

6.12 SECUKINUMAB, Injection 150 mg in 1 mL pre-filled pen, Cosentyx[®], Novartis Pharmaceuticals Australia Pty Ltd

1 Purpose of submission

- 1.1 The submission requested Authority Required (Section 85) listing of secukinumab (SEC) for the treatment of non-radiographic axial spondyloarthritis (nr-axSpA) in patients with objective signs of inflammation, defined as elevated C-reactive protein (CRP) and magnetic resonance imaging (MRI) evidence (i.e. CRP+ and MRI+), and meeting other criteria. This was the first submission to the PBAC for the requested indication; SEC is currently PBS listed for ankylosing spondylitis (AS), psoriatic arthritis and plaque psoriasis.
- 1.2 The basis for the requested listing was a cost-minimisation analysis to the other biologic disease-modifying anti-rheumatic drugs (bDMARDs) currently listed on the PBS for nr-axSpA: certolizumab pegol (CZP) and golimumab (GLM). If listed, SEC would be the third bDMARD available on the PBS for treatment of nr-axSpA.

Table 1: Key components of the clinical issue addressed by the submission

Component	Description
Population	Patients with nr-axSpA as defined by ASAS classification criteria. Patients must have objective signs of inflammation (OSI) as indicated by elevated C-reactive protein (CRP) and magnetic resonance imaging (MRI) evidence and have had an inadequate response to, or are intolerant to, at least two nonsteroidal anti-inflammatory drugs (NSAIDs) for a period of 3 months.
Intervention	Secukinumab (150 mg week 0,1,2,3 and 4 followed by same dose every month).
Comparator	Golimumab (50mg every month) and certolizumab (400mg week 0,2,4 then 200mg Q2W or 400mg Q4W).
Outcomes	Clinical response: proportion of patients meeting ASAS20 and BADAI 50 response criteria; change in safety and tolerability
Clinical claim	In patients with nr-axSpA, who have OSI as indicated by elevated CRP and MRI evidence, and an inadequate response, or are intolerant to, NSAIDs, secukinumab is non-inferior in effectiveness and safety compared to golimumab and certolizumab.

Abbreviations: ASAS=Assessment of SpondyloArthritis international Society; ASAS 20/40= Assessment of SpondyloArthritis international Society 20/40% response criteria; BASDAI50=50% improvement in Bath ankylosing spondylitis disease activity index; CRP=C-reactive protein; MRI=magnetic resonance imaging; nr-axSpA=non-radiographic axial spondyloarthritis; Q2W=every 2 weeks; Q4W=every 4 weeks. Source: Table 1.1, p2 of the submission.

2 Background

Registration status

- 2.1 The submission was made under the TGA/PBAC Parallel Process. At the time of the evaluation, the TGA Clinical Evaluation Report (Round 2), the TGA Delegate's Overview and Advisory Committee on Medicines (ACM) outcome were available. SEC was registered on the ARTG on 17 September 2020.

- 2.2 The approved TGA indication was “Cosentyx [secukinumab] is indicated for the treatment of adults with active non-radiographic axial spondyloarthritis (nr-axSpA) with objective signs of inflammation as indicated by elevated C-reactive protein (CRP) and/or MRI change, who have had an inadequate response to, or are intolerant to non-steroidal anti-inflammatory drugs (NSAIDs).”
- 2.3 Two dosing regimens were approved for SEC for nr-axSpA:
- SEC without loading: ‘150mg by subcutaneous injection every month.’
 - SEC with loading: ‘150mg by subcutaneous injection with initial dosing at Weeks 0, 1, 2, 3, and 4 followed by the same dose every month.’

The TGA delegate and the ACM considered that the choice between SEC with and without loading is best made clinically by the treating rheumatologist, taking account of patient factors that may contribute to increased experience of adverse reactions and the likelihood of a significant clinical response. In assessing the relative benefits and risk of the loading dose, the ACM determined that there was utility in a loading dose. Despite more frequent adverse events overall for SEC with loading, the ACM considered these were mild in nature. The ACM also considered that the earlier onset of response with loading was clinically important enough to outweigh the safety concerns, and offers advantages for some patients.

- 2.4 The TGA approval of two dosing regimens for SEC have flow on effects on the requested maximum quantities on the PBS, equi-effective doses in the cost-minimisation and financial estimates, which were updated in the Pre-Sub-Committee Response (PSCR) to include the SEC loading and no loading dosing regimens.

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

3 Requested listing

- 3.1 In the submission, the sponsor only presented proposed restrictions based on SEC with loading. However, the PSCR updated the restrictions to account for the TGA approval for loading and no loading dosing regimens for nr-axSpA. This has been included below in the grey fields. Changes made by the Secretariat have been included in italics and strikethrough.

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Name, restriction, manner of administration, form	Maximum quantity (packs)	Maximum quantity (units)	No. of repeats	Dispensed price for maximum quantity	Proprietary name and manufacturer
SECUKINUMAB					
With loading regimen					
<u>Initial 1, 2, 3</u>					
150mg/mL injection, 1mL pen device	4	4	0	\$3,985.50 [^]	Cosentyx® Novartis Pharmaceuticals
150mg/mL injection, 1mL pen device	1	1	3	\$1,025.12 [^]	
<u>Continuing, grandfather, balance of supply</u>					
150mg/mL injection, 1mL pen device	1	1	5	\$1,025.12 [^]	
No loading regimen					
<u>Initial 1, 2, 3</u>					
150mg/mL injection, 1mL pen device	1	1	74	\$1,025.12 [^]	
<u>Continuing, grandfather, balance of supply</u>					
150mg/mL injection, 1mL pen device	1	1	5	\$1,025.12 [^]	

[^] Updated during the evaluation using mark-ups current from 1 July 2020, assuming the same requested AEMP (\$952.13). The DPMQ presented in the submission was \$3,960.66 for the 4 pack of 150mg/mL initial treatment and \$1,008.74 for the 1 pack.

Note: grey fields were added in the Pre-Sub-Committee Response (PSCR) after TGA approval of loading and no loading dosing regimens for nr-axSpA

Category/Program:	GENERAL – General Schedule (Code GE)
PBS indication:	nr-axSpA
Treatment phase:	Initial treatment 1 (New patients or recommencement after a break of more than 5 years)
Restriction:	<input checked="" type="checkbox"/> Authority Required - In Writing
Treatment criteria:	<ul style="list-style-type: none"> • Must be treated by a rheumatologist; OR • Must be treated by a clinical immunologist with expertise in the management of nr-axSpA
Clinical criteria:	<ul style="list-style-type: none"> • Patient must not have received PBS-subsidised treatment with this drug for this condition in the last 5 years or more, AND • Patient must have had chronic lower back pain and stiffness for 3 or more months that is relieved by exercise but not rest, AND • Patient must have failed to achieve an adequate response following treatment with at least 2 non-steroidal anti-inflammatory drugs (NSAIDs), whilst completing an appropriate exercise program, for a total period of 3 months, AND • Patient must have one or more of the following: (a) enthesitis (heel); (b) uveitis; (c) dactylitis; (d) psoriasis; (e) inflammatory bowel disease; or (f) positive for Human Leukocyte Antigen B27 (HLA-B27), AND • The condition must not be radiographically evidenced on plain x-ray of Grade II bilateral sacroiliitis or Grade III or IV unilateral sacroiliitis, AND • The condition must be non-radiographic axial spondyloarthritis, as defined by Assessment of Spondyloarthritis International Society (ASAS) criteria, AND • The condition must be sacroiliitis with active inflammation and/or oedema on non-contrast Magnetic Resonance Imaging (MRI), AND • The condition must have presence of Bone Marrow Oedema (BMO) depicted as a hyperintense signal on a Short Tau Inversion Recovery (STIR) image (or equivalent), AND • The condition must have BMO depicted as a hypointense signal on a T1 weighted image (without gadolinium), AND <p>The treatment must not exceed a maximum of 20 weeks with this drug under this restriction.</p>

Prescriber criteria:	<p>The following criteria indicate failure to achieve an adequate response to NSAIDs and must be demonstrated at the time of the initial application:</p> <p>(a) a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) of at least 4 on a 0-10 scale; and</p> <p>(b) C-reactive protein (CRP) level greater than 10 mg per L.</p> <p>The assessment of the patient's response to the initial course of treatment must be made following a minimum of 12 weeks of treatment and submitted no later than 4 weeks from the cessation of that treatment course. If the response assessment is not submitted within these timeframes, the patient will be deemed to have failed this course of treatment.</p> <p>If a patient fails to demonstrate a response to treatment with this drug they will not be eligible to receive further PBS-subsidised treatment with this drug for this condition. Serious adverse reaction of a severity resulting in the necessity for permanent withdrawal of treatment is not considered as a treatment failure.</p>
Treatment phase:	Continuing treatment
Restriction:	<input checked="" type="checkbox"/> Authority Required - In Writing
Clinical criteria:	<ul style="list-style-type: none"> • Patient must have previously received this drug as their most recent course of PBS-subsidised biologic medicine treatment with for this condition, AND • Patient must have demonstrated an adequate response to treatment with this drug for this condition, AND <p>The treatment must not exceed a maximum of 24 weeks with this drug per authorised course under this restriction.</p>
Prescriber Instructions:	<p>An adequate response to therapy with this drug is defined as a reduction from baseline in the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score by 2 or more units (on a scale of 0-10) and 1 of the following:</p> <p>(a) a CRP measurement no greater than 10 mg per L; or</p> <p>(b) a CRP measurement reduced by at least 20% from baseline.</p>

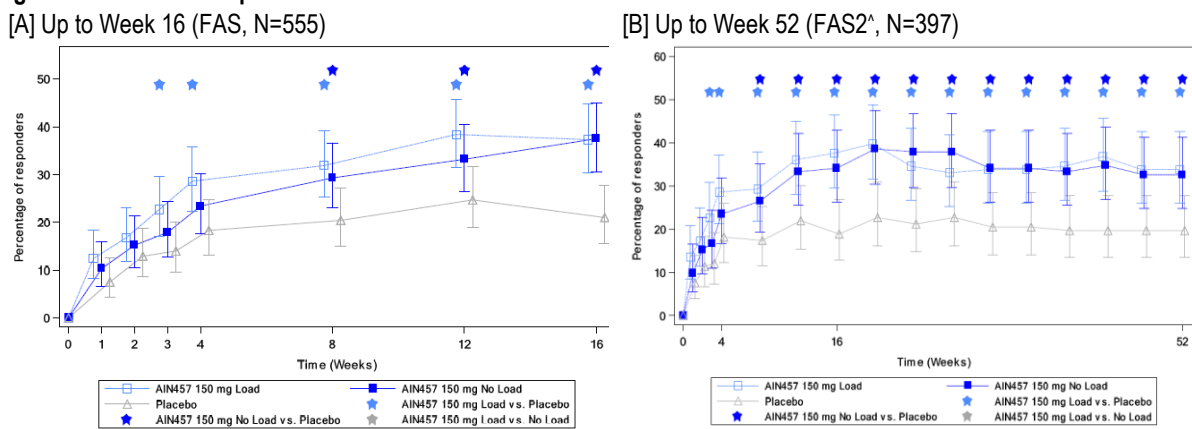
3.2 The approved Product Information (PI, p2) stated that SEC should be dosed monthly. It was noted the actual dosing in the trials occurred every four weeks rather than monthly, but the TGA Delegate considered this difference is unlikely to have a significant effect on efficacy or safety. The PSCR noted there has been inconsistency between the use of monthly and four-weekly dosing in the therapeutic relativity sheets, PIs, Public Summary Documents (PSDs), PBS restrictions and trials and maintained that monthly dosing should be used in the CMA. However, four-weekly dosing of SEC has been applied to the AS and psoriatic arthritis listings where the PBAC previously considered that “in practice patients would likely find four-weekly less confusing, noting that monthly use would lead to dosing on different days of the week” (paragraph 7.2, Secukinumab AS PSD March 2016 PBAC meeting) and “therefore considered four-weekly dosing was the most appropriate frame of reference for considering equi-effective doses.” (paragraph 7.2, Secukinumab AS PSD March 2016 PBAC meeting).

3.3 The sponsor requested a maximum of 20 weeks of initial therapy for SEC with no load regimen. The requested maximum quantity of 1 and 7 repeats for SEC no load regimen would provide for a maximum of 32 weeks of initial therapy (if doses are administered every 4 weeks). If doses were administered ‘monthly’ (i.e. every 30.44 days), then the requested maximum quantities would provide for even longer treatment duration

(34.8 weeks). Based on the requested maximum of 20 weeks initial therapy and assumed monthly administration from the cost-minimisation analysis, only one initial script plus 4 repeats is required for SEC no load. The pre-PBAC response agreed with this change.

