

5.22 SECUKINUMAB
powder for injection, 150 mg,
pre-filled syringe, 150 mg/mL, and
pre-filled pen, 150 mg/mL;
Cosentyx[®]; Novartis Pharmaceuticals Australia Pty Ltd

1 Purpose of Application

1.1 The major submission sought a General Schedule Authority Required listing for the treatment of severe chronic plaque psoriasis which is refractory to treatment with non-biological disease modifying anti rheumatic drugs (DMARDs) in patients meeting certain criteria.

2 Requested listing

2.1 The requested listing was similar to that of ustekinumab (and other bDMARDs including adalimumab, etanercept and infliximab) currently PBS listed for the treatment of severe chronic plaque psoriasis. An abbreviated version is shown below:

Name, Restriction, Manner of administration and form	Max Qty packs	Max Qty units	No. of Rpts	Dispensed Price for Max. Qty	Proprietary Name and Manufacturer	
SECUKINUMAB						
<u>Initial treatment</u>						
Powder for injection 150mg × 2	2	2 (4)	3	\$ [REDACTED]	Cosentyx	NV
Pre-filled syringe 150mg/mL × 2	2	2 (4)	3	\$ [REDACTED]	Cosentyx	NV
Pre-filled pen 150mg/mL × 2	2	2 (4)	3	\$ [REDACTED]	Cosentyx	NV
<u>Continuing Treatment</u>						
Powder for injection 150mg × 2	1	1 (2)	5	\$ [REDACTED]	Cosentyx	NV
Pre-filled syringe 150mg/mL × 2	1	1 (2)	5	\$ [REDACTED]	Cosentyx	NV
Pre-filled pen 150mg/mL × 2						

Severity:	Severe - The whole body (baseline PASI >15) OR the face, a palm of a hand or the sole of a foot (2 of 3 PASI symptom sub-scores rated as 'severe' or 'very severe' or 30% or more of the area is affected).
Condition:	Plaque psoriasis
Restriction:	Section 85 (General Schedule) Authority Required
Treatment phase:	Initial and continuing
Treatment criteria:	Must be initiated by a dermatologist. Treatment must be used as systemic monotherapy (other than methotrexate).

Clinical criteria:	<ul style="list-style-type: none"> • Failed to achieve an adequate response based on PASI assessment, contra-indicated or intolerant to at least 3 of the 4 following treatments: <ul style="list-style-type: none"> - phototherapy (UVB or PUVA) for 3 treatments per week for at least 6 weeks; - methotrexate at a dose of at least 10mg weekly for at least 6 weeks; - cyclosporin at a dose of at least 2 mg per kg per day for at least 6 weeks; - acitretin at a dose of at least 0.4 mg per kg per day for at least 6 weeks. • Initial Authority approval is limited to 16 weeks and patients must be assessed for response to an initial treatment course after at least 12 weeks of treatment. • Patients are required to demonstrate an adequate response or maintenance of an adequate response for continuing treatment. For patients with whole body psoriasis this is defined as a 75% reduction in PASI score from baseline (PASI 75 response). For patients with face, palm or sole psoriasis, response is defined as a reduction in all three PASI sub-scores to 'slight' or 'none' or 75% reduction in the area affected. • Continuing Authority approval is for 26 weeks (6 months equivalent).
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- 2.2 The submission also sought an increase in the number of treatments a patient can use in a treatment cycle from the current three biological agents to a proposed four agents, and to extend this to the restrictions of all PBS listed bDMARDs. No data directly supportive of this change was presented in the submission. Adalimumab, etanercept and infliximab are all anti-tumour necrosis factor (anti-TNF) agents, ustekinumab is an antibody against interleukin 12 and 23, whilst secukinumab is an antibody against interleukin 17. Therefore, even if the maximum number of treatments remain at three, it is possible for a patient to have tried and failed one biological agent in each class, including secukinumab, before the treatment cycle is over. The ESC noted that keeping the number of biologics per treatment cycle as three would mean that secukinumab is replacing one of three other agents. Increasing it to four is effectively the addition of a fourth line of therapy. This potential change had implications for the choice of comparator, the cost-minimisation analysis and the financial estimates, as the use of up to four agents compared to three agents results in greater drug treatment costs.
- 2.3 Following the review by the ESC, the sponsor, in its pre-PBAC response, withdrew the proposed increase in the number of treatments used per cycle.

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

3 Background

- 3.1 The submission was made under TGA/PBAC parallel processes.
- 3.2 Secukinumab was TGA registered for treatment of moderate to severe plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy on 8 January 2015.
- 3.3 Secukinumab had not previously been considered by the PBAC for any indication.

4 Clinical place for the proposed therapy

- 4.1 Psoriasis is a chronic autoimmune disease with predominantly skin and joint manifestations, with plaque psoriasis being the most common form. The major

manifestation is chronic inflammation of the skin characterised by disfiguring, scaling and erythematous plaques that may be painful or pruritic.

- 4.2 Secukinumab is expected to be used as an alternative to other existing bDMARDs (ustekinumab, adalimumab, etanercept and infliximab) in the treatment of severe chronic plaque psoriasis.

5 Comparator

- 5.1 The submission proposed ustekinumab as the main comparator based on current utilisation data, from a Medicare Australia data sample. Forty-four per cent of the patient sample had used ustekinumab, 37% adalimumab, 10% etanercept and 9% infliximab. Adalimumab, etanercept and infliximab were therefore nominated as secondary comparators. The evaluation considered the nominated comparators to be appropriate.
- 5.2 The ESC however considered that ustekinumab may not be the most appropriate comparator. Since the current PBS restrictions only allow three bDMARDs per treatment cycle, secukinumab is more likely to displace the least popular bDMARDs in current usage - that is infliximab and etanercept. Since there are three agents that have the same mechanism of action TNF-alpha inhibition, it is also likely clinicians will choose three drugs with different mechanisms per treatment cycle. This further supports the view that infliximab or etanercept would be replaced by secukinumab.

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

6 Consideration of the evidence

Sponsor hearing

- 6.1 The sponsor requested a hearing for this item.
- 6.2 The clinician presenting at the hearing addressed the issue of the appropriateness of ustekinumab and adalimumab as comparators. The clinician's view was that there is no established hierarchy in the selection of bDMARD treatments in severe chronic plaque psoriasis and that treatment selection depended on individual patient factors and individual drug characteristics. The clinician advocated for the use of ustekinumab and adalimumab as appropriate comparators in the submission and acknowledged that etanercept's efficacy in the condition appeared to be inferior to other existing bDMARDs. The clinician was also supportive of the submission's clinical claims.
- 6.3 The PBAC considered that the hearing was informative.

Consumer comments

- 6.4 There were no consumer comments received for this item.

