

**6.02 CERTOLIZUMAB PEGOL,
Injection 200 mg in 1 mL single use pre-filled syringe
Solution for injection 200 mg in 1 mL pre-filled pen,
Cimzia[®],
UCB Australia Pty Ltd.**

1 Purpose of Application

- 1.1 The Sponsor requested Authority Required listing of certolizumab pegol (CZP) for 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.
- 1.2 The key components of the clinical issue addressed by the submission are presented in Table 1. The requested listing was a cost-minimisation analysis to golimumab (GLM), which is a pharmacological analogue to CZP and the only biologic Disease Modifying Anti-rheumatic Drug (bDMARD) currently PBS listed for nr-axSpA.

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

Component	Description
Population	Adults 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) <u>and</u> 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	Certolizumab pegol subcutaneous injection. 400mg Week 0, 2, 4 then 200mg Q2W or 400mg Q4W.
Comparator	Golimumab subcutaneous injection. 50 mg on the same day each month (referred to as Q4W).
Outcomes	Clinical response: proportion of patients meeting ASAS20, ASAS40 and BASDAI50 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 to, or are intolerant to, NSAIDs, CZP is non-inferior in effectiveness and safety compared to GLM.

Abbreviations: ASAS=Assessment of SpondyloArthritis international Society; ASAS20/40=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, p18 of the submission

2 Requested listing

The abridged listing is provided below. Suggested additions are in italics and deletions are in strikethrough.

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Name, Restriction, manner of administration and form	Max. Qty (packs)	Max. Qty (units)	№.of Rpts	Dispensed Price for Max. Qty	Proprietary Name and Manufacturer	
CERTOLIZUMAB PEGOL						
<u>Initial 1 and initial 2</u>						
200mg/mL, 2x1mL pen device	3	6	0	\$ [REDACTED]	Cimzia® UCB Australia	
200mg/mL, 2x1mL syringe	3	6	0	\$ [REDACTED]		
200mg/mL, 2x1mL pen device	1	2	2	\$ [REDACTED]		
200mg/mL, 2x1mL syringe	1	2	2	\$ [REDACTED]		
<u>Continuing treatment</u>						
200mg/mL, 2x1mL pen device	1	2	5	\$ [REDACTED]		
200mg/mL, 2x1mL syringe	1	2	5	\$ [REDACTED]		

PBS Indication:	Active nr-axSpA
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
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
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 • The treatment must not exceed a maximum of 18-20 weeks with this drug under this restriction.
Population criteria	<ul style="list-style-type: none"> • <i>Patient must be aged 18 years or older</i>
Prescriber instructions:	<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.</p>

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	A patient who has failed treatment with this drug for this condition fewer than twice and who has a break in therapy of less than 5 years may re-commence a further course of treatment with this drug for this condition under the Initial 2 - Re-commencement of treatment after a break of less than 5 years.
Treatment phase:	Initial treatment 2 (Re-commencement of treatment after a break of less than 5 years)
Restriction:	<input checked="" type="checkbox"/> Authority Required - In Writing
Clinical criteria:	<ul style="list-style-type: none"> • Patient must have a documented history of non-radiographic axial spondyloarthritis, AND • Patient must have received prior PBS-subsidised treatment with this drug for this condition within the last five years, AND • Patient must not have failed PBS-subsidised treatment with this drug for this condition more than once within the last five years, AND • The treatment must not exceed a maximum of 18-20 weeks with this drug under this restriction.
Prescriber instruction:	<p>An application for Initial 2 treatment must be accompanied by BASDAI and CRP results of the most recent course of treatment with this drug for this condition within the last 5 years to demonstrate a response to treatment. The results must be conducted following a minimum of 12 weeks of treatment.</p> <p>When a patient has either failed or ceased to respond to treatment with this drug for this condition twice, they must have, at a minimum, a 5-year break in PBS-subsidised treatment with this drug for this condition before they are eligible to re-commence under the Initial 1 - New patient or recommencement after a break of more than 5 years.</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 PBS-subsidised treatment with this drug for this condition, AND • Patient must have demonstrated an adequate response to treatment with this drug for this condition, AND • The treatment must not exceed a maximum of 24 weeks with this drug per authorised course under this restriction.
Prescriber instruction:	<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 1-10) 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>

- 2.1 The Sponsor requested PBS listing of CZP 200mg as a prefilled syringe and pen device for initial and continuing treatment indications, with assessment of response after at least 12 weeks of initial treatment (in-line with the draft product information (PI)). The wording of the requested restriction was consistent with the current listing of GLM for nr-axSpA.
- 2.2 The recommended dose of CZP for adults with nr-axSpA in the draft PI is 400mg at Weeks 0, 2 and 4 (loading dose), followed by either 200mg every two weeks (Q2W) or 400mg every four weeks (Q4W) via subcutaneous (SC) injection. The requested maximum quantities and repeats provides for 18-20 weeks of initial treatment depending on the dose, and 24 weeks of continuing treatment (12 injections), consistent with the PBS indication for ankylosing spondylitis.

- 2.3 The requested approved ex-manufacturer price (AEMP) (\$██████████); and corresponding DPMQ of \$██████████) was based on the published price for GLM and a cost-minimisation analysis over six years of treatment. There is no special pricing arrangement for GLM, therefore the published price is the same as the effective price.
- 2.4 The Sponsor requested identical restriction criteria for CZP to GLM where patients are allowed to be treated with and fail to respond to GLM twice before undergoing a minimum 5 year break; therefore, patients may be eligible to initiate and fail bDMARD therapy four times (twice with GLM and twice with CZP) within a single treatment cycle. The submission did not present any evidence to support increasing the maximum number of treatment failures. The Pre-Sub-Committee Response (PSCR) stated that it was for patients' benefit to maintain the same restriction as GLM, given that treatment options for nr-axSpA are limited. The PBAC considered it appropriate to allow patients to be treated with and fail to respond to bDMARDs three times within a treatment cycle for consistency with listings for bDMARDs in other conditions.
- 2.5 The financial implications to the PBS associated with potentially increasing from two to four bDMARD therapies per treatment cycle were not addressed. The financial estimates presented in the submission assumed no market growth following PBS listing of CZP, and PBS listing of GLM is currently subject to a Risk Sharing Arrangement (RSA).

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

3 Background

Registration status

- 3.1 The submission was made under the TGA/PBAC Parallel Process and was not TGA registered at the time of PBAC consideration. The second round Clinical Evaluation Report, TGA Delegate's Overview and Advisory Committee on Medicines (ACM) meeting minutes were provided during the evaluation. The ACM supported the registration of CZP 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 magnetic resonance imaging (MRI) change, who have had an inadequate response to, or are intolerant to, nonsteroidal anti-inflammatory drugs (NSAIDs)". The requested PBS restriction is narrower than the TGA indication, which defines objective signs of inflammation as MRI+ and/or CRP+, and does not define the minimum disease severity (e.g. a minimum BASDAI).

Previous PBAC considerations

- 3.2 This was the first application of CZP to the PBAC for the treatment of nr-axSpA. CZP is currently PBS listed for rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis.

- 3.3 The PBAC recommended the PBS listing of GLM for nr-axSpA in July 2018 on the basis of acceptable cost-effectiveness compared to conventional care (represented by placebo plus background NSAID). The PBAC considered that the recommended restriction criteria identified patients with the highest clinical need and those who would benefit most; however, a RSA was required to limit use to the intended population given difficulties defining the population via the restriction.
- 3.4 The PBAC rejected etanercept twice for nr-axSpA (March 2015 and March 2016) on the basis of short-term trial evidence, poorly defined patient population and high and uncertain cost-effectiveness.

