

An addendum to this Public Summary Document has been included at the end of the document.

6.08 UPADACITINIB, Tablet 15 mg, Rinvoq[®], Abbvie Pty Ltd.

1 Purpose of submission

1.1 The Category 2 submission requested a General Schedule Authority Required (Written) listing for the treatment of non-radiographic axial spondyloarthritis (nr-axSpA).

1.2 Listing was requested on the basis of a cost-minimisation approach versus golimumab.

Table 1: Key components of the clinical issue addressed by the submission (as stated in the submission)

Component	Description
Population	Adults with active nr-axSpA
Intervention	Upadacitinib 15 mg tablet oral administered once daily
Comparator	Main comparator: <ul style="list-style-type: none"> Golimumab 50 mg subcutaneous injection administered monthly Secondary comparators: <ul style="list-style-type: none"> Certolizumab pegol subcutaneous injection. 400 mg Week 0, 2, 4 then 200 mg every two weeks or 400 mg every four weeks Secukinumab injection (LD). 150 mg Week 0, 1, 2, 3, 4 then 150 mg every month Secukinumab injection (NL). 150 mg every month Potential near market comparator: Ixekizumab 80 mg subcutaneous injection administered every four weeks
Outcomes	Efficacy: Proportion of patients meeting ASAS20, ASAS40 and BASDAI50 response criteria Safety: Frequency of AEs, serious AEs, AEs with reasonable possibility of being related to study treatment, AEs leading to withdrawal of study treatment
Clinical claim	In adult patients with active non-radiographic axial spondylarthritis: <ul style="list-style-type: none"> Upadacitinib is non-inferior in terms of effectiveness compared with golimumab, certolizumab pegol, secukinumab and ixekizumab Upadacitinib is non-inferior in terms of safety compared with golimumab, certolizumab pegol, secukinumab and ixekizumab

Source: Table 1.1, p27 of the submission, Section 2 of the submission and certolizumab pegol PSD November 2019, secukinumab PSD November 2020, ixekizumab PSD November 2021.

AE = adverse events, ASAS20 = Assessment of Spondyloarthritis International Society 20, ASAS40 = Assessment of Spondyloarthritis International Society 40, BASDAI50 = bath ankylosing spondylitis disease activity index 50, LD = loading dose, NL = no loading dose, nr-axSpA = non-radiographic axial spondyloarthritis, PSD = public summary document.

2 Background

Registration status

2.1 The submission was made under the TGA/PBAC Parallel Process. At time of PBAC consideration, the Round 2 Clinical Evaluation Report (CER) was available.

3 Requested listing

3.1 The requested restriction is consistent with the current PBS listing of golimumab (initial and continuing treatment) for the treatment of nr-axSpA. For brevity reasons, an abridged restriction is presented below.

MEDICINAL PRODUCT medicinal product pack	Dispensed Price for Max. Qty	Max. qty packs	Max. qty units	No. of Rpts	Available brands
UPADACITINIB (initial treatment)					
Upadacitinib 15 mg tablet, 28	\$1,271.40 published price	1	28	3	RINVOQ ^{®/™} , AbbVie Pty Ltd
UPADACITINIB (continuing treatment)					
Upadacitinib 15 mg tablet, 28	\$1,271.40 published price	1	28	5	RINVOQ ^{®/™} , AbbVie Pty Ltd