Clinical trials

6.5 The submission was based on an indirect comparison, using the method described by Bucher (1997), between:

- secukinumab – a meta-analysis of 4 trials; three providing a comparison of secukinumab and placebo and one comparing secukinumab and etanercept and placebo (n=1,377);
- ustekinumab – a meta-analysis of up to 6 trials (6 trials using the 45 mg dose and 4 trials using the 90 mg dose); five comparing ustekinumab and placebo and one comparing ustekinumab and etanercept (n=2,596);
- adalimumab – a meta-analysis of 4 trials comparing adalimumab and placebo (n=1,560); and
- infliximab – a meta-analysis of 6 trials comparing infliximab and placebo (n=1,255).

The primary comparison presented in the submission was between secukinumab and ustekinumab.

6.6 Details of the trials presented in the submission are provided in Table 1 below. Many of the trials had multiple publications, so only the primary publications are listed below. A further trial comparing infliximab and placebo (IFX6; Chaudhari 2001) was included in the Commentary for completeness.

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Trials and associated reports presented in the submission

Trial ID	Protocol title/ Publication title	Publication citation
SECUKINUMAB		
Secukinumab versus etanercept and placebo		
SEC ₂ (FIXTURE)	A randomized, double-blind, double-dummy, placebo controlled, multicenter study of subcutaneous secukinumab to demonstrate efficacy after twelve weeks of treatment, compared to placebo and etanercept, and to assess the safety, tolerability and long-term efficacy up to one year in subjects with moderate to severe chronic plaque-type psoriasis Langley RG, et al. Secukinumab in plaque psoriasis: results of two phase three trials.	25 Sept 2013 <i>New Engl J Med.</i> 2014 371(4): 326-38
Secukinumab versus placebo		
SEC ₁ (ERASURE)	A randomized, double-blind, placebo controlled, multicenter study of subcutaneous secukinumab to demonstrate efficacy after twelve weeks of treatment, and to assess the safety, tolerability and long-term efficacy up to one year in subjects with moderate to severe chronic plaque-type psoriasis Langley RG, et al. Secukinumab in plaque psoriasis: results of two phase three trials. <i>Ohtsuki M et al. Secukinumab efficacy and safety in Japanese patients with moderate-to-severe plaque psoriasis: Subanalysis from ERASURE, a randomized, placebo-controlled, phase 3 study.</i>	06 Sept 2013 <i>New Engl J Med.</i> 2014 371(4): 326-38 The Journal of Dermatology 2014, 41 (12): 1039-1046.
SEC ₃ (FEATURE)	A randomized, double-blind, placebo controlled, multicenter study of subcutaneous secukinumab in prefilled syringes to demonstrate efficacy after twelve weeks of treatment, and to assess the safety, tolerability, usability and long-term efficacy in subjects with chronic plaque-type psoriasis. <i>Blauvelt A, et al. Secukinumab administration by pre-filled syringe: efficacy, safety and usability results from a randomized controlled trial in psoriasis (FEATURE).</i>	05 Sept 2013 British Journal of Dermatology, Article first published online : 11 DEC 2014
SEC ₄ (JUNCTURE)	A randomised , double-blind, placebo-controlled, multicenter study of subcutaneous secukinumab in autoinjectors to demonstrate efficacy after 12 weeks of treatment, and to assess the safety, tolerability, usability and long-term efficacy in subjects with chronic plaque-type psoriasis. <i>Paul C, et al. Efficacy, safety and usability of secukinumab administration by autoinjector/pen in psoriasis: a randomized, controlled trial (JUNCTURE).</i>	16 Sept 2013 Journal of the European Academy of Dermatology and Venerology, Article first published online : 22 SEP 2014
USTEKINUMAB		
Ustekinumab versus etanercept		
UST ₁ (ACCEPT)	Griffiths CE, et al. Comparison of ustekinumab and etanercept for moderate-to-severe psoriasis (ACCEPT).	<i>N Engl J Med,</i> 2010;362:118–128
Ustekinumab versus placebo		
UST ₂ (PHOENIX 1)	Leonardi CL, et al. Efficacy and safety of ustekinumab, human interleukin-12/23 monoclonal antibody, in patients with psoriasis: 76-week results from a randomised, double blind, placebo-controlled trial (PHOENIX 1).	<i>The Lancet,</i> 2008; 371:1665–1674.
UST ₃ (PHOENIX 2)	Papp KA, et al. Efficacy and safety of ustekinumab, a human interleukin-12/23 monoclonal antibody, in patients with psoriasis: 52-week results from a randomised, double blind, placebo-controlled trial (PHOENIX 2).	<i>The Lancet,</i> 2008;371:1675–1684.
UST ₄ (PEARL)	Tsai TF, et al. Efficacy and safety of ustekinumab for the treatment of moderate-to-severe psoriasis: A phase III, randomized, placebo-controlled trial in Taiwanese and Korean patients (PEARL).	<i>J Dermatol Sci,</i> 2011;63:154–163.
UST ₅ (Igarashi 2012)	Igarashi A, et al. The Japanese Ustekinumab Study Group. Efficacy and safety of ustekinumab in Japanese patients with moderate- to-severe plaque-type psoriasis: Long-term results from a phase 2/3 clinical trial.	<i>J Dermatol,</i> 2012; 39:242–252.
UST ₆ (LOTUS)	Zhu X, et al. Efficacy and safety of ustekinumab in Chinese patients with moderate to severe plaque-type psoriasis: results from a phase 3 clinical trial (LOTUS).	<i>J Drugs Dermatol.</i> 2013 Feb;12(2):166-74
ADALIMUMAB		
Adalimumab versus placebo		
ADA ₁ (CHAMPION)	Saurat JH, et al. Efficacy and safety results from the randomized controlled comparative study of adalimumab vs. methotrexate vs. placebo in patients with	<i>Br J Dermatol.</i> 2008 Mar;158(3):558-66.