For more detail on the 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 with radiographic inflammation (i.e. ankylosing spondylitis) identifiable on x-ray and patients without radiographic inflammation (i.e. nr-axSpA). Ankylosing spondylitis and nr-axSpA 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.
- 4.2 Progression from nr-axSpA to ankylosing spondylitis occurs in approximately 10% of patients within 2 years of symptom onset, and approximately 50% of patients after 10 years. Presence of sacroiliitis on MRI and elevated serum CRP increase the likelihood of progression. If one or both factors are present, progression to ankylosing spondylitis is approximately 20% within the first 2 years.
- 4.3 CZP is a recombinant, humanised monoclonal antibody that binds to and inhibits human tumour necrosis factor alpha (TNF α), which is a pro-inflammatory cytokine in the pathogenesis of axSpA and other chronic inflammatory diseases. CZP can be used during pregnancy and breastfeeding. The PSCR and the pre-PBAC response further emphasised this point and stated that the clinical need for this patient population is high.
- 4.4 The PBAC noted that CZP is an alternative treatment to GLM at the same line of therapy in the clinical management algorithm, for patients with persistently high disease activity despite conventional treatments. First-line treatment includes NSAIDs up to the maximum dose and non-pharmacological treatment including tailored exercise programs.

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

5 Comparator

The submission nominated GLM as the main comparator, given it is currently the only bDMARD PBS listed for the treatment of nr-axSpA with objective signs of inflammation (MRI+ and CRP+). GLM also belongs to the same class as CZP (TNF α inhibitor) and has the same route of administration (SC injection).

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 submission did not identify any direct head-to-head randomised trials. The literature search identified two placebo-controlled trials of CZP (AS0006 and AS001), and one placebo-controlled trial of GLM (GO-AHEAD). Safety results from two ongoing CZP studies were also presented in the submission (AS0005, a Phase 3 randomised withdrawal trial comparing CZP to placebo; and AS0007, a Phase 4 open-label study of CZP). The trials and associated reports presented in the submission are shown in Table 2.

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Table 2: Trials and associated reports presented in the submission

Trial ID	Protocol title/ Publication title	Publication citation
Certolizumab vs placebo		
Study AS0006 C-axSpAnd NCT02552212 2015-001894-41 (EudraCT number)	Multicenter Study Evaluating Certolizumab Pegol Compared to Placebo in Subjects With axSpA Without X-ray Evidence of AS (C-AXSPAND). UCB Pharma (UCB BIOSCIENCES GmbH), (AS0006) Deodhar A, Gensler LS, Kay J, Maksymowych WP, Haroon N, Landewé R, Rudwaleit M, Hall S, Bauer L, Hoepken B, de Peyrecave N, Kilgallen B, van der Heijde D. A 52-Week Randomized Placebo-Controlled Trial of Certolizumab Pegol in Non-Radiographic Axial Spondyloarthritis.	24 September 2018 Rheumatol. 2019 July; 71(7):1101-1111
Study AS001 RAPID (NCT01087762)	Phase 3, Multicenter, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate Efficacy and Safety of Certolizumab Pegol in Subjects With Active Axial Spondyloarthritis (AS001) Landewé R, Braun J, Deodhar A, Dougados M, Maksymowych WP, Mease PJ, Reveille JD, Rudwaleit M, van der Heijde D, Stach C, Hoepken B, Fichtner A, Coteur G, de Longueville M, Sieper J. 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.	18 July 2016 Ann Rheum Dis. 2014 Jan; 73(1):39-47
Golimumab vs placebo		
Sieper et al., GO-AHEAD NCT01453725	Sieper J, van der Heijde D, Dougados M, Maksymowych WP, Scott BB, Boice JA, Berd Y, Bergman G, Curtis S, Tzontcheva A, Huyck S, Weng HH. A randomised, double-blind, placebo-controlled, sixteen week study of subcutaneous golimumab in patients with active nonradiographic axial spondyloarthritis. Sieper J., Van Der Heijde D., Maksymowych W.P., Braun J., Bergman G., Curtis S.P., Tzontcheva A., Philip G., Huyck S., Dougados M. Efficacy of golimumab for nonradiographic axial spondyloarthritis (nr-axSpA): Subgroup analysis by baseline MRI and C-reactive protein status. Dougados M., Bergman G., Maksymowych W.P., Curtis S., Huyck S., Tzontcheva A., Sieper J. Baseline demographic and disease characteristics associated with response to golimumab in patients with active nonradiographic axial spondyloarthritis. Van Der Heijde D., Dougados M., Maksymowych W., Bergman G., Curtis S.P., Tzontcheva A., Philip G., Huyck S., Sieper J. Long-term tolerability and efficacy of golimumab in active nonradiographic axial spondyloarthritis: Results from the open-label extension of a randomized, double-blind study. Van Der Heijde D., Dougados M., Maksymowych W.P., Braun J., Bergman G., Curtis S.P., Tzontcheva A., Philip G., Huyck S., Sieper J. Long-term efficacy and tolerability of golimumab in active nonradiographic axial spondyloarthritis: Results of the open-label extension of a randomized, double-blind study.	Arthritis & rheumatology 2015; 67:(10):2702-2712 Arthritis and Rheumatology 2016; 68(Suppl 10):943-945 Annals of the Rheumatic Diseases. Conference: EULAR 2015. 74(Suppl 2):275 Arthritis and Rheumatology Annual Scientific Meeting, ACR/ARHP 2015. 67(Suppl 10):1 Annals of the Rheumatic Diseases. Conference: EULAR 2016. 75(Suppl 2):808-809

Source: Table 2.4 and Table 2.5, pp56-59 of the submission.

6.4 Table 3 presents the key features of the included trials.

Table 3: Key features of the included evidence

Trial	N	Design/duration	Bias	Treatment arms	Population	Key efficacy outcomes
CZP vs PBO						
AS0006	317	R, MC, PC, DB 52wk / OL extension; rescue ≥Wk 0 ^a	Low	CZP 200mg Q2W PBO	nr-axSpA plus OSI [#]	1°: ASDAS-MI (Wk52) and ASAS40 (Wk12) 2°: Δ BASDAI (other: BASDAI50, ASAS20, ASDAS)
AS001	325 (147 [^])	R, MC, PC, DB 24wk / DSB and OL extension; bDMARD rescue in PBO arm wk16 ^b	Low	CZP 200mg Q2W CZP 400mg Q4W 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 ^c	Low	GLM 50mg PBO	nr-axSpA plus or minus OSI [#]	1°: ASAS20 (Wk16) 2°: ASAS40, BASDAI50, ASDAS

Abbreviations: AS=ankylosing spondylitis; ASAS20=Assessment of SpondyloArthritis international Society 20% response criteria; ASAS40=Assessment of SpondyloArthritis international Society 40% response criteria; ASDAS=Ankylosing Spondylitis Disease Activity Score; ASQOL= Ankylosing Spondylitis Quality of Life; 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; R=randomised; Q2W=every 2 weeks; Q4W=every 4 weeks.

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

[#] CRP>ULN defined as: in AS0006 ULN=9.99mg/L; in AS001 ULN=7.9mg/L; in GO-AHEAD ULN=9mg/L

^a 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 determined by the Investigator. Approximately 66% of patients randomised to placebo had discontinued treatment (61% switched to OL bDMARD) by Week 52 compared to 21% of patients randomised to CZP (13% switched to OL bDMARD). Patients who withdrew/discontinued or had missing data at the point of assessment) as non-responders in the full analysis set

^b ASAS20 non-responders in the placebo arm at Week 14 and Week 16 randomised to CZP 200mg Q2W or 400mg Q4W at Week 16. Approximately 61% of placebo patients discontinued by Week 24 (52% met the early escape criteria at Week 16) compared to 7% randomised to CZP treatment. Patients who withdrew/discontinued or had missing data at the point of assessment) as non-responders in the full analysis set.