- 3.4 The submission did not justify why 20 weeks of initial therapy is necessary. The PSCR argued that clinical response assessed in the trials varied between Week 12 for CZP and Week 16 for golimumab (GLM) and SEC, however the maximum duration for initial treatment on the PBS was 18-20 weeks for CZP and 16 weeks for GLM and SEC. The PSCR also argued that data from the key trial (PREVENT) also supported the requested 20 weeks of initial treatment with SEC, given the highest BASDAI50 response was achieved at Week 20 over the 52-week placebo-controlled treatment period. Further, 20 weeks of initial therapy with SEC provides an additional 4 weeks of treatment to cover the assessment period consistent with other PBS-listed treatments to ensure treatment continuity in accordance with QUM. The evaluation noted that a maximum of 16 weeks of initial treatment with SEC is listed for other PBS indications (AS, chronic plaque psoriasis and psoriatic arthritis) and the proportion achieving a clinical response in nr-axSpA was relatively stable after Week 12 as shown in Figure 1. Given this relationship, allowing up to 20 weeks of initial treatment with SEC may delay patients who do not respond to SEC from accessing a potentially more effective therapy by at least 4 weeks.

Figure 1: BASDAI50 response over time in the PREVENT trial



Abbreviations: AIN457=secukinumab; BASDAI50=50% improvement in Bath ankylosing spondylitis disease activity index; FAS=full analysis set

[^] The full analysis set 2 (N=397) comprised all patients from the randomized set to whom study treatment had been assigned and who had been in enrolled at least 379 (upper limit of visit window for primary endpoint) days before date cut off.

Source: Figures 11-10 and 11-24, p167 and p194 of Attachment 6_CSR2315.

- 3.5 The sponsor requested PBS listing of SEC 150mg as a pen device for initial and continuing treatment of nr-axSpA plus objective signs of inflammation (CRP+ and MRI+). The wording of the requested restrictions was based on the current PBS restrictions for CZP and GLM, with assessment of response after at least 12 weeks of initial treatment and every 24 weeks thereafter. The PBS population (MRI+ and CRP+) is narrower than the TGA indication (MRI+ and/or CRP+), as it does not define

objective signs of inflammation as either MRI+ or CRP+, or the minimum disease severity / activity.

- 3.6 Grandfathering was proposed in the submission to provide access to PBS subsidised SEC treatment for patients that are part of clinical trials and patient familiarisation program. The submission estimated there are currently 30 trial patients in Australia.

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

4 Population and disease

- 4.1 Axial spondyloarthritis (axSpA) is the spectrum of chronic inflammatory disease characterised by inflammation of the spine and sacroiliac (SI) joints. The Assessment of SpondyloArthritis international Society (ASAS) classification criteria differentiates between patients without radiographic inflammation (i.e. nr-axSpA) and patients with radiographic inflammation (i.e. AS) identifiable on x-ray.
- 4.2 Nr-axSpA and AS have similar clinical manifestations, disease activity and functional impairments. Chronic back pain is the leading symptom of the disease, which is often inflammatory in nature with pronounced stiffness and pain that improved with exercise. Progression from nr-axSpA to AS occurs in approximately 10-40% of patients within 2 to 10 years of symptom onset. Elevated serum CRP and presence of sacroiliitis on MRI, increases the likelihood of progression to AS.
- 4.3 SEC is a recombinant human monoclonal anti-human Interleukin-17A (IL-17A, IL-17) antibody and works to inhibit the release of pro-inflammatory cytokines, chemokines and mediators of tissue damage and reduces IL-17A-mediated contributions to autoimmune and inflammatory diseases. If listed, SEC would provide an alternative class of treatment (i.e. IL-17 inhibitor) to the other bDMARDs available on the PBS (i.e. tumour necrosis factor alpha (TNF α) inhibitors).

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

5 Comparator

- 5.1 The submission nominated GLM and CZP as the main comparators, given both are the only bDMARDs currently PBS listed for the treatment of nr-axSpA with objective signs of inflammation (MRI+ and CRP+). GLM and CZP have a different mechanism of action compared to SEC (TNF α inhibitors vs IL-17 inhibitor), but all three biologics have the same route of administration (SC injection) via pre-filled syringe or pen. The recommended dose for GLM is 50mg once a month, and the recommended dose for CZP is 400mg at Weeks 0, 2 and 4, followed by 200mg every 2 weeks (Q2W) or 400mg every 4 weeks (Q4W).

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

6 Consideration of the evidence

Sponsor hearing

6.1 There was no hearing for this item.

Consumer comments

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

Clinical trials

6.3 The literature search did not identify any direct head-to-head randomised trials comparing SEC to CZP or GLM in nr-axSpA. The submission was based on four placebo controlled randomised trials of SEC (PREVENT), GLM (GO-AHEAD) and CZP (C-axSpAnd and RAPID-axSpA).

Table 2: Trials and associated reports presented in the submission

Trial ID	Protocol title/ Publication title	Publication citation
Secukinumab vs placebo		
PREVENT INCT02696031	Study of Efficacy and Safety of Secukinumab in Patients With Non-radiographic Axial Spondyloarthritis (Internal clinical study report (2315))	02 May 2019
	Deodhar et al. Efficacy and safety of secukinumab in non-radiographic axial spondyloarthritis: design of a randomized, double-blind, placebo-controlled multicenter phase 3 study (PREVENT).	International journal of rheumatic diseases. 2018; 21:146
Golimumab vs placebo		
Sieper et al., GO-AHEAD NCT01453725	Sieper et al. A Randomized, Double-Blind, Placebo-Controlled, Sixteen-Week Study of Subcutaneous Golimumab in Patients With Active Nonradiographic Axial Spondyloarthritis.	Arthritis & Rheumatology. 2015; 67(10):2702-12
	Sieper et al. Efficacy of golimumab for nonradiographic axial spondyloarthritis: Subgroup analysis by baseline MRI and c-reactive protein status.	Annals of the Rheumatic Diseases. 2016; 75:813-4.
Certolizumab vs placebo		
C-axSpAnd NCT02552212	Deodhar et al. A Fifty-Two-Week, Randomized, Placebo-Controlled Trial of Certolizumab Pegol in Nonradiographic Axial Spondyloarthritis.	Arthritis and Rheumatology. 2019; 71(7):1101-11.
RAPID-axSpA NCT01087762	Landewé et al. Efficacy of certolizumab pegol on signs and symptoms of axial spondyloarthritis including ankylosing spondylitis: 24-week results of a double-blind randomised placebo-controlled Phase 3 study.	Annals of the rheumatic diseases. 2014; 73(1):39-47

Source: Table 2.12, pp29-34 of the submission.

6.4 Table 3 presents the key features of the included trials. All trials were multicentre (PREVENT included five study sites in Australia), double blind, randomised placebo-controlled trials. The duration of the double-blind phases ranged from 16 to 52 weeks, but all trials reported key clinical response outcomes at Week 12 to 16.

Table 3: Key features of the included evidence

Trial	N	Design/duration	Bias	Treatment arms	Population	Key efficacy outcomes
SEC vs PBO						
PREVENT	555	R, MC, PC, DB 52wk / DSB and OL extension; rescue ≥Wk20; DMARD rescue in PBO arm wk16 ^α	Low	- SEC 150mg Q4W (with loading) - SEC 150mg Q4W (without loading) - PBO	nr-axSpA plus OSI [#]	1°: ASAS40 (Wk 16) 2°: Δ BASDAI, BASDAI50, ASAS20, ASDAS-CRP [‡]
CZP vs PBO						
C-axSpAnd	317	R, MC, PC, DB 52wk / OL extension; rescue ≥Wk 0 ^β	Low	- CZP 200mg Q2W (with loading) - PBO	nr-axSpA plus OSI [#]	1°: ASDAS-MI (Wk52) and ASAS40 (Wk12) 2°: Δ BASDAI (other: BASDAI50, ASAS20, ASDAS)
RAPID-axSpA	325 (147 [^])	R, MC, PC, DB 24wk / DSB and OL extension; bDMARD rescue in PBO arm wk16 ^γ	Low	- CZP 200mg Q2W (with loading) - CZP 400mg Q4W (with loading) - PBO	AS and nr-axSpA plus OSI [#]	1°: ASAS20 (wk12) 2°: BASDAI50, ASAS40 (other: ASDAS)
GLM vs PBO						
GO-AHEAD	198 (158 [^])	R, MC, PC, DB 16wk/ OL extension; no rescue	Low	- GLM 50mg Q4W - PBO	nr-axSpA plus or minus OSI [#]	1°: ASAS20 (Wk16) 2°: ASAS40, BASDAI50, ASDAS

Abbreviations: AS=ankylosing spondylitis; ASAS20/40=Assessment of SpondyloArthritis international Society 20%/40% response criteria; ASDAS=Ankylosing Spondylitis Disease Activity Score; BASDAI(50)=50% improvement in Bath ankylosing spondylitis disease activity index; CZP=certolizumab pegol; DB=double blind; DSB=dose blind; GLM=golimumab; MC=multicentre; nr-axSpA=non-radiographic axial spondyloarthritis; OL=open label; OSI=objective signs of inflammation (defined as MRI+ and/or CRP+ in all trials); PBO=placebo; PC=placebo-control; SEC=secukinumab; R=randomised; Q2W=every 2 weeks; Q4W=every 4 weeks; wk=week

[^] pre-specified subgroup with nr-ax-SpA plus OSI (indicated by CRP+ and/or MRI+)

[#] CRP>ULN defined as: PREVENT ULN=5mg/L; C-axSpAnd ULN=9.99mg/L; RAPID-axSpA ULN=7.9mg/L; GO-AHEAD ULN=9mg/L

[‡] ASDAS-CRP (Ankylosing Spondylitis Disease Activity - C-reactive protein) inactive disease as defined by ASDAS <1.3

^α Background medications (e.g. NSAIDs and DMARDs) could be modified or added to treat signs and symptoms of nr-axSpA from Wk 16. Starting from Wk 20, all patients repeatedly (e.g. ≥2 consecutive visits) considered to be inadequate responders based on the clinical judgement of disease activity by the investigator and patient, received OL SEC or other biologics as standard of care. All other patients continued their original assigned treatment. Patients switching to a biologic (e.g. TNF α inhibitor) other than SEC were not allowed to receive further study medication and underwent a 12-week wash-out period.

^β Investigators could modify background medications (NSAIDs, corticosteroids, analgesics, SAARDs) during course of trial, and randomised therapy could be discontinued any time and subjects switched to OL CZP or other treatments if necessary.

^γ ASAS20 non-responders in the PBO arm at Wks 14 and 16 randomised to CZP 200mg Q2W or 400mg Q4W at Wk 16.

Source: constructed during the evaluation

6.5 In the trials, both GLM 50mg and SEC 150mg (after applicable loading doses) were administered every 4 weeks. The corresponding PIs however state that SEC is administered 'every month' (after loading doses) and GLM is administered 'once a month'. This slight difference in dosing frequencies between the trials and PIs may have implications for the cost-minimisation and financial estimates because dosing frequency determines the number of scripts required per year (see Economic analysis).

6.6 There were key differences in study design across the trials including:

- population (axSpA or nr-axSpA)

- presence of objective signs of inflammation (with or without)
 - definition of elevated CRP (CRP+ defined as serum level >5, 8, 9 or 10 mg/L),
 - prior bDMARD use (patients did not have prior use of TNF α inhibitors, i.e. TNF α inhibitor naïve, or patients had an inadequate response to prior TNF α inhibitors, i.e. TNF α inhibitor naïve + experienced); and
 - rescue / early escape during the double blind phase (not permitted, at any time or at Weeks 16 or 20).
 - There were also slight differences in the handling of missing data related to the Bath ankylosing spondylitis disease activity index (BASDAI) score and response outcome.
 - Discontinuations and withdrawals were much higher in the trials that permitted rescue / early escape (up to 66% versus 3%).
- 6.7 To control for differences in the definition of objective signs of inflammation, the submission presented results for patients with nr-axSpA using two definitions of objective signs of inflammation: broad (MRI+ and/or CRP+) in-line with the TGA indication ('TGA population'); and narrow (MRI+ and CRP+) in-line with the PBS indication ('PBS population'). The PBS population/subgroup in the trials also represented a small proportion of the total patients across the trials (15.8% in the PREVENT trial).
- 6.8 Despite presenting results for this PBS subgroup, there were still a number of differences across the trials that may violate the assumption of transitivity/exchangeability of the common reference arm and bias results of the indirect comparison (see para 6.4). As the submission did not present baseline characteristics for the PBS subgroup across the trials (a post-hoc subgroup in PREVENT and GO-AHEAD), it was unknown whether the comparison groups included in the indirect comparisons were balanced and sufficiently similar. It was also unclear what proportion of the PBS subgroup also met other PBS eligibility criteria, and whether such differences (between the trial and Australian settings) may have impacted the estimated treatment effects.

Comparative effectiveness

- 6.9 All of the trials measured treatment response as according to the BASDAI, ASAS20/40 response criteria and the Ankylosing Spondylitis Disease Activity Score (ASDAS), as either primary, secondary or other outcomes (see Table 3). As all trials enrolled patients with a BASDAI score of ≥ 4 at baseline, a 50% improvement in the BASDAI (i.e. BASDAI50) corresponded to a reduction from baseline in the BASDAI score of ≥ 2 .
- 6.10 In November 2017, "the ESC considered BASDAI50 was a clinically relevant outcome ... and has been recommended by ASAS [guidelines] as the response criteria used to determine treatment success" (paragraph 6.24, Golimumab PSD November 2017

PBAC meeting). “The ESC noted while the ASAS20 was the primary outcome measure used in GO-AHEAD, and the basis upon which the MCID was stated, the use of the BASDAI50 (a secondary endpoint in the trial) better reflects the preferred clinical measure for the assessment of response to treatment in nr-axSpA. It was agreed that this was the appropriate basis for the assessment of response and cost-effectiveness in this condition” (paragraph 6.14, Golimumab PSD November 2017 PBAC meeting).