Category / Program: General Schedule
Prescriber type: <input type="checkbox"/> <input checked="" type="checkbox"/> Medical Practitioners
Restriction type: <input checked="" type="checkbox"/> Authority Required (online PBS Authorities system) (Continuing treatment) <input checked="" type="checkbox"/> Authority Required (in writing only via post/HPOS upload) (Initial treatment)
Indication: Non-radiographic axial spondyloarthritis
Treatment Phase: Initial treatment 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
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:
The treatment must not exceed a maximum of 16 weeks with this drug under this restriction.
Treatment criteria:
Must be treated by rheumatologist; OR
Must be treated by a clinical immunologist with expertise in the management of non-radiographic axial spondyloarthritis.
AND
Population criteria:
Patient must be aged 18 years or older.
Treatment Phase: Initial treatment - Initial 2 (Change or re-commencement of treatment after a break in biological medicine of less than 5 years)
Treatment criteria:
Must be treated by rheumatologist; OR
Must be treated by a clinical immunologist with expertise in the management of non-radiographic axial spondyloarthritis.
AND
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:
Patient must not have failed PBS-subsidised therapy with this biological medicine for this PBS indication more than once in the current treatment cycle
AND
Clinical criteria:
The treatment must not exceed a maximum of 16 weeks with this drug under this restriction.
AND
Population criteria:
Patient must be aged 18 years or older
Treatment Phase: Initial treatment - Initial 3 (Recommencement of treatment after a break in biological medicine of more than 5 years)
Treatment criteria:
Must be treated by rheumatologist; OR
Must be treated by a clinical immunologist with expertise in the management of non-radiographic axial spondyloarthritis.
AND
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:
Patient must have had 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:
The treatment must not exceed a maximum of 16 weeks with this drug under this restriction.
AND
Population criteria:
Patient must be aged 18 years or older
Treatment Phase: Continuing treatment
Clinical criteria:
Patient must have received this drug as their most recent course of PBS-subsidised biological 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 rheumatologist; OR
Must be treated by a clinical immunologist with expertise in the management of non-radiographic axial spondyloarthritis.
Population criteria:
Patient must be aged 18 years or older

- 3.2 Upadacitinib will be the fourth agent for this indication. The Secretariat advised flow-on changes to other PBS-listed therapies to include upadacitinib in the list of eligible treatments for nr-axSpA will be required if recommended for listing. Currently, patients may trial each of the 3 existing agents before a 5-year break in PBS-subsidy is mandated. The PBAC considered it may be reasonable to review the design of treatment cycle requirements for bDMARDs/tsDMARDs broadly given the range of available treatments with different mechanisms of action since these requirements were originally devised.

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

4 Population and disease

- 4.1 Axial spondyloarthritis (axSpA) is a chronic disease spectrum involving inflammation of the axial skeleton that leads to progressive and irreversible damage causing significant spinal pain, a loss of spinal mobility and function. AxSpA presents as two clinical subtypes: with or without radiographic (e.g. evident on plain x-ray) evidence of inflammation based on the modified New York criteria. Patients with axSpA may have sacroiliitis visible on radiographic imaging (ankylosing spondylitis [AS]) or no radiographic evidence of sacroiliitis (nr-axSpA). Patients with nr-axSpA may show other signs of inflammation, such as elevated levels of CRP or evidence of inflammation detected by magnetic resonance imaging (MRI). Even though nr-axSpA patients, by nature, have less structural damage than AS patients, both nr-axSpA and AS are associated with similar substantial disease burden in terms of health-related quality of life (QoL), disease activity and functional impairment.
- 4.2 Upadacitinib is proposed as an additional treatment choice in the same line of therapy as other PBS listed biologic/targeted synthetic disease modifying anti-rheumatic drugs (bDMARDs/tsDMARDs) for adult patients with nr-axSpA.
- 4.3 Upadacitinib is an orally administered, small molecule, selective and reversible inhibitor of JAK1. In contrast to current PBS listed bDMARDs/tsDMARDs which are based around the antibody neutralisation of select inflammatory cytokines (i.e. TNF α and IL-17), JAK1 is a key choke point for signalling from a broad range of inflammatory cytokine receptors, blocking the effects of various interleukins and interferons, including those pathologically elevated in nr-axSpA.