^c 3% of patients discontinued randomised treatment

Source: constructed during the evaluation

- 6.5 All trials were multicentre (AS0006 included seven study sites in Australia), double-blind, randomised placebo-controlled trials of CZP or GLM at TGA approved doses. The duration of the double-blind phases ranged from 16 to 52 weeks, but all trials reported relevant outcomes at Weeks 12 or 16.
- 6.6 There were differences in study design in terms of population (axSpA or nr-axSpA), presence of objective signs of inflammation (with or without), definition of elevated CRP (CRP+ defined as serum level >8, 9 or 10 mg/L) and rescue / early escape during the double blind phase (not permitted, at any time or at Week 16). Discontinuations and withdrawals were much higher in the trials that permitted rescue / early escape (up to 61% versus 3%).
- 6.7 The submission presented indirect comparisons for trial patients with nr-axSpA meeting a broad definition of objective signs of inflammation in line the TGA indication (MRI+ and/or CRP+), and a narrow definition in line with the PBS indication (MRI+ and CRP+) in AS0006 and GO-AHEAD. The submission did not adequately justify the exclusion of AS001 from the indirect comparisons given the trial enrolled a relevant

subgroup with nr-axSpA and reported the relevant outcomes at Week 12 (unaffected by early placebo escape).

- 6.8 Differences in trial design mentioned above may potentially introduce bias into the indirect comparisons for the following reasons. The PBS subgroup (MRI+ and CRP+) was pre-specified in trial AS0006 but post-hoc in GO-AHEAD. Given limited data, it was unknown whether there was any imbalance in baseline characteristics for this subgroup, which may bias outcomes. Trial AS0006 permitted adjustment of background medications and early withdrawal (classified as non-responders) whereas GO-AHEAD did not permit any rescue / early escape during the double-blind period. These differences may potentially influence the magnitude of the treatment effects reported in each trial.
- 6.9 The definition of BASDAI50 response (a 50% improvement in the Bath ankylosing spondylitis disease activity index, BASDAI) may have also differed slightly across the trials. For example, trial AS0006 coded BASDAI as missing if more than 1 (of 5) major symptoms was missing and classified patients who discontinued or with missing data as BASDAI50 non-responders. In contrast, BASDAI was coded missing in GO-AHEAD if ≥ 2 (of 5) total symptoms was missing and used last-observation-carried-forward (LOCF) for missing data to classify patients as BASDAI50 responders (a sensitivity analysis classified patients who discontinued GLM due to adverse events (AEs) as BASDAI50 non-responders).

Comparative effectiveness

- 6.10 All of the trials measured treatment response according to the BASDAI and BASDAI50 as well as the Assessment of SpondyloArthritis international Society 20% / 40% response criteria (ASAS20, ASAS40) and the Ankylosing Spondylitis Disease Activity Score (ASDAS), as either primary, secondary or other outcomes (see Table 3). All trials enrolled patients with a BASDAI score of ≥ 4 at baseline, therefore BASDAI50 in the trials corresponded to a reduction from baseline in the BASDAI score of ≥ 2 if baseline was 4, ≥ 2.5 if baseline was 5, and so on.
- 6.11 Under the proposed PBS criteria, continued treatment is dependent on demonstrating and maintaining response to therapy, assessed after a minimum of 12 weeks following initial therapy (and every 24 weeks ongoing thereafter). Response is defined as a reduction from baseline in the BASDAI score by 2 or more units and one of the following: a CRP measurement no greater than 10mg/L or a CRP measurement reduced by at least 20% from baseline.
- 6.12 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”. “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” (paragraphs 6.14 and 6.24, Golimumab November 2017 Public Summary Document).

- 6.13 A recent update of the ASAS-EULAR guidelines (van der Heijde 2017) recommended that the ASDAS was favoured compared to the BASDAI for assessing disease activity and response/continuation of bDMARDs. The ASDAS is a relatively new index for measuring disease activity in axSpA, which combines patient-reported outcomes and levels of CRP into one index. The publication stated that ASDAS is a better index than BASDAI (for several reasons) and placed first in the treatment algorithm because it is the preferred measure.
- 6.14 Tables 4 and 5 present the indirect treatment comparisons between CZP (at Week 12) and GLM (at Week 16) for BASDAI50 and ASAS20 respectively, by baseline MRI+ and CRP+ status. The rationale for using Week 12 data for CZP and Week 16 for GLM was unclear; however, this difference was unlikely to favour CZP (e.g. the proportion with BASDAI50 at Week 16 was numerically larger compared to Week 12 in AS0006).

Table 4: BASDAI50 response in patients with nr-axSpA plus objective signs of inflammation, 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+)					
CZP 200mg Q2W v PBO (Wk 12)					
AS0006, 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)
AS001 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, 7)
Meta-analysis	80/205 (39.0)	31/208 (14.9)	2.98 (2.08, 4.27)	0.30 (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+)					
CZP 200mg Q2W v PBO (Wk 12)					
AS0006, 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+)					
CZP (meta) vs GLM			1.45 (0.86, 2.45)	0.0 (-0.17, 0.17)	
CZP (AS0006) vs GLM			1.43 (0.81, 2.54)	-0.02 (-0.20, 0.16)	
PBS population: nr-axSpA (MRI+ AND CRP+)					
CZP vs GLM			1.75 (0.66, 4.65)	0.00 (-0.31, 0.31)	

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; Q2W=every 2 weeks; Q4W every 4 weeks; wk=week;

‡ Patients (20 PBO and 19 GLM) who were MRI-/CRP- were excluded from the PSS analysis.

CRP>ULN defined as: in AS0006 ULN=9.99mg/L; in AS001 ULN=7.9mg/L; in GO-AHEAD ULN=9mg/L

Source: Table 2.57 and Table 2.58, pp123-124 of the submission; Report no. 1104 Indirect Treatment Comparison Attachment

Table 5: ASAS20 response in patients with nr-axSpA plus objective signs of inflammation, 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+)					
COMPARISON: CZP 200mg Q2W v PBO (Wk 12)					
AS0006, 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)
AS001 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)	1.87 (1.51, 2.33)	0.30 (0.21, 0.39)	3 (3, 5)
COMPARISON: 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+)					
COMPARISON: CZP 200mg Q2W v PBO (Wk 12)					
AS0006, 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)
COMPARISON: 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+)					
CZP (meta) vs GLM			0.91 (0.63, 1.33)	-0.09 (-0.26,0.08)	-
CZP (AS0006) vs GLM			0.99 (0.67, 1.48)	-0.06 (-0.24,0.11)	-
PBS population: nr-axSpA (MRI+ AND CRP+)					
CZP vs GLM			1.23 (0.61, 2.47)	0.08 (-0.20, 0.36)	

Abbreviations: ASAS20=Assessment of SpondyloArthritis international Society 20% 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; Q2W=every 2 weeks; Q4W=every 4 weeks; wk=week;

‡ Patients (20 PBO and 19 GLM) who were MRI-/CRP- were excluded from the PSS analysis.

CRP>ULN defined as: in AS0006 ULN=9.99mg/L; in AS001 ULN=7.9mg/L; in GO-AHEAD ULN=9mg/L

Source: Table 2.57 and Table 2.58, pp123-124 of the submission; Report no. 1104 Indirect Treatment Comparison Attachment

- 6.15 The results for BASDAI50 and ASAS20 demonstrated that CZP and GLM were more effective than placebo at producing a response at Week 12 or 16, across all of the populations. However, the submission noted that ASAS20 in trial AS001 was not significantly different for CZP 200mg Q2W and placebo (results were significant for CZP 400mg Q4W, not presented). BASDAI50 response rates were similar across the populations.
- 6.16 The indirect comparisons indicated that there were no statistically significant differences between CZP 200mg Q2W and GLM 50mg Q4W for BASDAI50 or ASAS20 response in any of the populations. Placebo response rates for ASAS20 were similar across the trials; however, placebo response for BASDAI50 was much higher in GO-AHEAD (29%) compared to the CZP trials (15-16%). The reason for this difference was unknown, but may be partially due to differences in trial design leading to high placebo discontinuation in the CZP trials and differences in the definition of BASDAI50 response assumed in the trials. The submission stated differences across the trials were unlikely to have any effect on the assumed transitivity of the common reference arms.