- 6.11 The submission nominated a non-inferiority margin of 0.43 using the relative risk (RR) statistic for the ASAS20, however none was nominated for ASAS40 and BASDAI50. At its November 2019 meeting, the PBAC stated that “...non-inferiority was demonstrated based on ASAS20 for all the populations, because the 95%CI of RR estimates all crossed 1 and the lower bounds were larger than 0.43 (which is the non-inferiority margin accepted for ankylosing spondylitis).” (paragraph 6.18, Certolizumab Pegol PSD November 2019 PBAC meeting). The PBAC also noted the lack of non-inferiority margin for BASDAI50, but considered the overall claim of non-inferiority (based on ASAS20 and BASDAI50) was reasonable (paragraphs 6.24 and 7.3, Certolizumab Pegol PSD November 2019 PBAC meeting).
- 6.12 Tables 4 and 5 present indirect comparisons between SEC, GLM and CZP for BASDAI50 and ASAS20 response respectively in the TGA and PBS populations. The outcomes were reported at Week 12 for CZP (C-axSpA and RAPID-axSpA) and Week 16 for SEC (PREVENT) and GLM (GO-AHEAD). The rationale for using different time points in the submission was unclear, however the PBAC has previously accepted the comparisons using Week 12 data for CZP and Week 16 for GLM in nr-axSpA (paragraph 6.14, Certolizumab Pegol PSD November 2019 PBAC meeting).

Table 4: BASDAI50 response in patients with nr-axSpA plus OSI defined according to the TGA population (MRI+ and/or CRP+) and PBS population (MRI+ and CRP+)

Trial	Drug n/N (%)	Control n/N (%)	RR (95%CI)	RD (95%CI)	NNT (95%CI)
TGA population: nr-axSpA (MRI+ AND/OR CRP+)^α					
SEC 150mg with load v PBO (Wk 12/16)					
PREVENT, ITT (N=555), Wk16	69/185 (37.3)	39/186 (21.0)	1.78 (1.27, 2.49)	0.16 (0.07, 0.25)	6 (4, 14)
SA: PREVENT, ITT (N=555), Wk12 [^]	71/185 (38.3)	46/186 (24.8)	1.55 (1.14, 2.12)	0.14 (0.04, 0.23)	7 (25, 4)
SEC 150mg no load v PBO (Wk 12/16)					
PREVENT, ITT (N=555), Wk 16	69/184 (37.5)	39/186 (21.0)	1.79 (1.28, 2.50)	0.17 (0.07, 0.26)	6 (4, 14)
SA: PREVENT, ITT (N=555), Wk12 [^]	62/184 (33.7)	46/186 (24.8)	1.36 (0.99, 1.88)	0.09 (-0.00, 0.18)	-
CZP 200mg Q2W v PBO (Wk 12)					
C-axSpAnd, ITT (N=317)	68/159 (42.8)	23/158 (14.6)	2.94 (1.93, 4.46)	0.28 (0.19, 0.38)	4 (3, 5)
RAPID-axSpA, PSS (N=96)	23/46 (50.0)	8/50 (16.0)	3.13 (1.56, 6.28)	0.34 (0.16, 0.52)	3 (2, 6)
Meta-analysis	91/205 (39.0)	31/208 (14.9)	2.99 (2.09, 4.28)	0.29 (0.21, 0.38)	3 (3, 5)
GLM v PBO (Wk 16)					
GO-AHEAD, PSS (N=158)	46/78 (59.0)	23/80 (28.8)	2.05 (1.39, 3.03)	0.30 (0.15, 0.45)	3 (2, 7)
PBS population: nr-axSpA (MRI+ AND CRP+)[*]					
SEC 150mg with load v PBO (Wk 16)					
PREVENT, PHS (N=88) ^β	15/30 (50.0)	3/25 (12.0)	4.17 (1.36, 12.77)	0.38 (0.16, 0.60)	3 (2, 6)
SEC 150mg no load v PBO (Wk 16)					
PREVENT, PHS (N=88) ^β	16/33 (48.5)	3/25 (12.0)	4.04 (1.32, 12.36)	0.36 (0.15, 0.58)	3 (2, 7)
CZP 200mg Q2W v PBO (Wk 12)					
C-axSpAnd, PSS (N=87)	21/45 (46.7)	6/42 (14.3)	3.27 (1.46, 7.30)	0.32 (0.14, 0.50)	3 (2, 7)
GLM v PBO (Wk 16)					
GO-AHEAD, PHS (N=53)	18/26 (69.2)	10/27 (37.0)	1.87 (1.07, 3.25)	0.32 (0.07, 0.58)	3 (2, 14)
Indirect comparisons					
TGA population: nr-axSpA (MRI+ AND/OR CRP+)					
SEC load v CZP (meta), Wk 16			0.60 (0.36, 0.97)	-0.13 (-0.25, 0)	-
SEC no load v CZP (meta), Wk 16			0.60 (0.37, 0.98)	-0.12 (-0.25, 0.01)	-
SEC load v GLM, Wk 16			0.87 (0.52, 1.45)	-0.14 (-0.31, 0.03)	-
SEC no load v GLM, Wk 16			0.87 (0.52, 1.46)	-0.13 (-0.31, 0.05)	-
SA: SEC load v CZP (meta), Wk 12			0.52 (0.32, 0.83)	-0.15 (-0.29, -0.01)	-
SA: SEC no load v CZP (meta), Wk 12			0.46 (0.28, 0.74)	-0.16 (-0.34, 0.02)	-
SA: SEC load v GLM, Wk 12			0.76 (0.46, 1.24)	-0.20 (-0.32, -0.08)	-
SA: SEC no load v GLM, Wk 12			0.66 (0.40, 1.10)	-0.21 (-0.38, -0.04)	-
PBS population: nr-axSpA (MRI+ AND CRP+)[*]					
SEC load v CZP (C-axSpAnd)			1.28 (0.32, 5.06)	0.06 (-0.22, 0.34)	-
SEC no load v CZP (C-axSpAnd)			1.24 (0.21, 4.9)	0.04 (-0.24, 0.32)	-
SEC load v GLM			2.23 (0.64, 7.78)	0.06 (-0.28, 0.40)	-
SEC no load v GLM			2.16 (0.62, 7.53)	0.04 (-0.29, 0.37)	-

Abbreviations: BASDAI50=50% improvement in Bath ankylosing spondylitis disease activity index; CRP=C-reactive protein; CZP=certolizumab pegol; GLM=golimumab; ITT=intention to treat; MRI=magnetic resonance imaging; nr-axSpA=non-radiographic axial spondyloarthritis; OSI=objective signs of inflammation; PBO=placebo; PSS=pre-specified subgroup; PHS=post-hoc subgroup; SA=sensitivity analysis; SEC=secukinumab; Q2W=every 2 weeks; Q4W every 4 weeks; wk=week;

[^] Sensitivity analysis was conducted using BASDAI50 response at Wk 12 estimated from Figure 11-10, p167 of Attachment 6_CSR2315.

^α In the TGA population, CRP>ULN defined as: PREVENT ULN=5mg/L; C-axSpAnd ULN=9.99mg/L; RAPID-axSpA ULN=7.9mg/L; GO-AHEAD ULN=9mg/L

^β PREVENT post-hoc PBS subgroup used MRI+ AND CRP+ (defined as >10mg/L)

Source: Table 2.52 and Table 2.54, pp92-96 of the submission; Attachment 11_Indirect comparison_nr-axSpA.xlsx and Attachment 11_Indirect comparison_nr-axSpA.rm5

* Note that the results presented are derived from ad-hoc/ post-hoc analyses conducted by the applicant specifically for the purposes of informing the PBAC consideration. These analyses were not part of the pre-specified statistical plan for study PREVENT. Interpretation of the results and their application should therefore be limited to seeking to understand the basis for the PBAC outcome and should not be used for any other purpose.

Table 5: ASAS20 response in patients with nr-axSpA plus OSI defined according to the TGA population (MRI+ and/or CRP+) and PBS population (MRI+ and CRP+)

Trial	Drug n/N (%)	Control n/N (%)	RR (95%CI)	RD (95%CI)	NNT (95%CI)
TGA population: nr-axSpA (MRI+ AND/OR CRP+)^α					
SEC 150mg with load v PBO (Wk 16)					
PREVENT, ITT (N=555)	105/185 (56.8)	85/186 (45.7)	1.24 (1.02, 1.52)	0.11 (0.01, 0.21)	-
SEC 150mg no load v PBO (Wk 16)					
PREVENT, ITT (N=555)	107/184 (58.2)	85/186 (45.7)	1.27 (1.04, 1.55)	0.12 (0.02, 0.23)	8 (4,50)
CZP 200mg Q2W v PBO (Wk 12)					
C-axSpAnd, ITT (N=317)	104/159 (65.4)	51/158 (32.3)	2.03 (1.57, 2.61)	0.33 (0.23, 0.44)	3 (2, 4)
RAPID-axSpA, PSS (N=96)	27/46 (58.7)	20/50 (40)	1.47 (0.97, 2.23)	0.19 (-0.01, 0.38)	-
Meta-analysis	131/205 (63.9)	71/208 (34.1)	1.80 (1.33, 2.44)	0.28 (0.15, 0.42)	4 (2, 7)
GLM v PBO (Wk 16)					
Go-AHEAD, PSS (N=158)	60/78 (76.9)	30/80 (37.5)	2.05 (1.51, 2.79)	0.39 (0.25, 0.54)	3 (2, 4)
PBS population: nr-axSpA (MRI+ AND CRP+)*					
SEC 150mg with load v PBO (Wk 16)					
PREVENT, PHS (N=88) ^β	21/30 (70.0)	7/25 (28.0)	2.50 (1.28, 4.89)	0.42 (0.18, 0.66)	2 (2, 6)
SEC 150mg no load v PBO (Wk 16)					
PREVENT, PHS (N=88) ^β	23/33 (69.7)	7/25 (28.0)	2.49 (1.28, 4.85)	0.42 (0.18, 0.65)	2 (2, 6)
CZP 200mg Q2W v PBO (Wk 12)					
C-axSpAnd, PSS (N=87)	39/45 (86.7)	13/42 (31.0)	2.80 (1.76, 4.46)	0.56 (0.39, 0.73)	2 (1, 3)
GLM v PBO (Wk 16)					
Go-AHEAD, PHS (N=53)	22/26 (84.6)	10/27 (37.0)	2.28 (1.36, 3.84)	0.48 (0.25, 0.70)	2 (1, 4)
Indirect comparisons					
TGA population: nr-axSpA (MRI+ AND/OR CRP+)					
SEC load v CZP (meta)			0.69 (0.48, 0.99)	-0.17 (-0.34, 0)	-
SEC no load v CZP (meta)			0.76 (0.49, 1.01)	-0.16 (-0.33, 0.01)	-
SEC load v GLM			0.60 (0.42, 0.87)	-0.28 (-0.46, -0.10)	-
SEC no load v GLM			0.62 (0.43, 0.89)	-2.70 (-0.45, -0.09)	-
PBS population: nr-axSpA (MRI+ AND CRP+)*					
SEC load v CZP (C-axSpAnd)			0.89 (0.39, 2.02)	-0.14 (-0.43, 0.15)	-
SEC no load v CZP (C-axSpAnd)			0.89 (0.40, 2.00)	-0.14 (-0.43, 0.15)	-
SEC load v GLM			1.10 (0.47, 2.56)	-0.06 (-0.39, 0.27)	-
SEC no load v GLM			1.09 (0.47, 2.54)	-0.06 (-0.39, 0.27)	-

Abbreviations: ASAS20/40=20%/40% improvement in Assessment of SpondyloArthritis international Society response criteria; CRP=C-reactive protein; CZP=certolizumab pegol; GLM=golimumab; ITT=intention to treat; MRI=magnetic resonance imaging; nr-axSpA=non-radiographic axial spondyloarthritis; OSI=objective signs of inflammation; PBO=placebo; PSS=pre-specified subgroup; PHS=post-hoc subgroup; SEC=secukinumab; Q2W=every 2 weeks; Q4W=every 4 weeks; wk=week;

^α In the TGA population, CRP>ULN defined as: PREVENT ULN=5mg/L; C-axSpAnd ULN=9.99mg/L; RAPID-axSpA ULN=7.9mg/L; GO-AHEAD ULN=9mg/L

^β PREVENT post-hoc PBS subgroup used MRI+ AND CRP+ (defined as >10mg/L)

Source: Table 2.52 and Table 2.54, pp92-96 of the submission; Attachment 11_Indirect comparison_nr-axSpA.xlsx and Attachment 11_Indirect comparison_nr-axSpA.rm5

* Note that the results presented are derived from ad-hoc/ post-hoc analyses conducted by the applicant specifically for the purposes of informing the PBAC consideration. These analyses were not part of the pre-specified statistical plan for study PREVENT. Interpretation of the results and their application should therefore be limited to seeking to understand the basis for the PBAC outcome and should not be used for any other purpose.