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	psoriasis (CHAMPION).	
ADA ₂ (REVEAL)	Menter A, et al. Adalimumab therapy for moderate to severe psoriasis: A randomized, controlled phase III trial.	<i>J Am Acad Dermatol.</i> 2008 Jan;58(1):106-15.
ADA ₃ (Gordon 2006)	Gordon KB, et al. Clinical response to adalimumab treatment in patients with moderate to severe psoriasis: double-blind, randomized controlled trial and open-label extension study.	<i>J Am Acad Dermatol.</i> 2006 Oct;55(4):598-606.
ADA ₄ (Asahina 2010)	Asahina A, et al. Adalimumab in Japanese patients with moderate to severe chronic plaque psoriasis: efficacy and safety results from a Phase II/III randomized controlled study.	<i>J Dermatol.</i> 2010 Apr;37(4):299-310.
INFLIXIMAB		
Infliximab versus placebo		
IFX ₁ (SPIRIT)	Gottlieb AB, et al. Infliximab induction therapy for patients with severe plaque-type psoriasis: a randomized, double-blind, placebo-controlled trial.	<i>J Am Acad Dermatol.</i> 2004 Oct;51(4):534-42.
IFX ₂ (EXPRESS)	Reich K, et al. Infliximab induction and maintenance therapy for moderate-to-severe psoriasis: a phase III, multicentre, double-blind trial.	<i>The Lancet.</i> 2005 Oct 15;366(9494):1367-74.
IFX ₃ (EXPRESS 2)	Menter A, et al. A randomized comparison of continuous vs. intermittent infliximab maintenance regimens over 1 year in the treatment of moderate-to-severe plaque psoriasis.	<i>J Am Acad Dermatol.</i> 2007 Jan;56(1):31-15.
IFX ₄ (Torii 2010)	Torii H, Nakagawa H. Infliximab monotherapy in Japanese patients with moderate-to-severe plaque psoriasis and psoriatic arthritis. A randomized, double-blind, placebo-controlled multicenter trial.	<i>J Dermatol Sci.</i> 2010 Jul;59(1):40-9.
IFX ₅ (Yang 2012)	Yang HZ, et al. Infliximab monotherapy for Chinese patients with moderate to severe plaque psoriasis: a randomized, double-blind, placebo-controlled multicenter trial.	<i>Chin Med J (Engl)</i> 2012 Jun;125(11):1845-51.
IFX ₆ (Chaudhari 2001)	Chaudhari U, et al. Efficacy and safety of infliximab monotherapy for plaque-type psoriasis: a randomised trial.	<i>The Lancet</i> 2001, 357 (9271): 1842-7.

Source: Table 9, pp 26-31 of the submission

- 6.7 The submission identified an ongoing head-to-head trial comparing secukinumab 300 mg and ustekinumab 45 mg and 90 mg (CLEAR, NCT02074982). The planned completion date is July 2015.
- 6.8 The key features of the direct randomised trials are summarised below.

Key features of the included evidence – indirect comparison

Trial	N ^b	Design/ duration ^c	Comparator	Risk of bias	Patient population	Outcome(s)	Use in modelled evaluation	
Secukinumab								
SEC ₁ (ERASURE)	738	R, DB, 12 weeks	PBO	Low ^a	Moderate to severe chronic plaque psoriasis	PASI 75 IGA mod 2011 at 12 weeks		
SEC ₂ (FIXTURE)	1306	R, DB, 12 weeks	ETN; PBO	Low ^a				
SEC ₃ (FEATURE)	177	R, DB, 12 weeks	PBO	Low ^a				
SEC ₄ (JUNCTURE)	182	R, DB, 12 weeks	PBO	Low ^a				
Meta-analysis	1377	Included all trials – relevant treatment arms only						PASI 75
Ustekinumab								
UST ₁ (ACCEPT)	903	R, SB, 12 weeks	ETN	Low ^a	Moderate to severe chronic plaque psoriasis	PASI 75 at 12 weeks	PASI 75	
UST ₂ (PHOENIX 1)	766	R, DB, 12 weeks	PBO	Low ^a				
UST ₃ (PHOENIX 2)	1230	R, DB, 12 weeks	PBO	Low ^a				
UST ₄ (PEARL)	121	R, DB, 12 weeks	PBO	Low ^a				
UST ₅ (Igarashi 2012)	158	R, DB, 12 weeks	PBO	Low ^a				
UST ₆ (LOTUS)	322	R, DB, 12 weeks	PBO	Low ^a				
Meta-analysis	2596	Included UST ₂ , UST ₃ , UST ₄ , UST ₅ , UST ₆						PASI 75
Adalimumab								
ADA ₁ (CHAMPION)	271	R, DB, 16 weeks	PBO	Low	Moderate to severe chronic plaque psoriasis	PASI 75 at 12/16 weeks		
ADA ₂ (REVEAL)	1212	R, DB, 16 weeks	PBO	Low ^a				
ADA ₃ (Gordon 2006)	147	R, DB, 12 weeks	PBO	Low ^a				
ADA ₄ (Asahina 2010)	235	R, DB, 16 weeks	PBO	Low				
Meta-analysis	1560	Included all trials – relevant treatment arms only						PASI 75
Infliximab								
IFX ₁ (SPIRIT)	249	R, DB, 10 weeks	PBO	Low	Moderate to severe chronic plaque psoriasis	PASI 75 at 10 weeks		
IFX ₂ (EXPRESS)	378	R, DB, 24 weeks	PBO	Low ^a				
IFX ₃ (EXPRESS 2)	835	R, DB, 14 weeks	PBO	Low				
IFX ₄ (Torii 2010)	54	R, DB, 16 weeks	PBO	Low ^a				
IFX ₅ (Yang 2012)	129	R, DB, 26 weeks	PBO	Low ^a				
IFX ₆ (Chaudhari 2001)	33	R, DB, 10 weeks	PBO	Low ^a				
Meta-analysis	1255	Included all trials – relevant treatment arms only						PASI 75

DB=double blind; SB=single blind; SEC=secukinumab; UST=ustekinumab; ADA=adalimumab; IFX=infliximab; PBO=placebo; ETN=etanercept

^a trial allowed cross-over over patients at some point (end of DB period), which would introduce bias

^b for trials, N represents entire population; for meta-analyses, N includes only relevant treatment arms

^c duration of the comparator controlled-phase of the trials

Source: compiled during the evaluation

Comparative effectiveness

6.9 Psoriasis Area Severity Index (PASI) 75 is an outcome previously accepted by the PBAC for therapies used in the treatment of psoriasis. The submission presented the results of the meta-analyses and indirect comparisons for PASI 75 response in the controlled, double-blind phase of the direct randomised trials (weeks 10-16) in terms of odds ratios (see table below). The relative risk and risk difference statistics and subsequent indirect comparisons were estimated using the method described by Bucher (1997) during the evaluation (estimates are provided in table below and under benefits/harms further below).

Results of PASI 75 response at the end of the controlled, double-blind phase of the direct randomised trials