- 6.17 Similar results were demonstrated for ASAS40, with the indirect comparisons indicating no statistically significant differences between CZP and GLM in any of the populations.
- 6.18 The submission concluded that non-inferiority was demonstrated based on ASAS20 for all the populations, because the 95%CI of the relative risk (RR) estimates all crossed 1 and the lower bounds were larger than 0.43 (which is the non-inferiority margin accepted for ankylosing spondylitis). The submission did not nominate a non-inferiority margin for BASDAI50 or ASAS40, but considered the evidence supported non-inferiority because there were no significant differences and all of the point estimates of the RR across the populations favoured CZP.
- 6.19 The trial publications did not report any other comparable outcomes by MRI / CRP status to support formal indirect comparison. However, the results for other potentially relevant outcomes were generally similar in the ITT populations of AS0006 (Week 12) and GO-AHEAD (Week 16). For example, the mean difference in CRP was -8.1mg/L for CZP versus placebo in AS0006 compared to -6.4mg/L for GLM versus placebo in GO-AHEAD. The mean difference in ASDAS score was -1.09 for CZP versus placebo at Week 12 in AS0006 compared to -1.05 for GLM versus placebo at Week 16 in GO-AHEAD.

Comparative harms

- 6.20 Table 6 summarises the key AEs in the safety populations to the end of the double-blind phases of the included trials. The submission did not present any safety outcomes by MRI / CRP status, or conduct an indirect comparison between CZP and GLM for safety outcomes due to differences in timing and reporting methods.

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

Trial ID	AS0006, Week 52 (nr-axSpA)		AS001, Week 24 (axSpA)		GO-AHEAD, Week 16 (nr-axSpA)	
	CZP n (%) N=159	PBO n (%) N=158	CZP# n (%) N=111	PBO^ n (%) N=107	GLM n (%) N=97	PBO n (%) N=100
Summary of treatment emergent adverse events (TEAEs)						
Any TEAEs	120 (75.5)*	101 (63.9)*	85 (76.6)*	67 (62.6)*	40 (41.2)	47 (47.0)
Serious TEAEs	8 (5.0)	3 (1.9)	4 (3.6)	5 (4.7)	1 (1.0)	2 (2.0)
Drug-related TEAEs	48 (30.2)*	23 (14.6)*	41 (36.9)*	22 (20.6)*	13 (13.4)	17 (17.0)
Withdrawal of treatment due to TEAEs	3 (1.9)	3 (1.9)	2 (1.8)	2 (1.9)	2 (2.1)	1 (1.0)
Common TEAEs						
Gastrointestinal disorders	32 (20.1)*	17 (10.8)*	15 (13.5)	15 (14.0)	-	-
General disorders & administration site	16 (10.1)*	9 (5.7)*	17 (15.3)	8 (7.5)	-	-
Infections & infestations	85 (53.5)*	53 (33.5)*	43 (38.7)*	25 (23.4)*	0	0
Nervous system disorders	20 (12.6)*	10 (6.3)*	12 (10.8)	12 (11.2)	-	-
Reproductive & breast disorders	6 (3.8)	2 (1.3)	-	-	-	-
Skin & subcutaneous disorders	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

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;

CZP 200mg Q2W treatment arm

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

* Risk difference p<0.05

Source: Tables 2.36 to 2.37, pp103-105, Table 2.41, p112, Table 2.46, p115 of the submission

6.21 During the double-blind phases of AS0006 and AS001, patients treated with CZP experienced a higher incidence of treatment emergent adverse events (TEAEs) including drug-related TEAEs. However, the submission stated that differences in duration of treatment exposure between groups confound the results, due to permitted placebo-escape to open label CZP treatment.

6.22 After correcting for duration of exposure in AS0006, incidence rates of TEAEs in were generally similar between CZP 200mg Q2W and placebo (195.2/100 subject-years and 207.2/100 subject-years, respectively). Incidence rates remained higher for patients on CZP for infections (89.7 vs 76.1/100 subject-years), gastrointestinal disorders (24.9 vs 19.5/100 subject-years), skin and subcutaneous disorders (18.5 vs 10.1/100 subject-years) and injection site reactions (5.0 vs 2.1/100 subject-years). Overall, the safety outcomes reported in the trials were consistent with the known safety profile of CZP and anticipated effects of TNF α inhibitors.

Benefits/harms

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

Clinical claim

- 6.24 The submission described CZP 200mg Q2W as non-inferior in terms of effectiveness and safety compared with GLM 50mg Q4W in patients with nr-axSpA meeting the broad TGA (MRI+ and/or CRP+) and narrow PBS (MRI+ and CRP+) definitions for objection signs of inflammation. Overall, the clinical claim of non-inferior efficacy and safety was generally reasonable despite the lack of a non-inferiority margin for BASDAI50 (the most relevant clinical outcome) and lack of formal comparison across safety. The results demonstrated point estimates of RR and RD either favoured CZP or showed minimal difference (i.e. close to zero or one) across all of the outcomes and populations. The PBAC has previously considered TNF α inhibitors (including CZP and GLM) are non-inferior in terms of safety for other indications.
- 6.25 The submission did not present any evidence or make any explicit claim for CZP 400mg Q4W (the other approved dosing regimen for CZP) versus GLM 50mg Q4W; however, results from trial AS001 found no notable differences between CZP 200mg Q2W and CZP 400mg Q4W. The PBAC has also considered CZP 200mg Q2W and CZP400mg Q4W are equi-effective in other indications.
- 6.26 The PBAC considered the claim of non-inferior comparative effectiveness and safety was supported by the clinical evidence.

Economic analysis

- 6.27 The submission presented a cost-minimisation analysis between CZP and GLM, and proposed that “CZP 200mg every 2 weeks or 400mg every 4 weeks is equivalent to GLM 50mg every 4 weeks” for nr-axSpA, based on the average doses in the trial, recommended doses in the PI and current formulations of CZP on the PBS.
- 6.28 The sponsor excluded the loading dose for CZP in the proposed equi-effective dose calculation, which is inconsistent with the therapeutic relativity sheets for bDMARDs, including CZP in other indications. The PBAC considered the equi-effective doses were CZP 400mg at Week 0, 2, 4 followed by 200mg every 2 weeks or 400mg every 4 weeks and GLM 50mg once a month.
- 6.29 The submission calculated the requested AEMP (\$ [REDACTED]) using a two-step process. The submission calculated AEMPs for CZP assuming five different time horizons (2-years, 3-years, 4-years, 5-years, and 6-years) and then weighted the estimated five AEMPs using persistence data from a DUSC review of ankylosing spondylitis (February 2016). The PBAC considered that the approach was poorly justified, may lead to significant incremental financial costs for CZP and was inconsistent with the cost-minimisation approach generally utilised for bDMARDs.
- 6.30 The requested AEMP (\$ [REDACTED]) was higher than the price calculated over the first two years of treatment, estimated during the evaluation as \$ [REDACTED] (CZP 200mg

Q4W) or \$ [REDACTED] (assuming [REDACTED], CZP 200mg Q2W and 400mg Q4W). In the Pre-PBAC response, the sponsor accepted the AEMP of the [REDACTED] weighted price of \$ [REDACTED] calculated over the first [REDACTED] years of treatment.