- 6.13 The results for BASDAI50 and ASAS20 demonstrated that the three bDMARDs (SEC, CZP and GLM) were more effective than placebo at producing a response to treatment at Weeks 12 or 16 across all the populations. Results in the PREVENT trial showed similar response rates for SEC 150mg with loading and SEC 150mg without loading for both outcomes.
- 6.14 The indirect comparisons in the TGA population found results generally favoured CZP over SEC (load and no load) for BASDAI and ASAS20, and GLM over SEC (load and no load) for ASAS20. In the PBS population however, there were no statistically significant differences between SEC (load and no load) compared to CZP and GLM for either BASDAI50 or ASAS20.
- 6.15 The submission noted that placebo response varied between the trials particularly for BASDAI50 (e.g. 12% to 37%), suggesting poor transitivity/exchangeability of the trials included in the analysis. As discussed above, there were a number of differences across the trials that would likely violate the assumption of transitivity (see Clinical trials). In addition, interpretation of results was also limited by the small patient numbers in the (post-hoc) PBS population and the fact that BASDAI50 was a secondary outcome in all trials. The submission however noted that past PBAC decisions were made using subgroup analyses of secondary endpoints.
- 6.16 The submission also presented results of a set of network meta-analyses (NMA) in the TGA population as a supplementary analysis to adjust for placebo response, baseline differences and different assumptions (i.e. independence of treatment effects, exchangeability, fixed versus random effects). Overall, SEC was found to perform similarly to CZP and GLM for BASDAI50, demonstrated by overlap in 95%CI. The results of the NMA were similar to the standard frequentist approach, and showed the point estimates favouring CZP and GLM over SEC.
- 6.17 The submission concluded that non-inferiority was supported by BASDAI50 and ASAS20 for the PBS population, given the relative risk (RR) point estimates were numerically but not statistically significantly non-inferior for SEC versus CZP and superior versus GLM. The evaluation noted the submission did not formally apply the nominated non-inferiority margin for ASAS20 to the results of the indirect comparison. Based on the nominated margin of 0.43 for the RR statistic, non-inferiority was satisfied between SEC (load and no load) and GLM but not CZP, given the lower 95%CI was below 0.43 (i.e. 0.39 for SEC load, and 0.40 for SEC no load).

Comparative harms

- 6.18 In the PREVENT trial, patients treated with SEC reported a higher incidence of any adverse events (AEs) and drug-related AEs up to Week 20 compared to placebo. Across the treatment arms, the incidence of serious AEs and AEs leading to discontinuations were low. The most commonly reported AEs were infections and infestations, gastrointestinal disorders, musculoskeletal and connective tissue disorders and nervous system disorders.

6.19 The submission compared safety outcomes in the double-blind treatment phases of the trials (Table 6), and conducted an indirect comparison using placebo as the common reference for patients with nr-axSpA. There was no statistically significant difference in any AEs between SEC (load and no load) and GLM or CZP. The risk of serious AEs and drug-related AEs was numerically lower for SEC compared to CZP but higher compared to GLM. Interpretation of the indirect comparisons was limited by differences in the timing of safety outcomes (Week 16 vs Week 52) and duration of treatment exposure i.e. placebo escape (from Week 20 vs entire double-blind period) across the trials.

Table 6: Summary of key adverse events (AEs) during the double-blind period of the included trials

Trial ID	PREVENT, Wk 20 (nr-axSpA)			C-axSpAnd, Wk 52 (nr-axSpA)		RAPID-axSpA, Wk 24 (axSpA)		GO-AHEAD, Wk 16 (nr-axSpA)	
	SEC no load N=184	SEC load N=185	PBO N=186	CZP N=159	PBO N=158	CZP# N=111	PBO^ N=107	GLM N=97	PBO N=100
Summary of AEs, n (%)									
Any AEs	107 (58.2)	118 (63.8)	100 (53.8)	120 (75.5)*	101 (63.9)*	85 (76.6)*	67 (62.6)*	40 (41.2)	47 (47.0)
Serious AEs	4 (2.2)	3 (1.6)	4 (2.2)	8 (5.0)	3 (1.9)	4 (3.6)	5 (4.7)	1 (1.0)	2 (2.0)
Drug-related AEs	39 (21.2)	49 (26.5)	26 (14.0)	48 (30.2)*	23 (14.6)*	41 (36.9)*	22 (20.6)*	13 (13.4)	17 (17.0)
Discontinuations due to AEs	4 (2.2)	0	3 (1.6)	3 (1.9)	3 (1.9)	2 (1.8)	2 (1.9)	2 (2.1)	1 (1.0)
Common AEs, n(%)									
Gastrointestinal disorders	25 (13.6)	33 (17.8)	20 (10.8)	32 (20.1)*	17 (10.8)*	15 (13.5)	15 (14.0)	-	-
General disorders & administration site	14 (7.6)	15 (8.1)	8 (4.3)	16 (10.1)*	9 (5.7)*	17 (15.3)	8 (7.5)	-	-
Infections & infestations	61 (33.2)	70 (37.8)	61 (32.8)	85 (53.5)*	53 (33.5)*	43 (38.7)*	25 (23.4)*	0	0
Nervous system disorders	12 (6.5)	24 (13.0)	11 (5.9)	20 (12.6)*	10 (6.3)*	12 (10.8)	12 (11.2)	-	-
Reproductive & breast disorders	2 (1.1)	1 (0.5)	2 (1.1)	6 (3.8)	2 (1.3)	-	-	-	-
Skin & subcutaneous disorders	12 (6.5)	15 (8.1)	12 (6.5)	24 (15.1)*	9 (5.7)*	17 (15.3)	14 (13.1)	10 (10.3)	6 (6.0)
Deaths	0	0	0	0	0	0	0	0	0

Abbreviations: axSpA=axial spondyloarthritis; CI=confidence interval; CZP=certolizumab pegol; GLM=golimumab; n=number of participants reporting data; N=total participants in group; nr-axSpA=non-radiographic axial spondyloarthritis; PBO=placebo; RD=risk difference; SEC=secukinumab; Q2W=every 2 weeks; wk=week;

CZP 200mg Q2W treatment arm

^ Entire PBO group, CZP data from PBO subjects were not utilized

* Risk difference p<0.05

Source: Tables 2.40 to 2.41, pp80-82 and Tables 2.43 to 2.51, pp84-90 of the submission, Attachment 6 CSR2315

6.20 Overall, safety outcomes reported in the trials were consistent with the known safety profile of SEC and anticipated effects of IL-17 inhibitor treatment as described in the proposed PI. The PBAC has previously considered SEC (with load) compared to GLM and/or CZP as non-inferior in safety for other indications including AS and psoriatic

arthritis (paragraph 7.5, Secukinumab AS PSD March 2016 PBAC meeting and paragraph 7.5, Secukinumab psoriatic arthritis PSD March 2016 PBAC meeting).

Benefits/harms

6.21 There were no expected clinically meaningful differences between the three bDMARDs (SEC, GLM and CZP) in efficacy and safety when used for the treatment of nr-axSpA with objective signs of inflammation in the proposed PBS population (MRI+ and CRP+).

Clinical claim

6.22 The submission described SEC as non-inferior in terms of effectiveness and non-inferior (or equivalent) in terms of safety compared with CZP and GLM in patients with nr-axSpA who meet the PBS (MRI+ and CRP+) definitions of objective signs of inflammation.

6.23 The clinical claim was based on the proposed dosing regimen SEC 150mg with loading. However the interpretation of the results was not different for SEC 150mg without loading in both the TGA and PBS populations. Similarly, the clinical claim was based on one of two approved dosing regimens for CZP (i.e. CZP 200mg Q2W), but results in RAPID-axSpA found no difference between CZP 200mg Q2W and CZP 400mg Q4W dosing regimens and both have been considered equi-effective in other indications.

6.24 Overall, the evaluation considered the clinical claim of non-inferior efficacy and safety may be reasonable, however the following key issues are noted:

- Interpretation of the evidence in the PBS population (MRI+ and CRP+) was limited by the very small number of trial patients meeting this criteria, the patient relevant outcome BASDAI50 being a secondary outcome in the trials, the lack of a non-inferiority margin for BASDAI50, and heterogeneity across the trials may violate the assumption of transitivity in the indirect comparisons.
- Results in the larger TGA population (MRI+ and/or CRP+) suggest that SEC may be inferior in effectiveness compared to CZP and GLM. For other indications including AS however, the PBAC has considered SEC is non-inferior to CZP and GLM (paragraph 7.4, Secukinumab AS PSD March 2016 PBAC meeting).

6.25 The PBAC considered that the claim of non-inferior comparative effectiveness was reasonable.

6.26 The PBAC considered that the claim of non-inferior comparative safety was reasonable.

Economic analysis

- 6.27 The submission presented a cost-minimisation analysis and proposed the following equi-effective doses, based on the recommended doses in the respective PIs:
- SEC 150mg at Week 0, 1, 2, 3 and 4, then monthly or SEC 150mg monthly (updated in PSCR)
 - GLM 50mg every month;
 - CZP 400mg at Week 0, 2, 4, then 200mg every 2 weeks or 400mg every 4 weeks.
- 6.28 The proposed equi-effective doses are consistent with the wording in the respective approved/draft PIs, but there are inconsistencies in the exact dosing frequency (four-weekly vs monthly) of GLM and SEC across the PIs, clinical trials, Therapeutic Relativity Sheets and PSDs. The PSCR argued that monthly dosing should be used in the cost-minimisation analysis for nr-axSpA given the PI and listings for SEC for psoriasis, AS and psoriatic arthritis listings were also based on monthly dosing. As discussed, the PBAC previously considered patients would likely find four-weekly dosing with SEC less confusing than monthly dosing, and “therefore considered four-weekly dosing was the most appropriate frame of reference for considering equi-effective doses.” (paragraph 7.2, Secukinumab AS PSD March 2016 PBAC meeting).
- 6.29 The cost-minimisation analysis in the submission calculated drug costs over the first 2 years of treatment based on current AEMPs of GLM and CZP, assuming 24 scripts of GLM, 28 scripts of CZP and 28 scripts of SEC with the requested AEMP of \$952.13, estimated based on the total cost of CZP, which was considered the lowest cost comparator.

Table 7: Results of the cost-minimisation analysis conducted over the first 2 years of treatment, presented in the submission.

	SEC (with loading)	GLM	CZP (200 Q2W)
AEMP / pack	\$952.13 ^a	\$1,181.07	\$952.13
Dose	SEC 150mg weeks 0, 1, 2, 3, 4 then every 4 weeks	50mg every 4 weeks	CZP 400mg weeks 0, 2, 4 then 200mg every 2 weeks.
Quantity / pack	1 x 150mg	1 x 50mg	2 x 200mg
Injections	28 x 150mg	24 x 50mg	56 x 200mg
Scripts	28	24	28
Total cost	\$26,659.64	\$28,346.68	\$26,659.64

Abbreviations: CZP=certolizumab pegol; GLM=golimumab; SEC=secukinumab; wk=week;

^a estimated AEMP based on cost-minimisation to CZP 200mg Q2W

Source: Tables 3.3 and 3.4, p112 of the submission and Attachment 12_Cost-minimisation analysis.xlsx.

- 6.30 The following issues were identified with the assumptions of the cost-minimisation analysis, and most were addressed in the PSCR:
- The estimated number of scripts for each treatment over the first 2 years for each treatment is dependent on the dosing frequencies assumed. The PSCR maintained

that monthly dosing should be used in the calculations, which underestimates the cost of treatment.

- The analysis did not include the SEC no load regimen, which requires fewer scripts than SEC with loading. This is however conservative, given the corresponding AEMP for SEC without loading would be larger. The PSCR updated this to 26 scripts to account for the SEC no load dosing regimen.
- The analysis did not include the CZP 400mg Q4W dosing regimen, which may be inappropriate given patients require 1 less 200mg injection over the first 2 years compared to the CZP 200mg Q2W dosing regimen. The PSCR added CZP 400 mg and capped injections at end of week 103.
- The submission incorrectly estimated the number of CZP scripts required for the first 2 years of treatment as 28 (provides 106 weeks of treatment), instead of 27.5. The PSCR updated this to 27.25 treatments (capped injections at the end of week 103).

6.31 Therefore, the PSCR presented an updated cost-minimisation analysis based on the revised equi-effective doses, assuming a 50:50 weighting on SEC load and no load dosing regimens and the dosing regimens for CZP and the associated script count adjustments for SEC and CZP, monthly dosing, price reduction of GLM in August 2020 and the AEMP/DPMQ based on an updated PBS pricing calculator (fees and mark-ups fees in 7CPA, effective 1 Jan 2021). This resulted in an increased AEMP of \$997.91 for SEC. There is no special pricing arrangement for CZP or GLM, therefore the published price is the same as the effective price.

Drug cost/patient/year: \$16,401.92 in submission; \$17,104.48 in PSCR

6.32 In the submission, assuming a DPMQ of \$1,025.12 (AEMP of \$952.13) and 16 scripts required for the first year of treatment inclusive of initial and continuing therapy with SEC 150mg with loading regimen, the cost per patient per year is \$16,401.92. Using the updated DPMQ of \$1,069.03 (AEMP of \$997.91) from the PSCR, the cost per patient per year increased to \$17,104.48.