Trial ID	Comparison	Test n/N (%)	Control n/N (%)	RD (95% CI)	NNT (95% CI)	RR (95% CI)	OR (95% CI)
Secukinumab – 12 weeks							
SEC ₁	SEC v PBO	200/245 (81.6)	11/246 (4.5)	0.77 (0.71, 0.82)	1.3 (1.2, 1.4)	18.3 (10.4, 32.6)	82.7 (38.7, 176.7)
SEC ₂		249/323 (77.1)	16/324 (4.9)	0.72 (0.67, 0.77)	1.4 (1.3, 1.5)	15.6 (9.8, 25.3)	66.0 (36.1, 120.6)
SEC ₃		44/59 (74.6)	0/59 (0.0)	0.75 (0.62, 0.84)	1.3 (1.2, 1.6)	89.0 (12.2, ∞)	341.7 (37.4, ∞)
SEC ₄		52/60 (86.7)	2/61 (3.3)	0.83 (0.71, 0.91)	1.2 (1.1, 1.4)	26.4 (7.7, 96.2)	191.8 (39.0, 943.8)
Meta-analysis – SEC v PBO				0.76 (0.72, 0.80)	1.3 (1.3, 1.4)	17.7 (12.4, 25.2)	82.2 (54.9, 126.2)
SEC ₂	SEC v ETN	249/323 (77.1)	142/323 (44.0)	0.33 (0.26, 0.40)	3 (2, 4)	1.8 (1.5, 2.0)	4.7 (3.3, 6.7)
Ustekinumab 45mg – 12 weeks							
UST ₂	UST v PBO	171/255 (67.1)	8/255 (3.1)	0.64 (0.57, 0.70)	1.6 (1.4, 1.8)	21.4 (11.0, 42.2)	62.9 (29.7, 133.2)
UST ₃		273/409 (66.7)	15/410 (3.7)	0.63 (0.58, 0.68)	1.6 (1.5, 1.7)	18.2 (11.2, 30.1)	52.9 (30.3, 92.1)
UST ₄		41/61 (67.2)	3/60 (5.0)	0.62 (0.48, 0.74)	1.6 (1.4, 2.1)	13.4 (4.8, 39.6)	39.0 (10.9, 139.8)
UST ₅		38/64 (59.4)	2/31 (6.5)	0.53 (0.35, 0.66)	1.9 (1.5, 2.9)	9.2 (2.8, 33.6)	21.2 (4.7, 96.6)
UST ₆		132/160 (82.5)	18/162 (11.1)	0.71 (0.63, 0.78)	1.4 (1.3, 1.6)	7.4 (4.9, 11.6)	37.7 (19.9, 71.3)
Meta-analysis – UST45 v PBO				0.64 (0.60, 0.69)	1.6 (1.4, 1.7)	13.1 (7.8, 22.0)	46.4 (33.0, 65.4)
UST ₁	UST v ETN	141/209 (67.5)	197/347 (56.8)	0.11 (0.02, 0.19)	9 (5, 50)	1.2 (1.0, 1.4)	1.6 (1.1, 2.3)
Ustekinumab 90mg – 12 weeks							
UST ₂	UST v PBO	170/256 (66.4)	8/255 (3.1)	0.63 (0.57, 0.69)	1.6 (1.4, 1.8)	21.2 (10.9, 41.8)	61.0 (28.8, 129.3)
UST ₃		311/411 (75.7)	15/410 (3.7)	0.72 (0.67, 0.76)	1.4 (1.3, 1.5)	20.7 (12.7, 34.0)	81.9 (46.7, 143.8)
UST ₅		42/62 (67.7)	2/31 (6.5)	0.61 (0.43, 0.74)	1.6 (1.4, 2.3)	10.5 (3.2, 38.2)	30.5 (6.6, 140.4)
Meta-analysis – UST90 v PBO				0.67 (0.60, 0.74)	1.5 (1.4, 1.7)	19.7 (13.4, 29.0)	68.7 (44.6, 105.7)
UST ₁	UST v ETN	256/347 (73.8)	197/347 (56.8)	0.15 (0.08, 0.22)	7 (5, 13)	1.3 (1.1, 1.4)	2.1 (1.6, 3.0)
Ustekinumab 45&90mg – 12 weeks							
UST ₂	UST v PBO	341/511 (66.7)	8/255 (3.1)	0.64 (0.59, 0.68)	1.6 (1.5, 1.7)	21.3 (11.0, 41.9)	61.9 (29.8, 147.8)
UST ₃		584/820 (71.2)	15/410 (3.7)	0.68 (0.64, 0.71)	1.5 (1.4, 1.6)	19.5 (12.0, 32.0)	65.2 (37.9, 119.7)
UST ₄		41/61 (67.2)	3/60 (5.0)	0.62 (0.48, 0.74)	1.6 (1.4, 2.1)	13.4 (4.8, 39.6)	39.0 (10.9, 139.8)
UST ₅		80/126 (63.5)	2/31 (6.5)	0.57 (0.41, 0.67)	1.8 (1.5, 2.4)	9.8 (3.0, 65.7)	25.2 (5.8, 223.7)
UST ₆		132/160 (82.5)	18/162 (11.1)	0.71 (0.63, 0.78)	1.4 (1.3, 1.6)	7.4 (4.9, 11.6)	37.7 (19.9, 71.3)
Meta-analysis – UST45&90 v PBO				0.66 (0.62, 0.69)	1.5 (1.4, 1.6)	13.5 (7.7, 23.4)	50.9 (36.4, 71.2)
UST ₁	UST v ETN	397/556 (71.4)	197/347 (56.8)	0.15 (0.08, 0.21)	7 (5, 13)	1.3 (1.1, 1.4)	1.9 (1.4, 2.5)
Adalimumab – 12 (ADA₃) or 16 weeks (ADA₁, ADA₂, ADA₄)							
ADA ₁	ADA v PBO	86/108 (79.6)	10/53 (18.9)	0.61 (0.46, 0.72)	1.6 (1.4, 2.2)	4.2 (2.5, 7.6)	16.8 (7.3, 38.6)
ADA ₂		578/814 (71.0)	26/398 (6.5)	0.64 (0.60, 0.68)	1.6 (1.5, 1.7)	10.9 (7.5, 15.8)	35.0 (22.9, 53.6)
ADA ₃		24/46 (52.2)	2/52 (3.9)	0.48 (0.33, 0.63)	2.1 (1.6, 3.0)	13.6 (3.9, 50.3)	28.6 (6.2, 131.9)
ADA ₄		27/43 (62.8)	2/46 (4.3)	0.58 (0.41, 0.72)	1.4 (1.4, 2.4)	14.4 (4.2, 53.1)	37.1 (7.9, 174.2)
Meta-analysis – ADA v PBO				0.61 (0.54, 0.67)	1.7 (1.5, 1.9)	8.6 (4.5, 16.6)	30.4 (21.2, 43.4)
Infliximab – 10 weeks							
IFX ₁	IFX v PBO	87/99 (87.9)	3/51 (5.9)	0.82 (0.70, 0.89)	1.2 (1.1, 1.4)	14.9 (5.5, 43.6)	116.0 (31.2, 431.3)
IFX ₂		242/301 (80.4)	2/77 (2.6)	0.78 (0.70, 0.83)	1.3 (1.2, 1.4)	31.0 (8.9, 112.5)	141.5 (33.7, 593.9)
IFX ₃		237/314 (75.5)	4/208 (1.9)	0.74 (0.68, 0.78)	1.4 (1.3, 1.5)	39.5 (15.6, 100.8)	157.0 (56.5, 436.4)
IFX ₄		24/35 (68.6)	0/19 (0.0)	0.69 (0.49, 0.82)	1.4 (1.2, 2.0)	27.2 (4.0, ∞)	83.1 (4.6, 1500.0)
IFX ₅		68/84 (81.0)	1/45 (2.2)	0.79 (0.67, 0.86)	1.3 (1.2, 1.5)	36.4 (7.0, 206.2)	187.0 (23.9, 1461)
IFX ₆		9/11 (81.8)	2/11 (18.2)	0.64 (0.22, 0.86)	1.6 (1.2, 4.5)	4.5 (1.6, 16.3)	20.3 (1.7, 293.5)
Meta-analysis – IFX v PBO				0.76 (0.73, 0.79)	1.3 (1.3, 1.4)	19.7 (9.1, 42.7)	121.9 (65.5, 266.8)

Source: Table 38, p117; Table 67, p174; Table 72, p182; Figure 17, p183 of the submission

Bold typography indicates statistically significant differences

RR and RD estimated during the evaluation using StatsDirect, NNT calculated during the evaluation as 1/RD. It is acknowledged that NNT should be whole numbers, however given the high response rates there was no delineation between the point estimates and 95% CIs.