Drug cost/patient/year: \$ [REDACTED]

- 6.31 Assuming a DPMQ of \$ [REDACTED] (AEMP of \$ [REDACTED]) and 15 scripts required for the first year of treatment inclusive of initial and continuing therapy, the cost per patient per year is \$ [REDACTED]. Fifteen scripts provides for 54 weeks of treatment on CZP 200mg Q2W or 56 weeks of treatment on CZP 400mg Q2W. The drug cost / patient / 52 weeks was \$ [REDACTED] for CZP 200mg Q2W (14.5 scripts) and \$ [REDACTED] (14 scripts).

Estimated PBS usage & financial implications

- 6.32 This submission was not considered by DUSC. The submission estimated the total number of patients with nr-axSpA (MRI+ and CRP+) each year based on epidemiological data and assumed all patients remained eligible for bDMARD treatment irrespective of previous treatment failure. The model used historical market data in ankylosing spondylitis to estimate the proportional use of initial and continuing therapy each year, and market-share assumptions to estimate the proportional use of CZP and GLM. The estimates are summarised in Table 7.

Table 7: Estimated use and financial implications to the PBS/RPBS of CZP

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Estimated number of eligible patients with nr-axSpA (MRI+ and CRP+)						
Eligible patients						
Incident						
Prevalent						
Estimated use of bDMARDs for nr-axSpA without CZP (current world with GLM only)						
GLM patients treated						
GLM scripts[^]						
GLM initial (0-16 weeks)						
GLM continuing (17-52 weeks)						
GLM continuing (52 weeks)						
GLM PBS/RPBS cost						
GLM net PBS/RPBS cost						
Estimated use of bDMARDs for nr-axSpA with CZP (proposed world with GLM and CZP)						
CZP patients treated	501	851	1,270	1,762	1,939	2,120
CZP (200mg) scripts						
CZP initial (0-16 weeks)						
CZP continuing (17-52 weeks)						
CZP continuing (52 weeks)						
CZP PBS/RPBS cost	\$	\$	\$	\$	\$	\$
CZP net PBS/RPBS cost	\$	\$	\$	\$	\$	\$
Estimated change in use of other medicines (proposed world with GLM and CZP)						
GLM patients treated						
GLM scripts						
GLM initial (0-16 weeks)						
GLM continuing (17-52 weeks)						
GLM continuing (52 weeks)						
GLM PBS/RPBS cost	-\$	-\$	-\$	-\$	-\$	-\$
GLM net PBS/RPBS cost	-\$	-\$	-\$	-\$	-\$	-\$
Estimated financial implication to government						
Net cost to PBS/RPBS	\$	-\$	-\$	-\$	-\$	-\$
Net cost to health budget	\$	-\$	-\$	-\$	-\$	-\$

Abbreviations: bDMARD=biologic disease-modifying anti-rheumatic drug; CRP=C-reactive protein; CZP=certolizumab pegol; GLM=golimumab; MRI=magnetic resonance imaging; nr-axSpA=non-radiographic axial spondyloarthritis;

[^] Corrected for the number of RPBS scripts for continuing therapy. The submission incorrectly calculated the number of continuing scripts (17-52 weeks) from the proportional distribution of initial therapy and the number of continuing scripts (52 weeks) as the sum of both initial and continuing scripts, which underestimated the RPBS cost.

Source: Tables 4.7, 4.11 to 4.19, pp154, 157-161 of the submission.

The redacted table shows that at Year 6, the estimated number of patients was less than 10,000 per year and the net cost to the PBS would be less than \$10 million for the first 6 year.

6.33 The ESC agreed with the evaluation that at the requested price, CZP is more costly than GLM for the first three years on treatment, and only becomes cost-saving for patients who remain on therapy for at least four years. The Sponsor stated in the pre-PBAC response that under the accepted pricing methodology calculated over the first 2 years of treatment, CZP would be cost saving after year 2 of listing.

- 6.34 The PBAC considered that the financial estimates presented in the submission were unreliable and uncertain because the methodology adopted was likely to overestimate the number of eligible and treated patients.

Financial Management – Risk Sharing Arrangements

- 6.35 The Sponsor expects to join the existing RSA with GLM upon listing, which addresses the uncertainty around the financial estimates presented 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 certolizumab (CZP) for the treatment of non-radiographic axial spondyloarthritis (nr-axSpA). The PBAC's recommendation for listing was based on, among other matters, its assessment, as described above, that the cost-effectiveness of CZP would be acceptable if it were cost-minimised to golimumab (GLM).
- 7.2 The PBAC considered the nominated comparator was appropriate and the equi-effective doses were CZP 400mg at Week 0, 2, 4 followed by 200mg every 2 weeks or 400mg every 4 weeks and GLM 50mg once a month. 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.
- 7.3 The PBAC considered the claim that CZP was non-inferior to GLM in terms of effectiveness and safety was adequately supported by the evidence provided in the submission. The PBAC noted the lack of a non-inferiority margin for BASDAI50 and the lack of formal comparison of safety but overall, considered the claim of non-inferiority was reasonable.
- 7.4 The PBAC noted the requested restriction criteria for CZP allowed for two failures within a treatment cycle, consistent with the current GLM restriction criteria, allowing for a total of four failures within a treatment cycle. The PBAC considered it appropriate that patients should be eligible to initiate and fail bDMARD therapy three times within a single treatment cycle for consistency with listings for bDMARDs in other conditions. The PBAC noted that there will be flow-on restriction changes to GLM regarding the number of treatment failures within a treatment cycle.

- 7.5 The PBAC noted the requested changes from the Australian Rheumatology Association that were recommended at its August 2017¹ meeting have been implemented for the biological medicines across multiple rheumatology indications and considered that it is appropriate to apply those changes to CZP and GLM for nr-axSpA, as follows. (1) Failure exclusions due to serious AEs (2) Request for removal of requirement to fail previous therapy (in this case NSAID and exercise) when recommencing after treatment break. The PBAC considered it was appropriate to include "If the requirement to demonstrate an elevated CRP cannot be met, the application must state the reason this criterion cannot be satisfied" consistent with the criteria for biologic medicines for other indications.
- 7.6 The PBAC considered the financial estimates provided in the submission were unreliable and considered that listing CZP for nr-axSpA on a cost minimisation basis as described in paragraph 7.2 should be cost-neutral to the PBS.
- 7.7 The PBAC recommended the written Authority Required listing of certolizumab for nr-axSpA and advised that it may be appropriate to explore other options for prescribing such as the Online PBS Authorities system, should that system provide suitable functionality.
- 7.8 The PBAC noted that its recommendation was on a cost-minimisation basis and advised that because CZP is not expected to provide a substantial and clinically relevant improvement in efficacy or reduction in toxicity over GLM and not expected to address a high and urgent unmet clinical need, the criteria prescribed by the National Health (Pharmaceuticals and Vaccines – Cost Recovery) Regulations 2009 for Pricing Pathway A were not met.
- 7.9 Under section 101(3BA) of the National Health Act 1953, the PBAC advised that CZP may be treated as interchangeable on an individual patient basis with GLM for nr-axSpA.
- 7.10 The PBAC advised that CZP is not suitable for prescribing by nurse practitioners.
- 7.11 The PBAC recommended that the Early Supply Rule should not apply to CZP.
- 7.12 The PBAC noted that this submission is not eligible for an Independent Review as it received a positive recommendation.