5 Comparator

- 5.1 The submission nominated golimumab (TNF α inhibitor) as the main comparator since it is the market leader among PBS listed bDMARDs/tsDMARDs for nr-axSpA. The submission nominated certolizumab pegol (TNF α inhibitor) and secukinumab (IL-17 inhibitor) as secondary comparators and ixekizumab (IL-17 inhibitor) as a near market comparator. The nominated comparators used in the submission are appropriate.

- 5.2 In the context of the cost-minimisation approach taken by the submission, a further consideration for PBAC is that, under Section 101(3B) of the *National Health Act 1953*, when the proposed medicine is substantially more costly than an alternative therapy, the committee cannot make a positive recommendation unless it is satisfied that, for some patients, the proposed medicine provides a significant improvement in efficacy and/or reduction of toxicity over the alternative therapy. If the committee is so satisfied, it must make a statement to this effect.
- 5.3 For the requested population, the following PBS listed medicines may be considered alternative therapies because they could be replaced in practice: golimumab, certolizumab pegol and secukinumab.

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 was based on two randomised, placebo-controlled trials of upadacitinib versus placebo (SELECT-AXIS 2) and golimumab versus placebo (GO-AHEAD). The PBAC previously considered the evidence from the GO-AHEAD trial in submissions of bDMARDs/tsDMARDs for nr-axSpA, with the most recent consideration at the November 2021 PBAC meeting for the requested listing of ixekizumab in the same target population.
- 6.4 The evidence for the efficacy and safety of upadacitinib compared with golimumab is informed by an indirect treatment comparison via the common placebo arm from the SELECT-AXIS 2 and GO-AHEAD trials.
- 6.5 The submission performed additional indirect treatment comparison analyses to assess the efficacy and safety of upadacitinib compared with certolizumab pegol and secukinumab (secondary comparators) and ixekizumab (near market comparator).
- 6.6 The submission conducted an indirect treatment comparison of upadacitinib versus golimumab in a subgroup of patients from the SELECT-AXIS 2 trial referred to as the PBS sub-population. The purpose of the subgroup analysis was to align the trial population with the proposed listing. The PBS sub-population was defined as patients with a positive MRI for sacroiliac joint inflammation and an elevated CRP level > ULN of 9 mg/L at baseline. Efficacy and safety outcomes for the PBS sub-population was a post-hoc analysis from the SELECT-AXIS trial data. The indirect treatment comparison

of upadacitinib versus the secondary comparators and the near market comparator was also conducted for the PBS sub-population. To account for discrepancies between trials that were used to inform the analysis, a second PBS sub-population was also considered in the submission, which was defined as patients with a positive MRI for sacroiliac joint inflammation and an elevated CRP level > ULN of 5 mg/L at baseline (as opposed to 9 mg/L). The first PBS sub-population (positive MRI and CRP > 9 mg/L) was largely consistent in terms of eligibility with the proposed listing (positive MRI and CRP > 10 mg/L) whereas the second PBS sub-population (positive MRI and CRP > 5 mg/L) was slightly different.