- 6.10 The results of the direct comparisons indicated that a statistically significantly greater proportion of patients achieve PASI 75 when treated with any bDMARD at the TGA-approved doses compared with placebo. A statistically significantly greater proportion of patients achieve PASI 75 when treated with secukinumab and ustekinumab compared with etanercept 100 mg weekly.

- 6.11 The results of the indirect comparisons presented as odd ratios are further summarised in the table below; where (i) a tick (✓) indicates that a statistically significantly greater proportion of patients achieved PASI 75 response, favouring secukinumab 300 mg at 12 weeks or (ii) no statistically significant (NS) differences were observed between treatments in the proportion of patients achieving PASI 75 response. N/A denotes that the comparison was not applicable.

Statistically significantly greater proportion of patients achieved PASI 75 response

Comparison	Common reference					
	Etanercept			Placebo		
	SEC - All	SEC ≤100kg	SEC >100kg	SEC - All	SEC ≤100kg	SEC >100kg
UST45 – all (12 weeks)	✓	N/A	N/A	✓	N/A	N/A
UST90 – all (12 weeks)	✓	N/A	N/A	NS	N/A	N/A
UST 45&90 – all (12 weeks)	✓	N/A	N/A	NS	N/A	N/A
UST45 ≤100kg (12 weeks)	N/A	✓	N/A	N/A	NS	N/A
UST90 >100kg (12 weeks)	N/A	N/A	NS	N/A	N/A	NS
ADA (12-16 weeks)	N/A	N/A	N/A	✓	N/A	N/A
IFX (10 weeks)	N/A	N/A	N/A	NS	N/A	N/A

- 6.12 The results for the comparison of secukinumab and ustekinumab were inconsistent, depending on whether etanercept or placebo is used as the common reference in the indirect comparison. It was noted that the etanercept response rates in the secukinumab and ustekinumab trials differed (in the ITT populations and in the sub-groups according to weight), which suggested there are exchangeability issues between these trials. The results of the indirect comparisons of secukinumab and ustekinumab using placebo as the common reference may be more reliable.
- 6.13 There were no statistically significant differences for the proportion of patients achieving a PASI 75 response between secukinumab (at 12 weeks) and ustekinumab (at 12 weeks), using placebo as the common reference and when ustekinumab was administered according to patient weight, as per the TGA-approved dosing or infliximab (at 10 weeks). A statistically significantly greater proportion of patients achieved PASI 75 response when treated with secukinumab at 12 weeks compared with adalimumab at 12-16 weeks.
- 6.14 With respect to the comparison with ustekinumab, the trials reported the PASI 75 response rate at 12 weeks. In practice, treatment response to ustekinumab is assessed at 28 weeks according to its current PBS restriction. Thus, the PASI 75 response rates for ustekinumab may have been underestimated.

Comparative harms

- 6.15 The submission stated that “across all the clinical trials, the safety profile of secukinumab showed no new or unexpected safety signals”. The submission did not conduct a complete comparison of the safety profile of secukinumab and the bDMARDs currently listed for psoriasis. It only presented an indirect comparison of the treatments in terms of the proportion of patients experiencing at least one adverse event. The available data suggested that like ustekinumab (ustekinumab draft PI), the most common adverse events during the induction phase of the secukinumab trials were nasopharyngitis and upper respiratory tract infections.

Infection rates were comparable for secukinumab 300 mg and the etanercept group and both were higher than in the placebo group. However, the incidence of serious infections was low and comparable across treatments.

- 6.16 Indirect comparisons of secukinumab to ustekinumab, adalimumab and infliximab using placebo as the common reference, showed no statistically significant differences in the proportion of patients experiencing at least one adverse event between the treatments (over an observation period ranging between 12 to 30 weeks).

Benefits/harms

- 6.17 A summary of the comparative benefits and harms for secukinumab versus ustekinumab, adalimumab and infliximab, using placebo as the common reference, is presented in table below.

Public Summary Document – March 2015 PBAC Meeting

Indirect comparison of PASI 75 response: summary of comparative benefits and harms for secukinumab compared with ustekinumab, adalimumab and infliximab

Trial	Week ^a	SEC	PBO/Comparator	RR (95% CI)	Event rate/100 patients*			RD (95% CI)	
					SEC	PBO/Comparator			
Benefits									
PASI 75: Indirect comparison - results of meta-analyses									
		SEC	PBO	Comp	RR (95% CI)	Event rate/100 patients*			RD (95% CI)
						SEC	PBO	Comp	
SEC All	12	545/687	29/690	-	17.7 (12.4, 25.2)	79	4	-	0.76 (0.72, 0.80)
UST45 ≤100kg	12	-	18/456	342/465	18.6 (11.8, 29.3)	-	4	74	0.70 (0.65, 0.74)
UST90 >100kg	12	-	5/209	67/103	29.2 (12.2, 69.8)	-	2	70	0.68 (0.61, 0.74)
ADA	12/16	-	40/549	715/1011	8.6 (4.5, 16.6)	-	7	71	0.61 (0.54, 0.67)
IFX	10	-	12/411	667/844	19.7 (9.1, 42.7)	-	3	79	0.76 (0.73, 0.79)
Indirect comparisons									
					2.1 (0.97, 4.3)	-			0.15 (0.07, 0.23)
					0.7 (0.3, 1.5)	-			0.0 (-0.05, 0.05)
Proportion patients with ≥1 adverse event: indirect comparison - results of meta-analyses									
	Week ^a	SEC	PBO	Comp	RR (95% CI)	Event rate/100 patients*			RD (95% CI)
						SEC	PBO	Comp	
SEC	12	388/690	340/694	-	1.15 (1.04, 1.27)	56	49	-	0.07 (0.02, 0.13)
UST45	12	-	452/918	514/949	1.08 (0.99, 1.18)	-	49	54	0.04 (-0.0, 0.09)
UST90	12	-	348/697	365/728	0.99 (0.80, 1.22)	-	50	50	-0.0 (-0.06, 0.05)
ADA	12/16	-	339/549	652/1009	1.03 (0.93, 1.13)	-	62	65	0.03 (-0.03, 0.09)
IFX	14-30	-	230/398	608/830	1.22 (1.12, 1.34)	-	58	73	0.14 (0.07, 0.22)
Indirect comparisons									
SEC v UST45					1.07 (0.93, 1.22)				0.03 (-0.04, 0.10)
SEC v UST90					1.16 (0.92, 1.47)				0.07 (-0.01, 0.15)
SEC v ADA					1.12 (0.97, 1.28)				0.04 (-0.04, 0.12)
SEC v IFX					0.93 (0.82, 1.25)				-0.07 (-0.16, 0.02)