Outcome:

Recommended

8 Recommended listing

- 8.1 *Add new indication as follows:*

¹ <http://www.pbs.gov.au/industry/listing/elements/pbac-meetings/pbac-outcomes/2017-08/positive-recommendations-2017-08.pdf>

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Add new indication to certolizumab pegol as follows:

Name, Restriction, Manner of administration and form	Max. Qty (Units)	Max. Qty (Packs)	Ne. of Rpts	PBS item code	Proprietary Name and Manufacturer	
Certolizumab pegol 200 mg/mL injection, 2 x 1 mL pen devices	2	1	5	NEW	Cimzia	UCB Australia Pty Ltd
Certolizumab pegol 200 mg/mL injection, 2 x 1 mL syringes	2	1	5	NEW	Cimzia	UCB Australia Pty Ltd

Initial treatment 1 Restriction Summary [NEW] / Treatment of Concept (ToC): [NEW]

Concept ID	Category / Program: General Schedule (Code GE)
	Prescriber type: <input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
	Restriction Level / Method: <input checked="" type="checkbox"/> Authority Required – In Writing
NEW	Administrative advice: TREATMENT OF ADULT PATIENTS WITH NON-RADIOGRAPHIC ANKYLOSING SPONDYLITIS <i>See end of restrictions for full explanatory note</i>
22964	Indication: Non-radiographic axial spondyloarthritis
edit	Treatment Phase: Initial treatment 1 - New patients
23582	Clinical criteria:
23581	Patient must not have received PBS-subsidised treatment with a biological medicine for this condition.
	AND
22968	Clinical criteria:
22966	Patient must have had chronic lower back pain and stiffness for 3 or more months that is relieved by exercise but not rest
	AND
11155	Clinical criteria:
11154	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
22972	Clinical criteria:
22971	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
22974	Clinical criteria:
22973	The condition must not be radiographically evidenced on plain x-ray of Grade II bilateral sacroiliitis or Grade III or IV unilateral sacroiliitis
	AND
22976	Clinical criteria:
22975	The condition must be non-radiographic axial spondyloarthritis, as defined by Assessment of Spondyloarthritis International Society (ASAS) criteria
	AND
22978	Clinical criteria:
22977	The condition must be sacroiliitis with active inflammation and/or oedema on non-contrast Magnetic Resonance Imaging (MRI)
	AND
22980	Clinical criteria:
22979	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
22982	Clinical criteria:

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22981	The condition must have BMO depicted as a hypointense signal on a T1 weighted image (without gadolinium)
	AND
12971	Clinical criteria:
	Patient must not receive more than 18 to 20 weeks of treatment, depending on the dosage regimen, under this restriction
	AND
8384	Population criteria:
8383	Patient must be aged 18 years or older
	AND
22985	Treatment criteria:
10111	Must be treated by a rheumatologist; or
22986	Must be treated by a clinical immunologist with expertise in the management of non-radiographic axial spondyloarthritis
	Prescribing 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.
edit 23012	Prescribing 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 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 initial application. CRP measure must be provided with the initial treatment application and must be no more than 1 month old at the time of application. <i>If the requirement to demonstrate an elevated CRP can not be met, the reason must be stated in the application.</i>
11161	Prescribing 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.
23014	Prescribing 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 must include the following: (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 completed BASDAI Assessment Form; and (iii) a copy of C-reactive protein (CRP) test result which must not be more than 1 month old at the time of application ; and (iv) a completed Exercise Program Self Certification Form included in the supporting information form; and (v) a copy of the MRI report; and (vi) details of the NSAIDs trialled, their doses and duration of treatment or 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 according to the relevant TGA-approved Product Information
11164	Administrative Advice: Details of the toxicities, including severity, which will be accepted for the purposes of administering this restriction can be found on the Department of Human Services website at www.humanservices.gov.au
11165	Administrative Advice: For details on the appropriate minimum exercise program that will be accepted for the purposes of administering this restriction, please refer to the Department of Human Services website at www.humanservices.gov.au

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7606	Administrative Advice: No increase in the maximum quantity or number of units may be authorised.
7607	Administrative Advice: No increase in the maximum number of repeats may be authorised.
7753 CAR	<p>Administrative Advice: Any queries concerning the arrangements to prescribe may be directed to the Department of Human Services 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 Department of Human Services website at www.humanservices.gov.au Applications for authority to prescribe should be forwarded to: Department of Human Services Complex Drugs Reply Paid 9826 HOBART TAS 7001</p>

Initial treatment 2 Restriction Summary [NEW] / ToC: [NEW]

Concept ID	Category / Program: General Schedule (Code GE)
	Prescriber type: <input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
	Restriction Level / Method: <input checked="" type="checkbox"/> Authority Required – In writing
NEW	Administrative advice: TREATMENT OF ADULT PATIENTS WITH NON-RADIOGRAPHIC ANKYLOSING SPONDYLITIS <i>See end of restrictions for full explanatory note</i>
22964	Indication: Non-radiographic axial spondyloarthritis
	Treatment Phase: Initial treatment 2 (Change or re-commencement of treatment after a break of less than 5 years)
	AND
22219	Clinical criteria:
22218	Patient must have received prior PBS-subsidised treatment with a biological medicine for this condition in this treatment cycle
	AND
24295	Clinical criteria:
24296	Patient must not have already failed, or ceased to respond to, PBS-subsidised treatment with this drug for this condition during the current treatment cycle.
	AND
23033	Clinical criteria:
23032	Patient must not have failed PBS-subsidised treatment with this drug for this condition more than once within the last five years
	AND
22984	Clinical criteria:
	Patient must not receive more than 18 to 20 weeks of treatment, depending on the dosage regimen, under this restriction
	AND
8384	Population criteria:
8383	Patient must be aged 18 years or older
	AND
22985	Treatment criteria:
10111	Must be treated by a rheumatologist; or
22986	Must be treated by a clinical immunologist with expertise in the management of non-radiographic axial spondyloarthritis
23034 edited	Prescribing Instructions: An application for Initial 2 treatment must be accompanied by BASDAI and CRP results of the most recent course of treatment with this drug for this condition within the last 5 years to demonstrate a response to treatment. The results must be conducted following a minimum of 12 weeks of treatment.
23037	Prescribing Instructions: The authority application must be made in writing and must include: (a) a completed authority prescription form; and

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	(b) a completed Non-radiographic axial spondyloarthritis PBS Authority Application - Supporting Information Form including: <ol style="list-style-type: none"> 1. a completed BASDAI Assessment Form; and 2. a copy of C-reactive protein (CRP) test result
7606	Administrative Advice: No increase in the maximum quantity or number of units may be authorised.
7607	Administrative Advice: No increase in the maximum number of repeats may be authorised.
7753 CAR	<p>Administrative Advice:</p> <p>Any queries concerning the arrangements to prescribe may be directed to the Department of Human Services on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday).</p> <p>Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Department of Human Services website at www.humanservices.gov.au</p> <p>Applications for authority to prescribe should be forwarded to:</p> <p>Department of Human Services Complex Drugs Reply Paid 9826 HOBART TAS 7001</p>

Initial treatment 3 Restriction Summary [NEW] / ToC: [NEW]

Concept ID	Category / Program: General Schedule (Code GE)
	Prescriber type: <input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
	Restriction Level / Method: <input checked="" type="checkbox"/> Authority Required – In writing
NEW	Administrative advice: TREATMENT OF ADULT PATIENTS WITH NON-RADIOGRAPHIC ANKYLOSING SPONDYLITIS <i>See end of restrictions for full explanatory note</i>
22964	Indication: Non-radiographic axial spondyloarthritis
	Treatment Phase: Initial treatment - Initial 3 (recommencement of treatment after a break in biological medicine of more than 5 years)
23588	Clinical criteria:
23589	Patient must have received prior PBS-subsidised treatment with a biological medicine for this condition
	AND
22968	Clinical criteria:
22966	Patient must have had chronic lower back pain and stiffness for 3 or more months that is relieved by exercise but not rest
	AND
23945	Clinical criteria:
23944	Patient must have (<i>had</i>) a break in treatment of 5 years or more from the most recently approved PBS-subsidised biological medicine for this condition
	AND
22972	Clinical criteria:
22971	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
22974	Clinical criteria:
22973	The condition must not be radiographically evidenced on plain x-ray of Grade II bilateral sacroiliitis or Grade III or IV unilateral sacroiliitis
	AND
22976	Clinical criteria:
22975	The condition must be non-radiographic axial spondyloarthritis, as defined by Assessment of Spondyloarthritis International Society (ASAS) criteria
	AND
22978	Clinical criteria:
22977	The condition must be sacroiliitis with active inflammation and/or oedema on non-contrast Magnetic Resonance Imaging

