is not immunogenic per se, and anti-drug antibodies are rare. Switching between brands of etanercept is unlikely to change this.
 - The ACPM has declared Brenzys a biosimilar for Enbrel. The ACPM was satisfied of the similar safety and efficacy of Brenzys and Enbrel in rheumatoid arthritis, psoriatic arthritis, plaque psoriasis, ankylosing spondylitis and non-radiographic axial spondyloarthritis.
- 7.7 The PBAC noted the consumer comments that expressed concern regarding potential 'a' flagging of biosimilars to reference biologics. The PBAC noted that the concerns raised were similar to those raised during the Committee's prior consideration of biosimilar infliximab, and biosimilars more broadly, and that the Department is currently undertaking a biosimilar awareness initiative to help address these concerns. The PBAC reiterated that it will make recommendations on whether to 'a' flag biosimilars on a case-by-case basis, and that pharmacy level substitution is not automatic.
- 7.8 The PBAC noted that the sponsor requested a partial 'a' flag for Brenzys, whereby substitution could only take place for etanercept treatment-naïve patients. The PBAC considered that such an 'a' flag would not work in practice as it relies on the dispenser knowing whether the patient is etanercept treatment naïve and this information is not always available to the dispenser.
- 7.9 The PBAC noted the potential for a Quality Use of Medicines issue relating to differences in auto injector presentations for Brenzys and Enbrel, but noted that any differences are likely to be minor and can be managed through the regular patient education and counselling on the use of the devices that is provided to patients by prescribers and pharmacists.
- 7.10 The PBAC noted the proposal from the sponsor in the pre-PBAC response that the PBAC recommend the authority listing of Brenzys (and other etanercept biosimilars) be streamlined, whilst the listing for Enbrel remains a written authority required. The sponsor considered this approach has the following benefits:
- to drive the uptake of both Brenzys and any future biosimilars to etanercept

which will generate significant savings for government through price disclosure;

- to provide etanercept biosimilars a point of differentiation from the originator and thereby give physicians a reason to prescribe biosimilar brands; and
- to maintain the primacy of clinician choice.

- 7.11 The PBAC did not consider streamlined listings would be appropriate because of the large potential for leakage into less severe disease. The PBAC however acknowledged the ongoing need to examine the uptake drivers for biosimilar medicines, and noted that the introduction of competition in the PBS etanercept market would make this bDMARD more cost-effective than many other bDMARDs currently subsidised for the same indications, making this a potential candidate for first line treatment in a cost-effective prescribing setting.
- 7.12 The PBAC considered the utilisation estimates presented in the submission were reasonable. As Brenzys is likely to only substitute for Enbrel or other future etanercept biosimilars, the PBAC considered the listing of Brenzys would not grow the overall market. The PBAC noted the submission estimated overall net savings to the PBAC of over \$150 million over the first five years of listing. This was based on the impact of the statutory 16% price reduction following the listing of a biosimilar brand. The financial estimates did not account for any potential impacts of price disclosure. In addition, the PBAC noted the financial estimates did not take into account the 5% statutory price reduction for etanercept that occurred in April 2016.
- 7.13 The PBAC advised that Brenzys and all other brands of etanercept are not suitable for prescribing by nurse practitioners.
- 7.14 The PBAC recommended that the Early Supply Rule should apply.
- 7.15 The PBAC noted that this submission is not eligible for an Independent Review as it received a positive recommendation.

Outcome:

Recommended

8 Recommended listing

- 8.1 Add new item: Etanercept (Brenzys), injection 50 mg

Listings same as for 50 mg etanercept (Enbrel) for the following indications:

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

9 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.

10 Sponsor's Comment

The sponsor had no comment.