^a outcome measured at week

Abbreviations: PBO = placebo; RD = risk difference; RR = risk ratio

Bold typography indicates statistically significant differences

Source: Compiled during the evaluation

- 6.18 On the basis of indirect evidence presented by the submission, for every 100 patients weighing ≤ 100 kg treated with secukinumab in comparison to ustekinumab 45 mg:
- Approximately 10 additional patients would have a PASI 75 response after 12 weeks of treatment. This difference should be interpreted with caution as the indirect comparison of these treatments, although statistically significantly different based on the Risk Difference, was not statistically significantly different when using the Relative Risk statistic.
- 6.19 On the basis of indirect evidence presented by the submission, for every 100 patients treated with secukinumab in comparison to adalimumab:
- Approximately 15 additional patients would have a PASI 75 response after 12 weeks of treatment. This is supported by the indirect comparison of these treatments using the RD and OR, but not RR statistics.
- 6.20 On the basis of indirect evidence presented by the submission, for every 100 patients weighing >100 kg treated with secukinumab in comparison to ustekinumab 90 mg, there were no differences in the proportion of patients achieving a PASI 75 response after 12 weeks of treatment. Similarly, on the basis of indirect evidence presented by the submission, for every 100 patients treated with secukinumab in comparison to infliximab, there were no differences in the proportion of patients achieving a PASI 75 response after 12 weeks of treatment.
- 6.21 While statistically significantly greater proportions of patients achieved a PASI response when treated with secukinumab compared with ustekinumab 45 mg (in those weighing ≤ 100 kg) and adalimumab at 12/16 weeks, there was no evidence to support a claim that those benefits would be maintained over the long term.
- 6.22 On the basis of indirect evidence presented by the submission, comparing secukinumab with ustekinumab (45 mg or 90 mg), adalimumab or infliximab, there were no differences in the proportion of patients experiencing at least one adverse event after 12 (or up to 30) weeks of treatment.

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

Clinical claim

- 6.23 The submission claimed that secukinumab:
- Is superior to etanercept 100 mg/week in comparative effectiveness and equivalent in comparative safety. The claim regarding efficacy was supported by direct clinical trials, but the claim regarding safety may not have been supported in the Australian setting as the TGA-approved dose for etanercept is 50 mg/week;
 - Has a strong trend towards superiority in terms of comparative effectiveness and equivalent in terms of comparative safety over ustekinumab 45 mg/90 mg. The claim is based on an indirect comparison from data for up to 12 weeks only. The results of the indirect comparisons indicate there were no statistically significant differences between treatments (non-inferiority criteria were not nominated by the

submission and no criteria have previously been accepted by the PBAC to assess non-inferiority). There were limited comparative safety data presented in the submission to support a claim of equivalent safety.

- Is superior in terms of comparative effectiveness and equivalent in terms of comparative safety over adalimumab 40 mg. The claim was possibly supported by the indirect comparison at 12 and 16 weeks but the PBAC has previously expressed (adalimumab March 2009 Public Summary Document) that in the absence of long term data there is no reason to assume superiority would be maintained in the long term. There were limited comparative safety data presented in the submission to support a claim of equivalent safety.
- Is non-inferior in terms of comparative effectiveness to infliximab over the short term (at 10 weeks) but secukinumab has greater effectiveness in the longer term compared to infliximab. The submission also claimed a trend of superiority in terms of comparative safety over infliximab. The results of the indirect comparisons indicated there were no statistically significant differences between treatments (non-inferiority criteria were not nominated by the submission and no criteria have previously been accepted by the PBAC to assess non-inferiority). There were no robust data to support the claim that secukinumab “has greater effectiveness in the longer follow-up compared to infliximab”. There were limited comparative safety data presented in the submission to support a claim of a trend of superior safety.

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

Economic analysis

- 6.24 A cost minimisation analysis versus ustekinumab over 100 weeks of treatment was presented. A cost minimisation analysis versus adalimumab was also conducted during the evaluation on the basis that whilst the indirect comparison of secukinumab and adalimumab indicated that secukinumab was superior to adalimumab in the proportion of patients achieving a PASI 75 response, this was over a period of 12 weeks and there was no direct head to head data presented to support the contention that this benefit is maintained over the long term.
- 6.25 The equi-effective doses were estimated as secukinumab 300 mg monthly (based on the draft PI) or every 4 weeks (based on clinical trials) and ustekinumab 59.38 mg every 12 weeks (based on the PI) for maintenance. It was further assumed that secukinumab 300 mg monthly (based on the draft PI) or every 4 weeks (based on clinical trials) is equivalent to adalimumab 40 mg fortnightly (based on the PI).
- 6.26 The results of the cost minimisation analysis of secukinumab to ustekinumab presented by the submission are shown in Table 6 below. The submission’s analysis assumed 12 scripts over a year for maintenance therapy for secukinumab based on monthly dosing, however dosing in the trials was every four weeks. Therefore, a cost minimisation assuming 13 doses per year (based on a 4-weekly dosing frequency) of secukinumab was conducted during the evaluation.

Cost-minimisation analysis of secukinumab to ustekinumab up to 99 weeks

	Ustekinumab	Secukinumab	
Ex-Factory price	\$4,455.06	\$ [REDACTED]	\$ [REDACTED]
Cost/mg	\$99.00	\$ [REDACTED]	\$ [REDACTED]
Average mg/dose	59.38 mg	300 mg	300 mg
Cost per average dose	\$5,878.20	\$ [REDACTED]	\$ [REDACTED]
Number of dose per year in maintenance	4.33	12	13
Dose in initiation (up to 16 weeks)	3	8	8
Dose in maintenance (17-100 weeks)	6	18.5	20
Total doses over 100 weeks^	9	26.5	28
Total cost over 100 weeks	\$52,904	\$ [REDACTED]	\$ [REDACTED]
Continuation Rate*	0.88	0.88	0.88
Weighted cost over 100 weeks	\$46,555	\$ [REDACTED]	\$ [REDACTED]

* Taken from DUSC review of bDMARDs for severe chronic plaque psoriasis

Text in italics indicates values calculated during evaluation. Key differences for sensitivity analysis are highlighted in bold

Source: Submission, Attachment 9, Section D_Cost-min calculation.xlsx

- 6.27 The submission assumed that patients will use 8 doses of secukinumab during the initiation phase (at weeks 0, 1, 2, 3, 4, 8, 12 and 16) and then one injection every month thereafter up to week 99 during the maintenance phase (18.5 doses), for a total of 26.5 doses over 100 weeks (from week 0 to week 99). Analysis conducted during the evaluation assumed that maintenance frequency is 4 weekly rather than monthly, resulting in 20 doses used in maintenance treatment. Treatment would be ongoing until the patient no longer demonstrates adequate response (i.e. do not achieve PASI 75 response).
- 6.28 The results of the cost minimisation analysis of secukinumab to adalimumab conducted by the evaluation are shown in Table 7 below. The use of 13 doses per year (based on a 4-weekly dosing frequency) of secukinumab was again considered in the evaluation and the results also presented alongside the use of 12 secukinumab doses.