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	(MRI)
	AND
22980	Clinical criteria:
22979	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
22982	Clinical criteria:
22981	The condition must have BMO depicted as a hypointense signal on a T1 weighted image (without gadolinium)
	AND
12971	Clinical criteria:
	Patient must not receive more than 18 to 20 weeks of treatment, depending on the dosage regimen, under this restriction
	AND
8384	Population criteria:
8383	Patient must be aged 18 years or older
	AND
22985	Treatment criteria:
10111	Must be treated by a rheumatologist; or
22986	Must be treated by a clinical immunologist with expertise in the management of non-radiographic axial spondyloarthritis
New Full	Prescribing 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 3 PBS Authority Application - Supporting Information Form
11161	Prescribing 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.
7606	Administrative Advice: No increase in the maximum quantity or number of units may be authorised.
7607	Administrative Advice: No increase in the maximum number of repeats may be authorised.
7753 CAR	Administrative Advice: Any queries concerning the arrangements to prescribe may be directed to the Department of Human Services 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 Department of Human Services website at www.humanservices.gov.au Applications for authority to prescribe should be forwarded to: Department of Human Services Complex Drugs Reply Paid 9826 HOBART TAS 7001

Balance of supply - initial 1, 2 and 3 treatment Restriction Summary [NEW] / ToC: [NEW]

Name, Restriction, Manner of administration and form	Max. Qty (Units)	Max. Qty (Packs)	No. of Rpts	PBS item code	Proprietary Name and Manufacturer	
Certolizumab pegol 200 mg/mL injection, 2 x 1 mL pen devices	2	1	0	NEW	Cimzia	UCB Australia Pty Ltd
Certolizumab pegol 200 mg/mL injection, 2 x 1 mL syringes	2	1	0	NEW	Cimzia	UCB Australia Pty Ltd

Concept ID	Category / Program: General Schedule (Code GE)
	Prescriber type: <input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
	Restriction Level / Method: <input checked="" type="checkbox"/> Authority Required – (Telephone/Emergency/Electronic)
NEW	Administrative Advice:

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	TREATMENT OF ADULT PATIENTS WITH NON-RADIOGRAPHIC ANKYLOSING SPONDYLITIS <i>Insert long common explanatory note here</i>
22964	Indication: Non-radiographic axial spondyloarthritis
	Treatment Phase: Initial treatment - Initial 1 (new patient), Initial 2 (change or recommencement 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
24321	Clinical criteria:
24318	Patient must have received insufficient therapy with this drug for this condition under the Initial 1 (new patient) restriction to complete 18 to 20 weeks treatment; or
24319	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 18 to 20 weeks treatment; or
24320	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 18 to 20 weeks treatment
	AND
11203	Clinical criteria:
11202	The treatment must provide no more than the balance of up to 18 to 20 weeks treatment available under the above restrictions
	AND
21932	Treatment criteria:
10111	Must be treated by a rheumatologist; or
21933	Must be treated by a clinical immunologist with expertise in the management of ankylosing spondylitis
23318 CAR	Administrative Advice: Authority approval for sufficient therapy to complete a maximum of 20 weeks of treatment may be requested by telephone by contacting the Department of Human Services on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday).

Grandfathering treatment Restriction Summary [NEW] / ToC: [NEW]

Name, Restriction, Manner of administration and form	Max.Qty (Units)	Max. Qty (Packs)	№.of Rpts	PBS item code	Proprietary Name and Manufacturer	
Certolizumab pegol 200 mg/mL injection, 2 x 1 mL pen devices	2	1	5	NEW	Cimzia	UCB Australia Pty Ltd
Certolizumab pegol 200 mg/mL injection, 2 x 1 mL syringes	2	1	5	NEW	Cimzia	UCB Australia Pty Ltd

Concept ID	Category / Program: General Schedule (Code GE)
	Prescriber type: <input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
	Restriction Level / Method: <input checked="" type="checkbox"/> Authority Required – In writing
NEW	Administrative advice: TREATMENT OF ADULT PATIENTS WITH NON-RADIOGRAPHIC ANKYLOSING SPONDYLITIS <i>See end of restrictions for full explanatory note</i>
22964	Indication: Non-radiographic axial spondyloarthritis
	Treatment Phase: Grandfathered patient
23039	Clinical criteria:
NEW	Patient must have previously received non-PBS subsidised therapy with this drug for this condition prior to [1 Month 20XX; insert listing date here]
	AND
22701	Clinical criteria:
22700	Patient must have demonstrated an adequate response to non-PBS subsidised treatment with this drug for this condition
	AND
23041	Clinical criteria:

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23040	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
23043	Clinical criteria:
23042	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
23045	Clinical criteria:
23044	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
22974	Clinical criteria:
22973	The condition must not be radiographically evidenced on plain x-ray of Grade II bilateral sacroiliitis or Grade III or IV unilateral sacroiliitis
	AND
22976	Clinical criteria:
22975	The condition must be non-radiographic axial spondyloarthritis, as defined by Assessment of Spondyloarthritis International Society (ASAS) criteria
	AND
23049	Clinical criteria:
23048	The condition must have been sacroiliitis with active inflammation and/or oedema on non-contrast Magnetic Resonance Imaging (MRI)
	AND
23047	Clinical criteria:
23046	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)
	AND
23051	Clinical criteria:
23050	The condition must have had BMO depicted as a hypointense signal on a T1 weighted image (without gadolinium)
	AND
23053	Clinical criteria:
23052	The treatment must not exceed a maximum of 24 weeks with this drug under this restriction
	AND
8384	Population criteria:
8383	Patient must be aged 18 years or older
	AND
22985	Treatment criteria:
10111	Must be treated by a rheumatologist; or
22986	Must be treated by a clinical immunologist with expertise in the management of non-radiographic axial spondyloarthritis
11158	<p>Prescribing Instructions: The application must include details of the NSAIDs trialled, their doses and duration of treatment.</p> <p>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.</p> <p>If treatment with NSAIDs is contraindicated according to the relevant TGA-approved Product Information, the application must provide details of the contraindication.</p> <p>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>
edit	Prescribing Instructions:

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23054	<p>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:</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 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>CRP measurement must be provided with the initial treatment application and must be no more than 1 month old at the time of initiating non-PBS subsidised treatment with this drug for this condition. <i>If the requirement to demonstrate an elevated CRP could not be met, the reason must be stated in the application.</i></p>
11161	<p>Prescribing Instructions:</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>
edit 23055	<p>Prescribing Instructions:</p> <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 40 -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>
23701	<p>Prescribing Instructions:</p> <p>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>
edit 23056 Full	<p>Prescribing Instructions:</p> <p>The authority application must be made in writing and must include:</p> <p>(a) a completed authority prescription form; and</p> <p>(b) a completed Non-radiographic axial spondyloarthritis Grandfathered PBS Authority Application - Supporting Information Form which must include the following:</p> <p>(i) a copy of the radiological report confirming the absence of Grade II bilateral sacroiliitis or Grade III or IV unilateral sacroiliitis; and</p> <p>(ii) evidence of failure to achieve an adequate response to NSAIDs prior to initiating non-PBS subsidised <i>treatment with this biological medicine</i> for this condition; and</p> <p>(iii) evidence of an adequate response to therapy with non-PBS subsidised <i>treatment with this biological medicine</i> for this condition following a minimum of 12 weeks of treatment with this drug for this condition <i>biological medicine</i>; and</p> <p>(iv) a copy of the MRI report; and</p> <p>(v) details of the NSAIDs trialled, their doses and duration of treatment or 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 according to the relevant TGA-approved Product Information.</p>
11164	<p>Administrative Advice:</p> <p>Details of the toxicities, including severity, which will be accepted for the purposes of administering this restriction can be found on the Department of Human Services website at www.humanservices.gov.au</p>
11165	<p>Administrative Advice:</p> <p>For details on the appropriate minimum exercise program that will be accepted for the purposes of administering this restriction, please refer to the Department of Human Services website at www.humanservices.gov.au</p>
7606	<p>Administrative Advice: No increase in the maximum quantity or number of units may be authorised.</p>
7607	<p>Administrative Advice: No increase in the maximum number of repeats may be authorised.</p>
7753 CAR	<p>Administrative Advice:</p> <p>Any queries concerning the arrangements to prescribe may be directed to the Department of Human Services on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday).</p> <p>Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Department of Human Services website at www.humanservices.gov.au</p> <p>Applications for authority to prescribe should be forwarded to:</p> <p>Department of Human Services Complex Drugs Reply Paid 9826 HOBART TAS 7001</p>