Estimated PBS usage & financial implications

6.33 This submission was not considered by DUSC. A unique market-share approach was used to estimate the financial impact of the proposed listing on the PBS, where the number of patients currently treated with a bDMARD for nr-axSpA was estimated from the PSDs (further information in paragraph 6.35-6.36).

6.34 Table 8 summarises the key inputs in the financial estimates. The submission assumed that the estimated market size implicitly included grandfathered patients (up to 30) and patients failing/recommencing treatment, rather than presenting these as separate costs, which was reasonable.

Table 8: Key inputs for financial estimates

Parameter	Value applied and source	Comment
Market size, patients treated with CZP.	Yr 1: 851; Yr 2: 1270; Yr 3: 1762; Yr 4: 1939; Yr 5: 2120; Yr 6: 2150. Source: Table 7, Certolizumab Pegol PSD November 2019 PBAC meeting.	The estimate may not be reliable and likely uncertain, given the PBAC considered the methodology used in the financial estimates for the listing of CZP was 'likely to overestimate the number of eligible and treated patients' (paragraph 6.43, Certolizumab Pegol PSD November 2019 PBAC meeting).
GLM market share (used to derived market size, patients treated with GLM)	Yr 1: 58% to Yr 5-6: 50% Source: Assumption. Linear interpolations applied from Yr 1 to reach 50%:50% in Yr 6 in terms of market share of eligible patients for GLM and CZP.	This assumption could not be verified and may be an underestimate, given GLM was the first bDMARD listed for nr-axSpA in December 2018 followed by CZP in June 2020. Utilisation in AS in recent years suggests up to 75%:25% market share between GLM and CZP.
SEC market share	Yr 1: 10% to Yr 6: 33% Source: Assumption. Linear interpolations applied from Yr 1 to reach 33%:33%:33% in Yr 6 in terms of market share of eligible patients for SEC, GLM and CZP, if SEC was listed on the PBS.	This assumption could not be verified. Utilisation data of SEC in AS suggests 25% to 44% market share in Year 2 and 3.
Total scripts / patient / year	SEC: 12; GLM: 12; CZP: 13 Source: Recommended dose and proposed listing	Based on the other parameters in the financial estimates, excluding loading doses may underestimate the financial impact of the proposed listing. The assumed script relativities reflect dosing for maintenance therapy only assuming SEC and GLM will be dosed every month, which is inconsistent with doses administered every 4 weeks in the trial evidence.
Script breakdown for SEC (Yr 1)	Initial 1: 18.3% Initial 2 (balance of supply): 28.8% Continuing: 52.8% Source: PBS/RPBS data for SEC in AS from Oct 2016-19	The submission applied the AS to nr-axSpA script adjustment for SEC on initial 2 (balance of supply) and continuing therapy, given differences in initial therapy (16 weeks vs 20 weeks) between SEC for AS and nr-axSpA, respectively.
Script breakdown for GLM (Yr 1)	Initial: 11.3% Continuing: 88.7% Source: PBS/RPBS data for GLM in AS from Sept 2010-19, but data from Yr 3 (2012-15) of listing was used.	Reasonable.
Script breakdown for CZP (Yr 1)	Initial 1:18.3% Initial 2 (balance of supply): 42% Continuing: 39.6% Source: PBS/RPBS data for SEC in AS from Oct 2016-19	The submission inappropriately did not apply the AS to nr-axSpA script adjustment for CZP on initial (balance of supply) and continuing therapy, despite inferring utilisation data of SEC in AS for CZP in nr-axSpA. This potentially underestimated the CZP script numbers (before the proposed listing of SEC), given differences in initial therapy (16 weeks vs 20 weeks) between SEC for AS and CZP for nr-axSpA, respectively.
AS to nr-axSpA script adjustment for SEC – initial therapy (Week 0 to 20)	33% Source: Recommended dose and proposed listing	Reasonable, given the requested restriction in nr-axSpA for SEC initial therapy is 20 weeks compared to the restriction in AS initial therapy for 16 weeks.

Abbreviations: AS=ankylosing spondylitis; bDMARD=biologic disease-modifying anti-rheumatic drug; CZP=certolizumab pegol; GLM=golimumab; MRI=magnetic resonance imaging; nr-axSpA=non-radiographic axial spondyloarthritis; Q2W=every 2 weeks; Q4W=every 4 weeks; SEC=secukinumab; Yr=year;

Source: Sections 4.1 to 4.2, pp115-128 of the submission.

6.35 The submission’s estimated number of eligible patients were replicated from the November 2019 PSD of CZP for nr-axSpA, which assumed all patients remained eligible for bDMARD treatment irrespective of past treatment failure (paragraph 6.32, Certolizumab Pegol PSD November 2019 PBAC meeting). The submission then estimated number of scripts as a function of: i) total scripts per year for continuing therapy, ii) proportional use of initial, continuing and balance of supply therapy each year based on PBS utilisation data for GLM and SEC in AS, and iii) script adjustment from AS to nr-axSpA given differences in initial therapy (16 weeks vs 20 weeks).

6.36 Table 9 summarises the submission’s estimated net financial implications for the proposed listing of SEC on the PBS/RPBS, based on the following assumptions:

- Market size (patients) was estimated from PSDs and assumptions;
- Number of scripts was estimated from annual scripts per patient required for maintenance dosing; and
- The split of initial and continuing scripts was estimated based on PBS dispensing data for AS, adjusted for differences in duration of treatment.

Table 9: Estimated use and financial implications to the PBS/RPBS of SEC, using updated DPMQ[^]

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Patients treated with a bDMARD	█ 1	█ 1	█ 1	█ 1	█ 1	█ 1
Estimated use of bDMARDs for nr-axSpA without SEC (current world with GLM and CZP)						
GLM patients treated	█ 1	█ 1	█ 1	█ 1	█ 1	█ 1
GLM scripts	█ 2	█ 2	█ 3	█ 3	█ 3	█ 3
CZP patients treated	█ 1	█ 1	█ 1	█ 1	█ 1	█ 1
CZP scripts	█ 2	█ 2	█ 3	█ 3	█ 3	█ 3
GLM and CZP net PBS/RPBS cost	█ 4	█ 5	█ 6	█ 4	█ 4	█ 4
Estimated use of bDMARDs for nr-axSpA with SEC (proposed world with SEC, GLM and CZP)						
SEC patients treated	█ 7	█ 7	█ 1	█ 1	█ 1	█ 1
SEC scripts	█ 1	█ 10	█ 1	█ 2	█ 2	█ 2
SEC net PBS/RPBS cost	█ 8	█ 8	█ 9	█ 9	█ 9	█ 5
Estimated change of use of other drugs (proposed world with SEC, GLM and CZP)						
GLM and CZP patients treated	█ 7	█ 7	█ 1	█ 1	█ 1	█ 1
GLM and CZP scripts	█ 1	█ 10	█ 10	█ 2	█ 2	█ 2
GLM and CZP net PBS/RPBS cost	-\$ █ 8	-\$ █ 8	-\$ █ 9	-\$ █ 9	-\$ █ 9	-\$ █ 5
Estimated financial implication to the government						
Net cost to PBS/RPBS	█ 8	-\$ █ 11	-\$ █ 11	-\$ █ 11	-\$ █ 11	-\$ █ 11
Net cost to health budget	█ 8	-\$ █ 11	-\$ █ 11	-\$ █ 11	-\$ █ 11	-\$ █ 11

Abbreviations: bDMARD=biologic disease-modifying anti-rheumatic drug; CZP=certolizumab pegol; GLM=golimumab; nr-axSpA=non-radiographic axial spondyloarthritis; SEC=secukinumab;

[^] DPMQs were updated during the evaluation using the 1 July, 2020 pricing calculator for SEC (Initial 1: \$3985.50, Initial 2 and Continuing: \$1025.12) GLM (\$1320.58) and CZP (Initial 1: \$3033.33, Initial 2 and Continuing: \$1031.23). The DPMQ was revised during the evaluation based on the requested AEMP of \$952.13 and the correct mark-ups.

Source: Tables 4.8, 4.13 to 4.18, pp121. 126-130 of the submission, Attachment 13_Utilisation and financial estimates.xlsx.

The redacted values correspond to the following ranges:

- ¹ 500 to < 5000
- ² 10,000 to < 20,000
- ³ 20,000 to < 30,000
- ⁴ \$30 million to < \$40 million
- ⁵ \$20 million to < \$30 million
- ⁶ \$50 million to < \$60 million
- ⁷ <500
- ⁸ \$0 to < \$10 million
- ⁹ \$10 million to < \$20 million
- ¹⁰ 5,000 to < 10,000
- ¹¹ net cost saving

6.37 Table 10 presents the updated financial estimates from the PSCR for the proposed listing of SEC, which was updated with the revised AEMPs and DPMQs (based on fees and mark-ups fees in 7CPA, effective 1 Jan 2021) of SEC, GLM and CZP. The estimates did not account for use of SEC no load regimen or adjust for the proportion of initial/continuing/balance of supply scripts.

Table 10: Financial implications to the PBS/RPBS of SEC updated in the PSCR^{^*}

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Patients treated with a bDMARD	■ ¹	■ ¹	■ ¹	■ ¹	■ ¹	■ ¹
Estimated use of bDMARDs for nr-axSpA without SEC (current world with GLM and CZP)						
GLM and CZP net PBS/RPBS cost	■ ²	■ ³	■ ⁴	■ ²	■ ²	■ ²
Estimated use of bDMARDs for nr-axSpA with SEC (proposed world with SEC, GLM and CZP)						
SEC net PBS/RPBS cost	■ ⁵	■ ⁵	■ ⁶	■ ⁶	■ ⁶	■ ³
Estimated change of use of other drugs (proposed world with SEC, GLM and CZP)						
GLM and CZP net PBS/RPBS cost	-■ ⁵	-■ ⁵	-■ ⁶	-■ ⁶	-■ ⁶	-■ ³
Net cost to PBS / RPBS	■ ⁵	■ ⁵	■ ⁵	■ ⁵	■ ⁵	■ ⁵

Abbreviations: bDMARD=biologic disease-modifying anti-rheumatic drug; CZP=certolizumab pegol; GLM=golimumab; nr-axSpA=non-radiographic axial spondyloarthritis; SEC=secukinumab;

[^] DPMQs were updated in the PSCR to include changes to distribution and dispensing fees in 7CPA effective 1 Jan 2021.

* The estimates did not account for use of SEC no load regimen or adjust for the proportion of initial/continuing/balance of supply scripts.

Source: Table 4 of the PSCR and Attachment 13_Utilisation and financial estimates.xlsx.

The redacted values correspond to the following ranges:

- ¹ 500 to < 5000
- ² \$30 million to < \$40 million
- ³ \$20 million to < \$30 million
- ⁴ \$50 million to < \$60 million
- ⁵ \$0 to < \$10 million
- ⁶ \$10 million to < \$20 million

6.38 The PSCR estimated the proposed listing of SEC with loading regimen would result in a cost to the PBS/RPBS of \$0 to < \$10 million (updated AEMPs and DPMQs) over the first 6 years. However, when the SEC volumes were updated in the pre-PBAC response to account for the no loading dose regimen, at the requested price, the proposed listing of SEC with loading regimen was estimated to result in a cost-saving to the PBS/RPBS of \$0 to < \$10 million (updated AEMPs and DPMQs) over the first 6 years. The estimated cost savings was unreliable and potentially underestimated the net cost to government. The financial estimates were driven by the assumed distribution of initial and continuing scripts, and the assumed number of scripts per patient per year (script relativities). The estimated market size (from patient numbers in a PSD and

scripts per patient per year for continuing therapy) and proportion of initial and continuing scripts (based on another indication with script adjustments) were not transparent, and the assumed script relativities ignored loading doses which underestimated cost to government for SEC (i.e. SEC 150mg with loading). The PBAC noted that the estimated utilisation of GLM and CZP was overestimated in the submission when compared to the current utilisation of GLM and CZP for nr-axSpA based on PBS dispensing data.

- 6.39 The submission noted potential uncertainty in the financial estimates which were inferred from the PSDs of GLM and CZP, but expected that SEC would join the existing RSA with GLM and CZP. The submission did not present any sensitivity analyses.

Financial Management – Risk Sharing Arrangements

- 6.40 The sponsor expects SEC to join the existing RSA with GLM and CZP upon listing, which would address the uncertainty around the assumptions and estimates in the submission.

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

7 PBAC Outcome

- 7.1 The PBAC recommended the Authority Required listing of secukinumab (SEC) for the treatment of non-radiographic axial spondyloarthritis (nr-axSpA). The PBAC's recommendation for listing was based on, among other matters, its assessment that the cost-effectiveness of SEC would be acceptable if it were cost-minimised to the lowest cost biologic disease-modifying anti-rheumatic drug (bDMARD) for this indication.
- 7.2 The PBAC considered the nominated comparators of golimumab (GLM) and certolizumab pegol (CZP) were appropriate and advised the equi-effective doses were:
- SEC: 150 mg at Week 0, 1, 2, 3 and 4, then SEC 150 mg every 4 weeks; or SEC 150 mg every 4 weeks
 - GLM: 50 mg every 4 weeks
 - CZP: 400 mg at Week 0, 2, 4, then 200 mg every 2 weeks; or CZP 400 mg every 4 weeks.
- 7.1 The PBAC reiterated its decision during the consideration of SEC at the March 2016 meeting that the 4-weekly dosing was the most appropriate frame of reference for considering equi-effective doses (para 7.2, SEC AS PSD March 2016 PBAC meeting). The PBAC advised the cost-minimisation analysis should use the approved ex-manufacturer price and be conducted over 2 years, consistent with the approach previously applied to bDMARDs for other indications.
- 7.2 The PBAC recommended that the listing of SEC for the initial treatment of nr-axSpA

should allow patients to be treated with or without loading doses. The PBAC agreed with the ACM advice that the choice between SEC with and without loading should be made clinically by the rheumatologist. The PBAC noted that the evidence provided in the submission demonstrated there was no difference in response rate between SEC with and without loading dose for the treatment of nr-axSpA. Additionally, the PBAC noted that it was likely that clinicians would initiate patients on SEC with the loading dose given SEC is TGA approved to be used with loading dose for ankylosing spondylitis (AS), plaque psoriasis and psoriatic arthritis.