6.7 Details of the trials presented in the submission are provided in Table 2.

Table 2: Trials and associated reports presented in the submission

Trial ID	Protocol title/ Publication title	Publication citation
SELECT-AXIS 2 NCT04169373	A Phase 3 Randomized, Placebo-Controlled, Double-Blind Program to Evaluate Efficacy and Safety of Upadacitinib in Adult Subjects with Axial Spondyloarthritis Followed by a Remission-Withdrawal Period (CSR M19-944 Week 14 Study 2 nr-axSpA).	December 2021
	A Phase 3 Randomized, Placebo-Controlled, Double-Blind Program to Evaluate Efficacy and Safety of Upadacitinib in Adult Subjects with Axial Spondyloarthritis Followed by a Remission-Withdrawal Period (Protocol for Study M19-944).	July 2021
GO-AHEAD NCT01453725	Sieper J, van der Heijde D, Dougados M et al. A randomized, double-blind, placebo-controlled, sixteen-week study of subcutaneous golimumab in patients with active nonradiographic axial spondyloarthritis.	Arthritis and Rheumatology 2015; 67(10): 1873-1883.
	van der Heijde D, Dougados M, Maksymowych W.P., et al. Long-term tolerability and efficacy of golimumab in active non-radiographic axial spondyloarthritis: results from open-label extension.	Rheumatology 2022; 61(2): 617-627.
	Maksymowych W, Tzontcheva A, Philip G, et al. Spondyloarthritis research consortium of Canada (SPARCC) baseline MRI SI joint score ≥ 2 better predicts response to golimumab than does assessment of spondyloarthritis international society (ASAS) MRI positivity in nonradiographic axial spondyloarthritis.	Arthritis and Rheumatology 2016; 68(S10): 905-907.
	Sieper J, Van Der Heijde D, Maksymowych W, 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: 813-814.
	Van Der Heijde D, Dougados M, Maksymowych W.P., et al. Long-term efficacy and tolerability of golimumab in active nonradiographic axial spondyloarthritis: results of the open-label extension of a randomized, double-blind study.	Annals of the Rheumatic Diseases 2016; 75: 808-809.

Source: Table 2.3, p49 of the submission.

nr-axSpA = non-radiographic axial spondyloarthritis; SPARCC= Spondyloarthritis research consortium of Canada; MRI= magnetic resonance imaging; SI= sacroiliac; ASAS= assessment of spondyloarthritis international society

6.8 The key features of the included randomised trials are summarised in Table 3.

Table 3: Key features of the included evidence- indirect comparison

Trial	N	Design/ duration	Risk of bias	Patient population	Outcome(s)
UPA vs PBO					
SELECT-AXIS 2	313	R, MC, PC, DB 52wk / OL extension	Low	nr-axSpA, ≥ 18 years of age, objective signs of inflammation ^a , inadequate response to ≥ 2 NSAIDs, prior treatment with at most 1 bDMARD ^b	Primary: ASAS40 at Wk 14 Secondary: ASAS20 and BASDAI50 at Wk 14
GLM vs PBO					
GO-AHEAD	197	R, MC, PC, DB 16wk / OL extension	Low	nr-axSpA, ≥ 18 to ≤ 45 years of age, objective signs of inflammation ^c , inadequate response to ≥ 1 NSAIDs, no prior treatment with bDMARD	Primary: ASAS20 at Wk 16 Secondary: ASAS40 and BASDAI50 at Wk 16

Source: Table 2.7, pp62-63 of submission, Attachment 2.4, Attachment 2.5 and Attachment 2.6.

ASAS20 = Assessment of Spondyloarthritis International Society 20; ASAS40 = Assessment of Spondyloarthritis International Society 40; BASDAI50 = bath ankylosing spondylitis disease activity index 50; bDMARD = biological disease-modifying antirheumatic drug; DB = double blind; GLM = golimumab; MC = multi-centre; nr-axSpA = non-radiographic axial spondyloarthritis; NSAID = non-steroidal anti-inflammatory drugs; OL = open label; PBO = placebo; PC = placebo controlled; R = randomised; UPA = upadacitinib.

^a Based on MRI of sacroiliac joints or based on hsCRP > 2.87 mg/L.

^b At least 20% with prior treatment with at most 1 bDMARD, but not exceeding 35% of total enrolled patients.

^c Based on ASAS classification criterion for the presence of sacroiliitis by MRI and have 1 SpA feature or be HLA-B27 positive and have ≥ 2 SpA features (where SpA features include CRP > 9 mg/L).

6.9 The key efficacy outcome measures of Assessment in Spondyloarthritis International Society 20 (ASAS20), Assessment in Spondyloarthritis International Society 40 (ASAS40) and Bath Ankylosing Spondylitis Disease Activity Index 50 (BASDAI50) have been validated in the nr-axSpA population and have previously been considered clinically relevant by the PBAC (paragraph 6.14, golimumab public summary document (PSD), November 2017 PBAC meeting; paragraph 6.12, certolizumab pegol, PSD, November 2019 PBAC meeting; paragraph 6.10, secukinumab, PSD, November 2020 PBAC meeting; paragraph 6.14, ixekizumab, PSD, November 2021 PBAC meeting). These outcomes were reported in the SELECT-AXIS 2 and GO-AHEAD trials as either primary or secondary endpoints.