Continuing treatment Restriction Summary [NEW] / ToC: [NEW]

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Name, Restriction, Manner of administration and form	Max. Qty (Units)	Max. Qty (Packs)	№.of Rpts	PBS item code	Proprietary Name and Manufacturer	
Certolizumab pegol 200 mg/mL injection, 2 x 1 mL pen devices	2	1	5	NEW	Cimzia	UCB Australia Pty Ltd
Certolizumab pegol 200 mg/mL injection, 2 x 1 mL syringes	2	1	5	NEW	Cimzia	UCB Australia Pty Ltd

Concept ID	Category / Program: General Schedule (Code GE)
	Prescriber type: <input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
	Restriction Level / Method: <input checked="" type="checkbox"/> Authority Required – In writing
NEW	Administrative advice: TREATMENT OF ADULT PATIENTS WITH NON-RADIOGRAPHIC ANKYLOSING SPONDYLITIS <i>See end of restrictions for full explanatory note</i>
22964	Indication: Non-radiographic axial spondyloarthritis
	Treatment Phase: Continuing treatment
23622	Clinical criteria:
	Patient must have received this drug as their most recent course of PBS-subsidised biological medicine treatment for this condition
	AND
23061	Clinical criteria:
23059	Patient must have demonstrated an adequate response to treatment with this drug for this condition
	AND
23089	Clinical criteria:
23088	The treatment must not exceed a maximum of 24 weeks with this drug per authorised course under this restriction
	AND
8384	Population criteria:
8383	Patient must be aged 18 years or older
	AND
22985	Treatment criteria:
10111	Must be treated by a rheumatologist; or
22986	Must be treated by a clinical immunologist with expertise in the management of non-radiographic axial spondyloarthritis
edit 23055	Prescribing 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 40 -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.
23062	Prescribing Instructions: The patient remains eligible to receive continuing treatment with the same drug in courses of up to 24 weeks providing they continue to sustain the response. It is recommended that a patient be reviewed in the month prior to completing their current course of treatment.
edit 23063 Full	Prescribing 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 PBS Authority Application - Supporting Information including evidence of adequate response to therapy with <i>this</i> PBS-subsidised <i>biological medicine</i> .
7606	Administrative Advice: No increase in the maximum quantity or number of units may be authorised.
7607	Administrative Advice: No increase in the maximum number of repeats may be authorised.
7753 CAR	Administrative Advice: Any queries concerning the arrangements to prescribe may be directed to the Department of Human Services 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 Department of Human Services website at www.humanservices.gov.au

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Applications for authority to prescribe should be forwarded to: Department of Human Services Complex Drugs Reply Paid 9826 HOBART TAS 7001
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Balance of supply – continuing treatment and grandfathered patients Restriction Summary [new] / ToC: [new]: Authority Required

Name, Restriction, Manner of administration and form	Max. Qty (Units)	Max. Qty (Packs)	№.of Rpts	PBS item code	Proprietary Name and Manufacturer	
Certolizumab pegol 200 mg/mL injection, 2 x 1 mL pen devices	2	1	0	NEW	Cimzia	UCB Australia Pty Ltd
Certolizumab pegol 200 mg/mL injection, 2 x 1 mL syringes	2	1	0	NEW	Cimzia	UCB Australia Pty Ltd

Concept ID	Category / Program: General Schedule (Code GE)
	Prescriber type: <input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
	Restriction Level / Method: <input checked="" type="checkbox"/> Authority Required – (Telephone/Emergency/Electronic)
NEW	Administrative advice: TREATMENT OF ADULT PATIENTS WITH NON-RADIOGRAPHIC ANKYLOSING SPONDYLITIS <i>See end of restrictions for full explanatory note</i>
22964	Indication: Non-radiographic axial spondyloarthritis
	Treatment Phase: Continuing and Grandfathered treatment - balance of supply
new	Clinical criteria: Patient must have received insufficient therapy with this drug under the grandfathered patient restriction to complete 24 weeks of treatment; or Patient must have received insufficient therapy with this drug under the Continuing treatment restriction to complete 24 weeks of treatment
	AND
10472	Clinical criteria:
10471	The treatment must provide no more than the balance of up to 24 weeks treatment available under the above restriction
	AND
22985	Treatment criteria:
10111	Must be treated by a rheumatologist; or
22986	Must be treated by a clinical immunologist with expertise in the management of non-radiographic axial spondyloarthritis
19604 CAR	Administrative Advice: Authority approval for sufficient therapy to complete a maximum of 24 weeks of treatment may be requested by telephone by contacting the Department of Human Services on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday).

Concept ID	Administrative Advice: TREATMENT OF ADULT PATIENTS WITH NON-RADIOGRAPHIC ANKYLOSING SPONDYLITIS
NEW	The following information applies to the prescribing under the Pharmaceutical Benefits Scheme (PBS) of certolizumab pegol and golimumab for adult patients with non-radiographic axial spondyloarthritis. Where the term 'biological medicine' appears in notes and restrictions, it refers to certolizumab pegol and golimumab only. A patient is eligible for PBS-subsidised treatment with only 1 of the 2 biological medicines at any one time. 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.

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<p>Serious adverse reaction of a severity resulting in the necessity for 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 paediatric patient cannot trial and fail, or cease to respond to, the same PBS-subsidised biological medicine more than twice.</p> <p>Once a patient has either failed or ceased to respond to treatment 3 times, 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 certolizumab pegol and golimumab</p> <p>(a) Initial treatment.</p> <p>Applications for initial treatment should be made where:</p> <p>(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)</p> <p>(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</p> <p>(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</p> <p>(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> <p>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>(b) Continuing treatment.</p> <p>For the first continuing treatment course of PBS-subsidised biological medicine, it is recommended that a patient is reviewed for response following a minimum of 12 weeks of therapy under the Initial 1, Initial 2 or Initial 3 treatment restrictions. For second and subsequent 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> <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 drug providing they have demonstrated an adequate response to treatment. The patient remains eligible to receive continuing biological medicine treatment with the same drug in courses of up to 24 weeks providing they continue to sustain the response.</p> <p>A patient must be assessed for response to a course of continuing therapy, and the assessment must be conducted within 1 month of the last dose. 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 of a severity resulting in the necessity for permanent withdrawal of treatment.</p> <p>(2) Swapping therapy.</p> <p>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</p>

<p>severity (i.e. the C-reactive protein (CRP) levels and the BASDAI), 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. 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 of a severity resulting in the necessity for permanent withdrawal of treatment.</p> <p>(3) Baseline measurements to determine response. A response to treatment is based on the baseline measurements of the BASDAI and CRP documented in the patient's medical records at the time of the first authority application for a biological medicine.</p> <p>For a new patient, the BASDAI used to determine the baseline 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. Therefore CRP level must be used to determine response.</p> <p>(4) 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>

8.2 Flow-on changes to GLM are to be confirmed for item numbers 11516D, 11521J, 11538G, 11560K.

This restriction 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.