- 7.3 The PBAC advised that the requested duration of initial treatment of 20 weeks was clinically appropriate given the loading dose would likely be used for SEC and patients would be able to be assessed between week 16-20 which is consistent with CZP treatment.
- 7.4 The PBAC noted the indirect comparisons in the ITT trial populations generally favoured CZP over SEC for BASDAI50 and ASAS20, and GLM over SEC for ASAS20. The PBAC noted there were a number of key differences in study design across the trials (paragraph 6.6) which may confound the indirect comparisons. The PBAC noted the indirect comparisons based on the PBS population subgroup demonstrated there were no statistically significant differences between SEC compared to CZP and GLM for BASDAI50 or ASAS20, although the comparison was based on small patient numbers. The PBAC recalled it had previously considered SEC to be non-inferior to CZP and GLM in other indications including AS. The PBAC considered that, overall, the clinical claim of non-inferior comparative efficacy between SEC, GLM and CZP was reasonable.
- 7.5 The PBAC considered that the clinical claim of non-inferior comparative safety between SEC, GLM and CZP was reasonable. The PBAC noted that there was no significant difference in the comparative safety between SEC (with and without loading), GLM and CZP.
- 7.6 The PBAC considered the market share approach presented in the submission was inappropriate given the market size was estimated from patient numbers in PSDs and assumptions which were unreliable and overestimated compared to the actual utilisation of GLM and CZP for nr-axSpA based on PBS dispensing data. The PBAC advised that the listing for SEC for nr-axSpA on a cost minimisation basis as described in paragraph 7.2 should not result in any additional cost to the PBS.
- 7.7 The PBAC noted the PSCR and Pre-PBAC response updated the cost minimisation based on a 50:50 weighting for SEC with and without loading compared with GLM and CZP. The PBAC considered that there is currently no clinical evidence on utilisation of the loading dose versus no loading dose, but it would be likely that a 70:30 weighting, for with and without loading doses respectively, to occur given the loading dose is currently TGA approved for SEC for AS, plaque psoriasis and psoriatic arthritis and clinicians would be familiar with using the loading dose regimen.

- 7.8 The PBAC recommended that SEC be included within the current Risk Sharing Arrangements for GLM and CZP and considered that this arrangement would address the uncertainty around the assumptions and estimates in the submission.
- 7.9 The PBAC considered the following in relation to the restrictions for SEC:
- the maximum permitted treatment failures of biologic medicines should remain at '3', but that each drug should only be trialled once in a treatment cycle. The PBAC noted that there will be flow-on restriction changes to GLM and CZP regarding the number of treatment failures within a treatment cycle. The PBAC also advised that the NOTE for GLM and CZP should be modified to include SEC in the list of biological medicines.
 - the authority approval/methods of SEC should be aligned with the listings for GLM and CZP. The PBAC considered that the delayed assessment through the written-only method would allow accurate screening for PBS eligibility non-compliance for authority applications without a history use of the biological medicine. However, as noted previously for CZP in November 2019, in situations where Services Australia has confirmed patient details regarding diagnosis, disease severity and past relevant treatments through a prior written application, such situations (Initial 2 – change of treatment; Initial 3 – re-commencement after a specified break, Continuing treatment, Balance of Supply requests) need not warrant further applications through the written channel. In these situations, an immediate assessment Authority Required (online/telephone) listing should suffice.
 - The PBAC discussed the practicality of creating separate listings for the loading dose regimen and the no loading dose regimen and considered a single listing that permits either situation (loading doses/no loading doses) would be reasonable, particularly noting that all the listings for SEC are Authority Required listings, whereby the prescriber would be interacting with Services Australia for each new prescription. Although the initial treatment listings would list a stated number of zero repeats, requests for increased repeats would be permitted for patients not utilising the loading doses such that the prescriber could request more than zero repeats. Therefore, when the no loading dose regimen is prescribed, a prescriber instruction directing prescribers to request the maximum quantity of 1 and maximum of 4 repeats should be included; and Services Australia should only approve a maximum quantity of 1 pack (not 5 packs per prescription).
- 7.10 The PBAC noted that its recommendation was on a cost-minimisation basis and advised that, because SEC is not expected to provide a substantial and clinically relevant improvement in efficacy, or reduction of toxicity, over GLM or CZP, or not expected to address a high and urgent unmet clinical need given the presence of an alternative therapy, the criteria prescribed by the *National Health (Pharmaceuticals and Vaccines – Cost Recovery) Regulations 2009* for Pricing Pathway A were not met.

7.11 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 indication as follows:

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Available brands
SECUKINUMAB secukinumab 150 mg/mL injection, 1 mL pen device	NEW	5	5	0	Cosentyx
Initial treatment 1 Restriction Summary [NEW] / Treatment of Concept (ToC): [NEW] (Based on Restriction Summary 10432 attached to certolizumab, 12027B, 12063X)					
	Category/program: GENERAL – General Schedule (Code GE)				
	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners				
	Restriction type: <input checked="" type="checkbox"/> Authority Required – delayed/non-immediate assessment by Services Australia (postal lodgement or electronic upload)				
	Administrative advice: TREATMENT OF ADULT PATIENTS WITH NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS (see restriction flow-on section at the end of this section for details)				
	Administrative Advice: No increase in the maximum quantity or number of units may be authorised.				
	Indication: Non-radiographic axial spondyloarthritis				
	Treatment Phase: Initial treatment - Initial 1 (New patient)				
	Clinical criteria:				
	Patient must not have received PBS-subsidised treatment with a biological medicine for this condition				
	AND				
	Clinical criteria:				
	Patient must have had chronic lower back pain and stiffness for 3 or more months that is relieved by exercise but not rest				
	AND				
	Clinical criteria:				
	Patient must have failed to achieve an adequate response following treatment with at least 2 non-steroidal anti-inflammatory drugs (NSAIDs), whilst completing an appropriate exercise program, for a total period of 3 months				
	AND				
	Clinical criteria:				
	Patient must have one or more of the following: (a) enthesitis (heel); (b) uveitis; (c) dactylitis; (d) psoriasis; (e) inflammatory bowel disease; or (f) positive for Human Leukocyte Antigen B27 (HLA-B27)				
	AND				
	Clinical criteria:				
	The condition must not be radiographically evidenced on plain x-ray of Grade II bilateral sacroiliitis or Grade III or IV unilateral sacroiliitis				
	AND				
	Clinical criteria:				
	The condition must be non-radiographic axial spondyloarthritis, as defined by Assessment of Spondyloarthritis International Society (ASAS) criteria				
	AND				
	Clinical criteria:				
	The condition must be sacroiliitis with active inflammation and/or oedema on non-contrast Magnetic Resonance Imaging (MRI)				
	AND				

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	Clinical criteria:
	The condition must have presence of Bone Marrow Oedema (BMO) depicted as a hyperintense signal on a Short Tau Inversion Recovery (STIR) image (or equivalent)
	AND
	Clinical criteria:
	The condition must have BMO depicted as a hypointense signal on a T1 weighted image (without gadolinium)
	AND
	Clinical criteria:
	Patient must not receive more than 20 weeks of treatment under this restriction.
	AND
	Population criteria:
	Patient must be aged 18 years or older
	Treatment criteria:
	Must be treated by a rheumatologist; or
	Must be treated by a clinical immunologist with expertise in the management of non-radiographic axial spondyloarthritis
	Prescriber Instructions: The stated maximum quantity of 5 with zero repeats is intended for a patient undergoing the loading dose regimen of 150 mg administered at weeks 0, 1, 2, 3, and 4 (a total of 5 doses) followed by monthly administration thereafter. State in the application whether a loading dose regimen is intended or not. Where a loading dose regimen is intended, request a maximum quantity of 5 and zero repeats to cover doses at weeks 0, 1, 2, 3 and 4. Doses at week 8, 12, and 16 can be sought under the relevant 'Balance of supply' listing. Where no loading dose regimen is intended, request a maximum quantity of 1 and seek an increase in the number of repeats from zero to 4 repeats to cover dosing at weeks 4, 8, 12 and 16. . Where increased repeats are sought, the maximum quantity sought must not be greater than 1.
	Prescriber Instructions: The application must include details of the NSAIDs trialed, their doses and duration of treatment. If the NSAID dose is less than the maximum recommended dose in the relevant TGA-approved Product Information, the application must include the reason a higher dose cannot be used. If treatment with NSAIDs is contraindicated according to the relevant TGA-approved Product Information, the application must provide details of the contraindication. If intolerance to NSAID treatment develops during the relevant period of use which is of a severity to necessitate permanent treatment withdrawal, the application must provide details of the nature and severity of this intolerance.
	Prescriber Instructions: The following criteria indicate failure to achieve an adequate response to NSAIDs and must be demonstrated at the time of the initial application: (a) a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) of at least 4 on a 0-10 scale; and (b) C-reactive protein (CRP) level greater than 10 mg per L. The baseline BASDAI score and CRP level must be determined at the completion of the 3-month NSAID and exercise trial, but prior to ceasing NSAID treatment. All measures must be no more than 4 weeks old at the time of initial application.
	Prescriber Instructions: If the requirement to demonstrate an elevated CRP level could not be met, the reason must be stated in the application. Treatment with prednisolone dosed at 7.5 mg or higher daily (or equivalent) or a parenteral steroid within the past month (intramuscular or intravenous methylprednisolone or equivalent) is an acceptable reason.
	Prescriber Instructions: The assessment of the patient's response to the initial course of treatment must be made following a minimum of 12 weeks of treatment and submitted no later than 4 weeks from the cessation of that treatment course. If the response assessment is not conducted within these timeframes, the patient will be deemed to have failed this course of treatment in this treatment cycle.
	Prescriber Instructions: The authority application must be made in writing and must include: (a) a completed authority prescription form; and (b) a completed Non-radiographic axial spondyloarthritis initial PBS Authority Application - Supporting Information Form which seeks details of:

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	(i) the radiological report confirming the absence of Grade II bilateral sacroiliitis or Grade III or IV unilateral sacroiliitis; and (ii) a baseline BASDAI score; and (iii) a baseline C-reactive protein (CRP) level; and (iv) a completed Exercise Program Self Certification Form included in the supporting information form; and (v) the MRI report; and (vi) the NSAIDs trialled, their doses and duration of treatment. If applicable, the reason a higher dose cannot be used where the NSAID dose is less than the maximum recommended dose in the relevant TGA-approved Product Information or details of the contraindication or intolerance according to the relevant TGA-approved Product Information must be included.
	Prescriber Instructions: The baseline BASDAI score and CRP level must also be documented in the patient's medical records.
	Administrative advice: Any queries concerning the arrangements to prescribe may be directed to Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday). Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Services Australia website at www.servicesaustralia.gov.au Applications for authority to prescribe should be submitted online using the form upload facility in Health Professional Online Services (HPOS) at www.servicesaustralia.gov.au/hpos Or mailed to: Services Australia Complex Drugs Reply Paid 9826 HOBART TAS 7001
Initial treatment 2 Restriction Summary [NEW] / ToC: [NEW] <i>(Based on Restriction Summary 10522 attached to certolizumab, 12027B, 12063X)</i>	
	Category / Program: General Schedule (Code GE)
	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners
	Restriction type: <input checked="" type="checkbox"/> Authority Required – immediate/real-time assessment by Services Australia (online/telephone)
	Administrative Advice: No increase in the maximum quantity or number of units may be authorised.
	Administrative advice: <i>(see restriction flow-on changes at the end of this section for details)</i>
	Indication: Non-radiographic axial spondyloarthritis
	Treatment Phase: Initial treatment 2 (Change or re-commencement of treatment after a break in biological medicine of less than 5 years)
	Clinical criteria:
	Patient must have received prior PBS-subsidised treatment with a biological medicine for this condition in this treatment cycle
	AND
	Clinical criteria:
	Patient must not have failed, or ceased to respond to, PBS-subsidised treatment with biological medicines more than three times for this PBS-indication during the current treatment cycle
	AND
	Clinical criteria: <i>Patient must not have failed PBS-subsidised therapy with this biological medicine for this PBS-indication more than once in the current treatment cycle</i>
	AND
	Clinical criteria:
	Patient must not receive more than 20 weeks of treatment under this restriction.
	AND
	Population criteria:
	Patient must be aged 18 years or older
	AND
	Treatment criteria:

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	Must be treated by a rheumatologist; or
	Must be treated by a clinical immunologist with expertise in the management of non-radiographic axial spondyloarthritis
	<p>Prescribing Instructions: An application for Initial 2 treatment must indicate whether the patient has demonstrated an adequate response (an absence of treatment failure), failed or experienced an intolerance to the most recent supply of biological medicine treatment.</p> <p>A new baseline Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score and C-reactive protein (CRP) level may be provided at the time of this application.</p>
	<p>Prescribing Instructions: An adequate response to therapy with this biological medicine is defined as a reduction from baseline in the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score by 2 or more units (on a scale of 0-10) and 1 of the following:</p> <p>(a) a CRP measurement no greater than 10 mg per L; or</p> <p>(b) a CRP measurement reduced by at least 20% from baseline.</p>
	<p>Prescribing Instructions: The assessment of the patient's response to the most recent supply of biological medicine must be conducted following a minimum of 12 weeks of treatment.</p>
	<p>Prescribing Instructions: BASDAI scores and CRP levels must be documented in the patient's medical records.</p>
	<p>Prescribing Instructions: The assessment of the patient's response to the initial course of treatment must be conducted following a minimum of 12 weeks of treatment and no later than 4 weeks from the cessation of that treatment course. If the response assessment is not conducted within these timeframes, the patient will be deemed to have failed this course of treatment in this treatment cycle.</p>
	<p>Prescribing Instructions: The following must be provided at the time of application and documented in the patient's medical records:</p> <p>(a) the BASDAI score; and</p> <p>(b) the C-reactive protein (CRP) level.</p>
	<p>Prescriber Instructions: The stated maximum quantity of 5 with zero repeats is intended for a patient undergoing the loading dose regimen of 150 mg administered at weeks 0, 1, 2, 3, and 4 (a total of 5 doses) followed by monthly administration thereafter.</p> <p>State in the application whether a loading dose regimen is intended or not.</p> <p>Where a loading dose regimen is intended, request a maximum quantity of 5 and zero repeats to cover doses at weeks 0, 1, 2, 3 and 4. Doses at week 8, 12, and 16 can be sought under the relevant 'Balance of supply' listing.</p> <p>Where no loading dose regimen is intended, request a maximum quantity of 1 and seek an increase in the number of repeats from zero to 4 repeats to cover dosing at weeks 4, 8, 12 and 16. Where increased repeats are sought, the maximum quantity sought must not be greater than 1.</p>
	<p>Administrative Advice: Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday).</p>
<p>Initial treatment 3 Restriction Summary [NEW] / ToC: [NEW] (based on Restriction Summary 10516 attached to attached to certolizumab, 12027B, 12063X)</p>	
	<p>Category/program: GENERAL – General Schedule (Code GE)</p>
	<p>Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners</p>
	<p>Restriction type: <input checked="" type="checkbox"/> Authority Required – immediate/real-time assessment by Services Australia (online/telephone)</p>
	<p>Administrative Advice: No increase in the maximum quantity or number of units may be authorised.</p>
	<p>Administrative advice: (see restriction flow-on changes at the end of this section for details)</p>
	<p>Indication: Non-radiographic axial spondyloarthritis</p>

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	Treatment Phase: Initial treatment 3 (Recommencement of treatment after a break in biological medicine of more than 5 years)
	Clinical criteria:
	Patient must have received prior PBS-subsidised treatment with a biological medicine for this condition
	AND
	Clinical criteria:
	Patient must have had chronic lower back pain and stiffness for 3 or more months that is relieved by exercise but not rest
	AND
	Clinical criteria:
	Patients must have a break in treatment of 5 years or more from the most recently approved PBS-subsidised biological medicine for this condition
	AND
	Clinical criteria:
	Patient must have one or more of the following: (a) enthesitis (heel); (b) uveitis; (c) dactylitis; (d) psoriasis; (e) inflammatory bowel disease; or (f) positive for Human Leukocyte Antigen B27 (HLA-B27)
	AND
	Clinical criteria:
	The condition must not be radiographically evidenced on plain x-ray of Grade II bilateral sacroiliitis or Grade III or IV unilateral sacroiliitis
	AND
	Clinical criteria:
	The condition must be non-radiographic axial spondyloarthritis, as defined by Assessment of Spondyloarthritis International Society (ASAS) criteria
	AND
	Clinical criteria:
	The condition must be sacroiliitis with active inflammation and/or oedema on non-contrast Magnetic Resonance Imaging (MRI)
	AND
	Clinical criteria:
	The condition must have presence of Bone Marrow Oedema (BMO) depicted as a hyperintense signal on a Short Tau Inversion Recovery (STIR) image (or equivalent)
	AND
	Clinical criteria:
	The condition must have BMO depicted as a hypointense signal on a T1 weighted image (without gadolinium)
	AND
	Clinical criteria:
	Patient must not receive more than 20 weeks of treatment under this restriction.
	AND
	Population criteria:
	Patient must be aged 18 years or older
	Treatment criteria:
	Must be treated by a rheumatologist; or
	Must be treated by a clinical immunologist with expertise in the management of non-radiographic axial spondyloarthritis
	Prescriber Instructions: The following must be provided at the time of application and documented in the patient's medical records: (a) a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score of at least 4 on a 0-10 scale; and (b) C-reactive protein (CRP) level greater than 10 mg per L.
	Prescriber Instructions: The BASDAI score and CRP level must be no more than 4 weeks old at the time of this application.
	Prescriber Instructions: If the requirement to demonstrate an elevated CRP level could not be met, the reason must be stated in the application. Treatment with prednisolone dosed at 7.5 mg or higher daily (or equivalent) or a parenteral steroid within the past month (intramuscular or intravenous methylprednisolone or equivalent) is an acceptable reason.

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	<p>Prescriber Instructions: The assessment of the patient's response to the initial course of treatment must be conducted following a minimum of 12 weeks of treatment and no later than 4 weeks from the cessation of that treatment course. If the response assessment is not conducted within these timeframes, the patient will be deemed to have failed this course of treatment in this treatment cycle.</p>
	<p>Prescriber Instructions: The stated maximum quantity of 5 with zero repeats is intended for a patient undergoing the loading dose regimen of 150 mg administered at weeks 0, 1, 2, 3, and 4 (a total of 5 doses) followed by monthly administration thereafter. State in the application whether a loading dose regimen is intended or not. Where a loading dose regimen is intended, request a maximum quantity of 5 and zero repeats to cover doses at weeks 0, 1, 2, 3 and 4. Doses at week 8, 12, and 16 can be sought under the relevant 'Balance of supply' listing. Where no loading dose regimen is intended, request a maximum quantity of 1 and seek an increase in the number of repeats from zero to 4 repeats to cover dosing at weeks 4, 8, 12 and 16. Where increased repeats are sought, the maximum quantity sought must not be greater than 1.</p>
	<p>Administrative advice: Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday).</p>

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Available brands
SECUKINUMAB secukinumab 150 mg/mL injection, 1 mL pen device	NEW	1	1	0	Cosentyx
Balance of supply - initial 1, 2 and 3 treatment Restriction Summary [NEW] / ToC: [NEW] (Based on Restriction Summary 10518 attached to attached to certolizumab, 12013G, 12040Q)					
	Category/program: GENERAL – General Schedule (Code GE)				
	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners				
	Restriction type: <input checked="" type="checkbox"/> Authority Required – immediate/real-time assessment by Services Australia (online/telephone)				
	Administrative advice: (see restriction flow-on changes at the end of this section for details)				
	Administrative Advice: No increase in the maximum quantity or number of units may be authorised.				
	Indication: Non-radiographic axial spondyloarthritis				
	Treatment Phase: Initial 1 (New patient), Initial 2 (Change or re-commencement of treatment after a break in biological medicine of less than 5 years) or Initial 3 (Recommencement of treatment after a break in biological medicine of more than 5 years) - balance of supply				
	Clinical criteria: Patient must have received insufficient therapy with this drug for this condition under the Initial 1 (new patients) restriction to complete 20 weeks treatment, OR				
	Patient must have received insufficient therapy with this drug for this condition under the Initial 2 (change or recommencement of treatment after a break in biological medicine of less than 5 years) restriction to complete 20 weeks treatment, OR				
	Patient must have received insufficient therapy with this drug for this condition under the Initial 3 (recommencement of treatment after a break in biological medicine of more than 5 years) restriction to complete 20 weeks treatment				
	AND				
	Clinical criteria: The treatment must provide no more than the balance of up to 20 weeks treatment				
	AND				
	Treatment criteria: Must be treated by a rheumatologist; OR				
	Must be treated by a clinical immunologist with expertise in the management of non-radiographic axial spondyloarthritis				
	Administrative advice:				

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Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday).

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
SECUKINUMAB					
secukinumab 150 mg/mL injection, 1 mL pen device	NEW	1	1	5	Cosentyx
Continuing treatment Restriction Summary 10430 / ToC: 10431 (currently attached to certolizumab, 12028C, 12005W)					
Category/program: GENERAL – General Schedule (Code GE)					
Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners					
Restriction type: <input checked="" type="checkbox"/> Authority Required – immediate/real-time assessment by Services Australia (online/telephone)					
Administrative advice: (see restriction flow-on changes at the end of this section for details)					
Administrative Advice: No increase in the maximum quantity or number of units may be authorised.					
Administrative Advice: No increase in the maximum number of repeats may be authorised.					
Administrative Advice: Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday).					
Indication: Non-radiographic axial spondyloarthritis					
Treatment Phase: Continuing treatment					
Clinical criteria:					
Patient must have received this drug as their most recent course of PBS-subsidised biologic medicine treatment for this condition					
AND					
Clinical criteria:					
Patient must have demonstrated an adequate response to treatment with this drug for this condition					
AND					
Clinical criteria:					
The treatment must not exceed a maximum of 24 weeks with this drug per authorised course under this restriction.					
Treatment criteria:					
Must be treated by a rheumatologist; or					
Must be treated by a clinical immunologist with expertise in the management of non-radiographic axial spondyloarthritis					
Prescriber instructions: An adequate response to therapy with this drug is defined as a reduction from baseline in the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score by 2 or more units (on a scale of 0-10) and 1 of the following: (a) a CRP measurement no greater than 10 mg per L; or (b) a CRP measurement reduced by at least 20% from baseline.					
Prescriber instructions: If the requirement to demonstrate an elevated CRP level could not be met under an initial treatment restriction, a reduction in the BASDAI score from baseline will suffice for the purposes of administering this continuing treatment restriction.					
Prescriber instructions: The patient remains eligible to receive continuing treatment with the same biological medicine in courses of up to 24 weeks providing they continue to sustain an adequate response. It is recommended that a patient be reviewed in the month prior to completing their current course of treatment.					

Grandfathering treatment Restriction Summary [NEW] / ToC: [NEW]
(based on Restriction Summary 10458 attached to certolizumab, 12013G, 12040Q)

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	Category/program: GENERAL – General Schedule (Code GE)
	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners
	Restriction type: <input checked="" type="checkbox"/> Authority Required – delayed/non-immediate assessment by Services Australia (postal lodgement or electronic upload)
	Administrative advice: (see restriction flow-on changes at the end of this section for details)
	Administrative Advice: No increase in the maximum quantity or number of units may be authorised.
	Administrative Advice: No increase in the maximum number of repeats may be authorised.
	Indication: Non-radiographic axial spondyloarthritis
	Treatment Phase: Grandfather treatment
	Clinical criteria: Patient must have previously received non-PBS subsidised therapy with this drug for this PBS indication prior to [1 Month 20XX; insert listing date here]
	AND
	Clinical criteria: Patient must have had chronic lower back pain and stiffness for 3 or more months that was relieved by exercise but not rest, prior to initiating non-PBS subsidised treatment with this drug for this condition
	AND
	Clinical criteria: Patient must have had failed to achieve an adequate response following treatment with at least 2 non-steroidal anti-inflammatory drugs (NSAIDs), whilst completing an appropriate exercise program, for a total period of 3 months, prior to initiating non-PBS-subsidised treatment with this drug for this condition
	AND
	Clinical criteria: Patient must have had one or more of the following: (a) enthesitis (heel); (b) uveitis; (c) dactylitis; (d) psoriasis; (e) inflammatory bowel disease; or (f) positive for Human Leukocyte Antigen B27 (HLA-B27); prior to initiating non-PBS subsidised treatment with this drug for this condition
	AND
	Clinical criteria: The condition must not be radiographically evidenced on plain x-ray of Grade II bilateral sacroiliitis or Grade III or IV unilateral sacroiliitis prior to commencing non-PBS subsidised treatment with this biological medicine
	AND
	Clinical criteria: The condition must have been diagnosed as non-radiographic axial spondyloarthritis, as defined by Assessment of Spondyloarthritis International Society (ASAS) criteria, prior to having commenced non-PBS subsidised treatment with this biological medicine
	Clinical criteria: The condition must have been sacroiliitis with active inflammation and/or oedema on non-contrast Magnetic Resonance Imaging (MRI) prior to commencing non-PBS subsidised treatment with this biological medicine
	AND
	Clinical criteria: The condition must have had presence of Bone Marrow Oedema (BMO) depicted as a hyperintense signal on a Short Tau Inversion Recovery (STIR) image (or equivalent) prior to commencing non-PBS subsidised treatment with this biological medicine
	AND
	Clinical criteria: The condition must have had BMO depicted as a hypointense signal on a T1 weighted image (without gadolinium) prior to commencing non-PBS subsidised treatment with this biological medicine
	AND
	Clinical criteria: The treatment must not exceed a maximum of 24 weeks with this drug under this restriction
	AND
	Population criteria: Patient must be aged 18 years or older
	Treatment criteria: Must be treated by a rheumatologist; or