6.10 The key difference between the two trials were:

- The SELECT-AXIS 2 included patients aged ≥ 18 years whereas the GO-AHEAD trial recruited patients aged ≥ 18 to ≤ 45 years of age.
- The SELECT-AXIS 2 trial included patients previously exposed to bDMARDs/tsDMARDs (IL-17 or TNFα± inhibitors) with inadequate responders to bDMARDs/tsDMARDs representing 31.4% of patients from the upadacitinib treatment arm and 34.4% of patients from the placebo treatment arm. This is different to the GO-AHEAD trial which excluded patients with any prior bDMARD exposure.
- The SELECT-AXIS 2 trial included patients that had failed ≥ 2 NSAIDs whereas the GO-AHEAD trial included patients that had failed ≥ 1 NSAIDs.

- The SELECT-AXIS 2 defined ULN as high-sensitivity C-reactive protein (hsCRP) > 2.87 mg/L for the laboratory assessment of CRP levels whereas the GO-AHEAD trial defined ULN as CRP > 9 mg/L.
- 6.11 Several other Australian population characteristics were not addressed by either trial; i.e., prior exercise (a requirement in the PBS restriction) and bone marrow oedema. While the SELECT-AXIS 2 and GO-AHEAD trials allowed patients to present with either a positive MRI for sacroiliac joint inflammation (positive MRI) or elevated CRP level > ULN, the PBS initiation criteria for bDMARD required both. This was addressed by the subgroup analysis from the submission which considered a PBS sub-population defined as patients with a positive MRI and elevated CRP, consistent with the previous considerations from the PBAC for bDMARDs/tsDMARDs in nr-axSpA (paragraph 6.8, certolizumab pegol, PSD, November 2019 PBAC meeting; paragraph 6.8, secukinumab, PSD, November 2020 PBAC meeting; paragraph 6.4, ixekizumab, PSD, November 2021 PBAC meeting).
- 6.12 The submission assessed the transitivity assumption for the indirect treatment comparison analysis and reported no significant differences between trial populations of the SELECT-AXIS 2 and the GO-AHEAD trial that may impact the measure of comparative treatment effect. In the PBS sub-population (positive MRI and CRP > 9 mg/L), prior bDMARD exposure was tested for treatment effect variation and found to not be a modifier of treatment effect based on the ASAS20 outcome. The sample size of the PBS sub-population was small and therefore it was uncertain whether the presence of a positive MRI and elevated CRP level were true treatment effect modifiers. Similar conclusions of the treatment effect modifier test have been reported in previous PBAC submissions where the PBAC previously stated that it was unclear if the presence of positive MRI and elevated CRP (i.e., objective signs of inflammation) were treatment effect modifiers in the GO-AHEAD trial data (paragraph 6.11, golimumab, PSD, July 2018 PBAC meeting).
- 6.13 Differences in age, and restrictions to prior bDMARD and NSAID exposure between the SELECT-AXIS 2 and GO-AHEAD trials may limit the exchangeability of studies in the indirect treatment comparison of upadacitinib with golimumab.
- 6.14 The submission assessed the trial characteristics for studies used in the indirect treatment comparison for secondary and near market comparators. The clinical studies for secukinumab, certolizumab pegol and ixekizumab (RAPID-axSpA, C-axSpAnd, PREVENT and COAST-X trials) were all phase III, multicentre, randomised, double blind, placebo-controlled trials, had a similar design, and all have previously been seen by the PBAC and determined to have a low risk of bias. Assessments of transitivity were not performed. There were some differences in the eligibility criteria between the RAPID-axSpA, C-axSpAnd, PREVENT and COAST-X trials with the SELECT-AXIS 2 trial such as age and prior medication exposure that could impact exchangeability.