Cost-minimisation analysis of secukinumab to adalimumab up to 99 weeks assuming 13 secukinumab doses per year

	Adalimumab	Secukinumab	
Cost per dose (Ex-factory price)	\$1630.00	\$ [REDACTED]	\$ [REDACTED]
Number of dose per year in maintenance	13	12	13
Dose in initiation (up to 16 weeks)	5	8	8
Dose in maintenance (17-100 weeks)	20.5	18.5	20
Total doses over 100 weeks	25.5	26.5	28
Total cost over 100 weeks	\$41,565	\$ [REDACTED]	\$ [REDACTED]
Continuation Rate*	0.88	0.88	0.88
Weighted cost over 100 weeks	\$36,577	\$ [REDACTED]	\$ [REDACTED]

Source: Constructed during evaluation

* Taken from DUSC review of bDMARDs for severe chronic plaque psoriasis

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

Drug cost/patient:

- 6.29 At the requested DPMQ for secukinumab, and using the current ustekinumab and adalimumab prices, the cost per patient per year will be:

DPMQ prices

	Initiation	12 months of maintenance
Secukinumab	\$ [REDACTED] (4 scripts at \$ [REDACTED] /script)	\$ [REDACTED] (13 scripts at \$ [REDACTED] /script)
Ustekinumab 45 mg	\$13,805.28 (3 scripts at \$4,601.76/script)	\$18,407.04 (4 scripts at \$4,601.76/script)
Adalimumab	\$8,874 (5 scripts at \$1,774.70/script)	\$23,071 (13 scripts at \$1,774.70/script)

Estimated PBS usage & financial implications

- 6.30 The submission was not considered by DUSC.
- 6.31 The submission used a market share approach to estimate PBS usage and the overall financial impact, relying primarily on PBS data. The evaluation considered this was a reasonable and appropriate approach.

Estimated use and financial implications

	Year 1	Year 2	Year 3	Year 4	Year 5
Estimated extent of use					
Patient years of treatment	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
Scripts ^a	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
Estimated net cost to PBS/RPBS/MBS					
Net cost to PBS/RPBS	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]
Net cost to MBS	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]
Estimated total net cost					
Net cost to PBS/RPBS/MBS	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]

^a Assuming 9.3 scripts per patient year as estimated by the submission, based on estimated 34% of patients initiating treatment (4 scripts) and 66% of patients continuing treatment (12 scripts).

Source: Submission, Attachment 10, Section E_Usage and financial estimates.xlsx

- 6.32 The redacted table above shows that under the proposed listing, the expected secukinumab use will come from the currently listed bDMARDs: ustekinumab, adalimumab, etanercept and infliximab. The expected number of patients on secukinumab at Year 5 is estimated to be less than 10,000.
- 6.33 However, the evaluation considered the submission's estimates of financial impact may not have been reasonable as the cost per patient year of secukinumab was likely to have been underestimated since the submission assumed only 12 scripts per patient year for continuation instead of 13.
- 6.34 The submission's estimated savings were mainly derived from a reduction in the number of patient years of ustekinumab, which was assumed to have a higher cost per patient year (\$23,401.63) compared to secukinumab (\$ [REDACTED]). This however was not reflective of any real savings, but instead reflected the difference in the relative doses of secukinumab to ustekinumab assumed in the cost minimisation analysis (2.4 to 1) and in the financial estimates (2.9 to 1). Given that the submission had proposed listing on a cost minimisation basis in which the costs of a course of treatment with ustekinumab and secukinumab are equal, estimated cost savings in the financial estimates were not considered to be attainable by the evaluation.
- 6.35 Nonetheless, given that secukinumab is unlikely to lead to market growth and will only substitute for existing bDMARDs if the limit of three bDMARDs per treatment

cycle is retained, the overall estimated financial impact on the government budget is likely to be low.

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

Financial Management – Risk Sharing Arrangements

- 6.36 The sponsor indicated a willingness to enter into a special pricing arrangement as exists for the comparators.

7 PBAC Outcome

- 7.1 The PBAC recommended listing secukinumab as a General Schedule Authority Required benefit for the treatment of severe chronic plaque psoriasis which is refractory to treatment with non-biological disease modifying anti rheumatic drugs (DMARDs) in patients meeting certain criteria, on a cost-minimisation basis with adalimumab. The equi-effective doses are estimated as secukinumab 300 mg every 4 weeks (based on the clinical trials) is equivalent to adalimumab 40 mg fortnightly (based on the Product Information).
- 7.2 The PBAC noted that adalimumab, etanercept and infliximab are all anti-tumour necrosis factor (anti-TNF) agents, ustekinumab is an antibody against interleukin 12 and 23, whereas secukinumab is an antibody against interleukin 17. The PBAC therefore considered it likely that secukinumab would be prescribed as an alternative to these existing PBS listed bDMARDs in severe chronic plaque psoriasis. Whilst the PBAC noted the ESC advice that secukinumab may displace infliximab and etanercept (the least popular bDMARDs in current usage based on a sample of Medicare Australia claims data), the PBAC considered a comparison against ustekinumab and adalimumab to be reasonable since these two agents are currently the most frequently used bDMARDs in severe chronic plaque psoriasis.
- 7.3 With respect to the clinical claims made by the submission, the PBAC's view was that secukinumab is likely to be non-inferior to ustekinumab in terms of comparative efficacy and safety. The results of the indirect comparisons presented in the submission indicated there was no statistically significant difference in the proportion of patients achieving a PASI 75 response at 12 weeks between secukinumab and ustekinumab. The indirect nature of the comparison from data that examined outcomes after only 12 weeks of treatment, combined with the fact that several of the indirect comparisons using placebo as a common reference did not show a statistical significance between secukinumab and ustekinumab in efficacy after 12 weeks of treatment, further supported this view. The ongoing head-to-head trial comparing secukinumab 300 mg and ustekinumab 45 mg and 90 mg (CLEAR, NCT02074982) is due for completion in July 2015 and the results of this trial will be informative. The PBAC noted the limited comparative safety data presented in the submission to support a claim of equivalent safety, but considered that the results from the limited safety data suggested that the claim was reasonable.
- 7.4 The PBAC was also of the view that secukinumab is likely to be non-inferior to adalimumab in efficacy and safety. Despite the submission's claim of superior

efficacy and equivalent comparative safety to adalimumab, the PBAC did not accept this claim for the following reasons:

- Although there is data on adalimumab after 52 weeks of treatment (from the REVEAL study), the questionable exchangeability of the trials meant that the PBAC was not confident that an initial advantage favouring secukinumab would be maintained beyond 16 weeks. The PBAC noted the evaluation's suggestion that the REVEAL results favour adalimumab but also noted the explanation in the sponsor's pre-PBAC response (p.4) regarding the interpretation of the REVEAL results. This response claimed that the REVEAL results favoured an interpretation that secukinumab is superior to adalimumab in the long term. Together with the questionable exchangeability of the REVEAL study with secukinumab trials, the absence of direct head to head trials comparing secukinumab and adalimumab beyond 16 weeks of treatment meant that the PBAC could not confidently rule out the possibility of no difference in efficacy between the treatments beyond 16 weeks.
- Although the result for relative risk (RR) favoured secukinumab [RR: 17.7, 95%CI: 12.4, 25.2] compared to adalimumab [RR: 8.8, 95%CI: 4.5, 16.6], there was overlap between the confidence intervals for this measure. This was in contrast to the result for risk difference (RD) which also favoured secukinumab [RD: 0.76, 95%CI: 0.72, 0.8] compared to adalimumab [RD: 0.61, 95%CI: 0.54, 0.67] but for which the confidence intervals did not overlap.

- 7.5 Compared to infliximab, the PBAC accepted the claim that secukinumab is likely to be non-inferior in efficacy over the short and long term as the results at 10 weeks showed no statistically significant difference between treatments. However, the PBAC further noted the limited comparative safety data, so did not accept the claim that secukinumab has superior safety compared to infliximab.
- 7.6 The PBAC noted that compared to etanercept in the FIXTURE trial, of those patients who were PASI 75 responders at week 12, a statistically significantly greater proportion of patients treated with secukinumab 300 mg (84.3%) compared with etanercept 100 mg/week (72.5%), maintained a PASI 75 response at week 52. Based the results of the trial, the PBAC accepted that secukinumab is superior to etanercept in terms of efficacy. The PBAC noted that this conclusion appears at odds with its earlier conclusions that secukinumab is non-inferior to adalimumab and that adalimumab is non-inferior to etanercept. However, the PBAC also noted that there is emerging evidence of variation in response to TNF-alfa inhibitors in psoriasis, with etanercept appearing to be less effective than other agents. The conclusions reached by PBAC in respect of this application are consistent with this evidence.
- 7.7 The PBAC noted the submission's cost-minimisation analysis of secukinumab versus ustekinumab and evaluation's cost-minimisation analysis of secukinumab versus adalimumab were both relevant considerations. The PBAC observed the proposed price for secukinumab to be substantially more costly than the alternative therapy of adalimumab. For secukinumab to be PBS-listed at a substantially more costly price than adalimumab, the PBAC needed to be satisfied that secukinumab for some patients, provides a significant improvement in efficacy or reduction of toxicity over adalimumab. Based on the evidence presented in the submission and the material before the Committee, the PBAC was not satisfied that secukinumab provides a significant improvement in efficacy or reduction of toxicity over adalimumab.

Therefore, there was no basis for secukinumab to have a price advantage over adalimumab.

- 7.8 The submission's financial estimates of cost savings appeared unrealistic as the PBAC agreed with the evaluation advice that listing on a cost minimisation basis should in theory entail no or minimal budgetary impact on the PBS. It was noted that there was a difference between the relative dose of secukinumab to ustekinumab in the cost minimisation analysis (2.9 to 1) and in the financial estimates (2.4 to 1) which was the key driver for the disparity between the request to list on a cost-minimisation basis and the submission's estimated cost savings. The PBAC did not consider this difference justified.
- 7.9 In terms of implementing a PBS restriction, the PBAC recommended a listing based on existing bDMARD restrictions in severe chronic plaque psoriasis. The PBAC considered that it would be appropriate for the number of bDMARD therapies that a patient may trial per treatment cycle remain at three as no data directly supportive of changing to four therapies was presented in the submission and the sponsor had accepted that the current arrangements in its pre-PBAC response (p.1). The PBAC noted that keeping the maximum number of treatments at three would still allow a patient to have tried and failed one biological agent from each available class of bDMARD, including secukinumab, before the treatment cycle is over. Retaining the number of therapies attempted at three would also ensure that the listing would truly be in line with a cost-minimisation recommendation.
- 7.10 The PBAC noted the Department's advice that the sponsor's request to list multiple presentations of the drug on the same day may require a price reduction as set out in the revised explanatory memorandum to the *National Health Amendment (Pharmaceutical Benefits Scheme) Bill 2007 (Cth)*.
- 7.11 The PBAC recommended that the Safety Net 20 Day Rule should not apply.
- 7.12 The PBAC considered that secukinumab is not suitable for inclusion in the PBS medicines for prescribing by nurse practitioners.
- 7.13 Advice to the Minister under subsection 101(3BA) of the Act
In accordance with subsection 101(3BA) of the Act the PBAC advised that it is of the opinion that, on the basis of the material available to it at its March 2015 meeting, secukinumab should not be treated as interchangeable on an individual patient basis with any other drugs.
- 7.14 The PBAC noted that etanercept was the comparator of the current PBS bDMARD psoriasis listings, including ustekinumab. The PBAC recommended to the Minister that a cost-effectiveness review of the PBS bDMARDs for psoriasis be undertaken because there is emerging evidence of variations in response to TNF-alfa inhibitors in psoriasis, with etanercept appearing to be less efficacious than other agents.

Outcome:
Recommended

8 Recommended listing

8.1 Add new item:

Name, Restriction, Manner of administration and form	Max. Qty (packs)	Max. Qty (units)	No. of Rpts	Proprietary Name and Manufacturer	
SECUKINUMAB					
Injections 150 mg in 1 mL single use pre-filled syringes, 2	1	2	5	Cosentyx	NV
Injections 150 mg in 1 mL single use pre-filled pens, 2	1	2	5	Cosentyx	NV
Powder of injection 150 mg, 2	1	2	5	Cosentyx	NV

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
Episodicity:	Chronic
Severity:	---
Condition:	plaque psoriasis
PBS Indication:	Chronic plaque psoriasis
Treatment phase:	To be finalised
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
Treatment criteria:	To be finalised
Clinical criteria:	To be finalised
Population criteria:	To be finalised
Prescriber Instructions:	To be finalised
Administrative Advice	To be finalised
Cautions	To be finalised

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.