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	Must be treated by a clinical immunologist with expertise in the management of non-radiographic axial spondyloarthritis
	<p>Prescriber Instructions: The application must include details of the NSAIDs trialled, their doses and duration of treatment. If the NSAID dose is less than the maximum recommended dose in the relevant TGA-approved Product Information, the application must include the reason a higher dose cannot be used. If treatment with NSAIDs is contraindicated according to the relevant TGA-approved Product Information, the application must provide details of the contraindication. If intolerance to NSAID treatment develops during the relevant period of use which is of a severity to necessitate permanent treatment withdrawal, the application must provide details of the nature and severity of this intolerance.</p>
	<p>Prescriber Instructions: The following criteria indicate failure to achieve an adequate response to NSAIDs and must have been demonstrated prior to initiation of non PBS subsidised treatment with this drug for this condition: (a) a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) of at least 4 on a 0-10 scale; and (b) C-reactive protein (CRP) level greater than 10 mg per L.</p>
	<p>Prescriber Instructions: The BASDAI must be determined at the completion of the 3-month NSAID and exercise trial, but prior to ceasing NSAID treatment. The BASDAI must be no more than 1 month old at the time of initiating non-PBS subsidised treatment with this drug for this condition.</p>
	<p>Prescriber Instructions: If the requirement to demonstrate an elevated CRP level could not be met, the reason must be stated in the application. Treatment with prednisolone dosed at 7.5 mg or higher daily (or equivalent) or a parenteral steroid within the past month (intramuscular or intravenous methylprednisolone or equivalent) is an acceptable reason.</p>
	<p>Prescriber Instructions: The assessment of the patient's response to the initial course of treatment must be made following a minimum of 12 weeks of treatment and submitted no later than 4 weeks from the cessation of that treatment course. If the response assessment is not submitted within these timeframes, the patient will be deemed to have failed this course of treatment.</p>
	<p>Prescriber Instructions: A Grandfathered patient may qualify for PBS-subsidised treatment under this restriction once only. For continuing PBS-subsidised treatment, a Grandfathered patient must qualify under the continuing treatment criteria.</p>
	<p>Prescriber Instructions: The authority application must be made in writing and must include: (a) a completed authority prescription form; and (b) a completed Non-radiographic axial spondyloarthritis Grandfathered PBS Authority Application - Supporting Information Form which seeks details of: (i) a copy of the radiological report confirming the absence of Grade II bilateral sacroiliitis or Grade III or IV unilateral sacroiliitis; and (ii) a BASDAI score and CRP level that substantiates failure to achieve an adequate response to NSAIDs prior to initiating non-PBS subsidised treatment with this biological medicine for this condition; and (iii) the MRI report; and (iv) the NSAIDs trialled, their doses and duration of treatment. If applicable, the reason a higher dose cannot be used where the NSAID dose is less than the maximum recommended dose in the relevant TGA-approved Product Information or details of the contraindication or intolerance according to the relevant TGA-approved Product Information must be included.</p>
	<p>Prescriber Instructions: The baseline BASDAI score and CRP level must also be documented in the patient's medical records.</p>
	<p>Administrative advice: Any queries concerning the arrangements to prescribe may be directed to Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday). Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Services Australia website at www.servicesaustralia.gov.au Applications for authority to prescribe should be submitted online using the form upload facility in Health Professional Online Services (HPOS) at www.servicesaustralia.gov.au/hpos Or mailed to: Services Australia Complex Drugs Reply Paid 9826 HOBART TAS 7001</p>

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MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
SECUKINUMAB					
secukinumab 150 mg/mL injection, 1 mL pen device	NEW	1	1	0	Cosentyx
Balance of supply – continuing treatment and grandfathered patients Restriction Summary 10501 / ToC: 10489 : currently attached to certolizumab, 12013G, 12040Q					
	Category/program: GENERAL – General Schedule (Code GE)				
	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners				
	Restriction type: <input checked="" type="checkbox"/> Authority Required – immediate/real-time assessment by Services Australia (online/telephone)				
	Administrative advice: (see restriction flow-on changes at the end of this section for details)				
	Administrative Advice: No increase in the maximum quantity or number of units may be authorised				
	Indication: Non-radiographic axial spondyloarthritis				
	Treatment Phase: Continuing treatment or Grandfather patient - balance of supply				
	Clinical criteria:				
	Patient must have received insufficient therapy with this drug for this condition under the Continuing treatment restriction to complete 24 weeks of treatment, OR				
	Patient must have received insufficient therapy with this drug for this condition under the Grandfathered patient restriction to complete 24 weeks of treatment				
	AND				
	Clinical criteria:				
	The treatment must provide no more than the balance of up to 24 weeks treatment available under the continuing treatment restriction or the grandfather restriction				
	Treatment criteria:				
	Must be treated by a rheumatologist; or				
	Must be treated by a clinical immunologist with expertise in the management of non-radiographic axial spondyloarthritis				
	Administrative Advice: Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday).				

Flow on changes to NOTE for secukinumab, golimumab and certolizumab pegol restrictions for non-radiographic ankylosing spondylitis:

8.2 Amend the explanatory NOTE (concept 25935) to include secukinumab in the list of biological medicines:

Concept lineage	
11538G	golimumab 50 mg/0.5 mL injection, 0.5 mL pen device
11521J	golimumab 50 mg/0.5 mL injection, 0.5 mL pen device
11560K	golimumab 50 mg/0.5 mL injection, 0.5 mL syringe
11516D	golimumab 50 mg/0.5 mL injection, 0.5 mL syringe
12027B	certolizumab pegol 200 mg/mL injection, 2 x 1 mL pen devices
12063X	certolizumab pegol 200 mg/mL injection, 2 x 1 mL syringes
12013G	certolizumab pegol 200 mg/mL injection, 2 x 1 mL pen devices
12040Q	certolizumab pegol 200 mg/mL injection, 2 x 1 mL syringes
12028C	certolizumab pegol 200 mg/mL injection, 2 x 1 mL pen devices
12005W	certolizumab pegol 200 mg/mL injection, 2 x 1 mL syringes
	Administrative Advice:

Concept lineage	TREATMENT OF ADULT PATIENTS WITH NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS
	<p>The following information applies to the prescribing under the Pharmaceutical Benefits Scheme (PBS) of <i>secukinumab</i>, certolizumab pegol and golimumab for adult patients with non-radiographic axial spondyloarthritis.</p> <p>Where the term 'biological medicine' appears in notes and restrictions, it refers to <i>secukinumab</i>, certolizumab pegol and golimumab only.</p> <p>A patient is eligible for PBS-subsidised treatment with only 1 of the 2-3 biological medicines at any one time.</p> <p>Under these arrangements, within a single treatment cycle, a patient may continue to receive long-term treatment with a biological medicine while they continue to show a response to therapy.</p> <p>A serious adverse reaction requiring permanent withdrawal of treatment, including serious infusion or injection related reactions, Steven's Johnson Syndrome, development of a demyelinating lesion, progressive multifocal leukoencephalopathy and malignancy related to treatment with the biological medicine, is not considered as a treatment failure.</p> <p>Within the same treatment cycle, a patient cannot trial and fail, or cease to respond to, the same PBS-subsidised biological medicine more than twice <i>once</i>.</p> <p>Once a patient has either failed or ceased to respond to treatment 3 times (twice once with the same <i>any</i> biological medicine, once with another biological medicine) within the same treatment cycle, they are deemed to have completed a treatment cycle and they must have, at a minimum, a 5-year break in PBS-subsidised biological medicine therapy before they are eligible to commence the next cycle. The 5-year break is measured from the date of the last prescription for PBS-subsidised biological medicine treatment in the most recent cycle to the date of the first application for initial treatment with a biological medicine under the new treatment cycle.</p> <p>A patient who has failed fewer than 3 trials of biological medicine therapy in a treatment cycle and who has a break in therapy of less than 5 years may commence a further course of treatment within the same treatment cycle.</p> <p>A patient who has failed 3 trials or fewer of biological medicine therapy in a treatment cycle and who has a break in therapy of more than 5 years may commence a new treatment cycle.</p> <p>There is no limit to the number of treatment cycles a patient may undertake in their lifetime.</p> <p>How to prescribe PBS-subsidised biological medicine treatment with <i>secukinumab</i>, certolizumab pegol and golimumab</p> <p>(1) Initial treatment.</p> <p>Applications for initial treatment should be made where:</p> <ul style="list-style-type: none"> (i) a patient has received no prior PBS-subsidised biological medicine treatment in this treatment cycle and wishes to commence such therapy (Initial 1 - New patient) (ii) a patient has received prior PBS-subsidised (initial or continuing) biological medicine therapy and wishes to trial an alternate agent (Initial 2 - Change or Recommencement of treatment after a break in therapy of less than 5 years) [further details are under 'Swapping therapy' below]; or (iii) a patient wishes to recommence treatment with a specific biological medicine following a break in PBS-subsidised therapy of less than 5 years with the same agent (Initial 2 - Change or Recommencement of treatment after a break in therapy of less than 5 years); or (iv) a patient wishes to recommence treatment with a biological medicine following a break in PBS-subsidised therapy of more than 5 years (Initial 3 - Recommencement of treatment after a break in biological medicine of more than 5 years). <p>With the exception of grandfathered patients, a patient must be assessed for response to a course of initial PBS-subsidised treatment following a minimum of 12 weeks of therapy.</p> <p>(2) Continuing treatment.</p> <p>For continuing courses of PBS-subsidised biological medicine it is recommended that a patient be reviewed the month prior to completing their current course of treatment to ensure uninterrupted biological medicine supply.</p>

Concept lineage	
	<p>Following the completion of an initial treatment course with a specific biological medicine, a patient may qualify to receive up to 24 weeks of continuing treatment with that biological medicine provided they have demonstrated an adequate response to treatment. The patient remains eligible to receive continuing biological medicine treatment in courses of up to 24 weeks provided they continue to sustain an adequate response.</p> <p>A patient must be assessed for response to a course of continuing therapy, and the assessment must be conducted no later than 4 weeks from the cessation of that treatment course. Where a response assessment is not conducted within the required timeframe, the patient will be deemed to have failed to respond to treatment with that biological medicine, unless the patient has experienced a serious adverse reaction requiring permanent treatment withdrawal.</p> <p>(3) Swapping therapy. Once initial treatment with the first PBS-subsidised biological medicine is approved, a patient may swap to an alternate biological medicine within the same treatment cycle without having to requalify with respect to the indices of disease severity (i.e. the C-reactive protein (CRP) level and the BASDAI score), or the prior NSAID therapy and exercise program requirements.</p> <p>To ensure a patient receives the maximum treatment opportunities allowed under these arrangements, it is important that they are assessed for response to every course of treatment.</p> <p>A patient who is not able to complete a minimum of 12 weeks of an initial treatment course will be deemed to have failed treatment with that biological medicine unless the patient has experienced a serious adverse reaction requiring permanent treatment withdrawal.</p> <p>(4) Baseline measurements to determine response. A response to treatment is based on the baseline BASDAI score and CRP level documented in the patient's medical records.</p> <p>For a new patient, the BASDAI score used to determine baseline disease severity must be measured while the patient is receiving NSAID therapy and completing their exercise program.</p> <p>To ensure consistency in determining response, the same indices of disease severity used to establish baseline must be used for all subsequent continuing treatment applications.</p> <p>Prescribers may provide new baseline measurements any time that an 'Initial treatment' authority application is submitted and the eligibility for continuing treatment must be assessed according to these revised baseline measurements.</p> <p>(5) Recommencement of treatment after a 5-year break in PBS-subsidised therapy. A patient who wishes to trial a second or subsequent course of treatment following a break in PBS-subsidised biological medicine therapy of at least 5 years, must qualify under the Initial 3 treatment restriction. The same clinical criteria and indices of disease severity (i.e. the C-reactive protein (CRP) levels and the BASDAI) as for the Initial 1 (New patient) restriction will need to be met, but a re-trial of NSAID therapy and exercise therapy is not required.</p>

8.3 Replace the relevant criterion (concept 25962) only when secukinumab proceeds to list for this indication of non-radiographic axial spondyloarthritis, to read as follows:

Concept lineage	
11538G	golimumab 50 mg/0.5 mL injection, 0.5 mL pen device
11560K	golimumab 50 mg/0.5 mL injection, 0.5 mL syringe
12027B	certolizumab pegol 200 mg/mL injection, 2 x 1 mL pen devices
12063X	certolizumab pegol 200 mg/mL injection, 2 x 1 mL syringes
	Clinical criteria:
	Patient must not have failed PBS-subsidised therapy with this biological medicine for this PBS-indication twice or more in the current treatment cycle.
	<i>Patient must not have failed PBS-subsidised therapy with this biological medicine for this PBS-indication more than once in the current treatment cycle.</i>

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

9 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.

10 Sponsor's Comment

The sponsor had no comment.