Comparative effectiveness

- 6.15 The submission stated that the ASAS20, ASAS40 and BASDAI50 efficacy outcomes do not have a defined and uniformly accepted minimal clinically important difference (MCID) but that they were themselves clinically important outcomes.
- 6.16 The PBAC previously considered whether established MCIDs from AS are applicable for nr-axSpA, specifically with ASAS20 (the primary endpoint of the GO-AHEAD trial) and had noted that it was not apparent whether MCIDs from AS should apply (paragraph 6.13, golimumab, PSD, November 2017 PBAC meeting).
- 6.17 The submission determined non-inferiority by the application of a non-inferiority margin for ASAS20 using the risk ratio (RR) statistic of 0.43 and determined non-inferiority for ASAS40 and BASDAI50 outcomes through no statistically significant differences for RR and odds ratio (OR) statistics between upadacitinib and each comparator. This is consistent with previously accepted claims of non-inferiority in nr-axSpA (paragraph 6.18, certolizumab pegol, PSD, November 2019 PBAC meeting; paragraph 6.11, secukinumab, PSD, November 2020 PBAC meeting; paragraph 6.15, ixekizumab, PSD, November 2021 PBAC meeting).
- 6.18 Table 4 and Table 5 present the results of the ASAS20, ASAS40 and BASDAI50 outcomes from the SELECT-AXIS 2 and GO-AHEAD trials respectively. Outcomes were reported at Week 14 for the double-blind period of the SELECT-AXIS 2 trial and Week 16 for the double-blind period of the GO-AHEAD trial.

Table 4: Achievement of key outcomes in the SELECT-AXIS 2 trial at week 14

Outcome	UPA n/N (%)	PBO	RR (95% CI)	OR (95% CI)	RD (95% CI)
ASAS20	104/156 (67)	69/157 (44)	1.52 (1.23, 1.87)	2.55 (1.61, 4.03)	0.23 (0.12, 0.33)
ASAS40 ^a	70/156 (45)	35/157 (22)	2.01 (1.43, 2.83)	2.84 (1.74, 4.63)	0.23 (0.12, 0.33)
BASDAI50	66/156 (42)	35/157 (22)	1.90 (1.34, 2.68)	2.56 (1.56, 4.18)	0.20 (0.10, 0.30)

Source: Table 2.1, p74 of the submission.

ASAS20 = Assessment of Spondyloarthritis International Society 20, ASAS40 = Assessment of Spondyloarthritis International Society 40, BASDAI50 = bath ankylosing spondylitis disease activity index 50, CI = confidence interval, n = number of participants with event, N = total participants in group, OR = odds ratio, PBO = placebo, RD = risk difference, RR = risk ratio, UPA = upadacitinib.

^a Primary outcome measure.

Table 5: Achievement of key outcomes in the GO-AHEAD trial at week 16

Outcome	GLM n/N (%)	PBO n/N (%)	RR (95% CI)	OR (95% CI)	RD (95% CI)
ASAS20 ^a	69/97 (71)	40/100 (40)	1.78 (1.35, 2.33)	3.69 (2.04, 6.68)	0.31 (0.18, 0.44)
ASAS40	55/97 (57)	23/100 (23)	2.47 (1.65, 3.67)	4.38 (2.37, 8.11)	0.34 (0.21, 0.47)
BASDAI50	56/97 (58)	30/100 (30)	1.92 (1.36, 2.71)	3.18 (1.77, 5.73)	0.28 (0.14, 0.41)

Source: Table 2.1, p74 of the submission.

ASAS20 = Assessment of Spondyloarthritis International Society 20, ASAS40 = Assessment of Spondyloarthritis International Society 40, BASDAI50 = bath ankylosing spondylitis disease activity index 50, CI = confidence interval, GLM = golimumab, n = number of participants with event, N = total participants in group, OR = odds ratio, PBO = placebo, RD = risk difference, RR = risk ratio.

^a Primary outcome measure.

- 6.19 The clinical effectiveness of upadacitinib and golimumab on all three outcome measures were demonstrated by the SELECT-AXIS 2 and GO-AHEAD trials respectively, with significantly more patients with either bDMARD intervention achieving an ASAS20, ASAS40 and BASDAI50 response compared to patients with placebo.

- 6.20 The Pre-Sub-Committee Response (PSCR) presented additional results for the SELECT-AXIS 2 study out to week 52 and noted the statistically significant results over placebo for ASAS20, ASAS40 and BASDAI50 were maintained.
- 6.21 Table 6 presents the efficacy results for the indirect treatment comparison of upadacitinib versus golimumab after 14/16 weeks of treatment for the full trial population.

Table 6: Indirect treatment comparisons of upadacitinib versus golimumab at Week 14/16 via placebo for full trial population

Trial type or estimate	Trial ID	Intervention n/N (%)	Placebo n/N (%)	RR (95% CI) ^a	OR (95% CI) ^b	RD (95% CI) ^c
ASAS20						
UPA vs PBO	SELECT-AXIS 2	104/156 (67)	69/157 (44)	1.52 (1.23, 1.87)	2.55 (1.61, 4.03)	0.23 (0.12, 0.33)
GLM vs PBO	GO-AHEAD	69/97 (71)	40/100 (40)	1.78 (1.35, 2.33)	3.69 (2.04, 6.68)	0.31 (0.18, 0.44)
Indirect comparison effect UPA vs GLM				0.85 (0.61, 1.20)	0.69 (0.33, 1.46)	-0.08 (-0.25, 0.09)
ASAS40						
UPA vs PBO	SELECT-AXIS 2	70/156 (45)	35/157 (22)	1.76 (1.44, 2.15)	1.76 (1.44, 2.15)	1.76 (1.44, 2.15)
GLM vs PBO	GO-AHEAD	55/97 (57)	23/100 (23)	2.39 (1.79, 3.19)	2.39 (1.79, 3.19)	2.39 (1.79, 3.19)
Indirect comparison effect UPA vs GLM				0.82 (0.48, 1.38)	0.65 (0.29, 1.42)	-0.11 (-0.28, 0.05)
BASDAI50						
UPA vs PBO	SELECT-AXIS 2	66/156 (42)	35/157 (22)	1.90 (1.34, 2.68)	1.90 (1.34, 2.68)	1.90 (1.34, 2.68)
GLM vs PBO	GO-AHEAD	56/97 (58)	30/100 (30)	2.56 (1.56, 4.18)	2.56 (1.56, 4.18)	2.56 (1.56, 4.18)
Indirect comparison effect UPA vs GLM				0.99 (0.61, 1.61)	0.80 (0.37, 1.73)	-0.08 (-0.24, 0.09)

Source: Table 2.19, p87 of the submission.

ASAS20 = Assessment of Spondyloarthritis International Society 20, ASAS40 = Assessment of Spondyloarthritis International Society 40, BASDAI50 = bath ankylosing spondylitis disease activity index 50, CI = confidence interval, GLM = golimumab, n = number of participants with event, N = total participants in group, OR = odds ratio, PBO – placebo, RD = risk difference, RR = risk ratio, UPA = upadacitinib.

^a RR < 1 favours upadacitinib.

^b OR < 1 favours upadacitinib.

^c RD < 0 favours upadacitinib.

- 6.22 There were no significant differences in response rates between upadacitinib and golimumab for any outcome after 14/16 weeks of treatment in the full trial population. Using the non-inferiority margin on the relative risk for ASAS20, as previously accepted by the PBAC, upadacitinib was non-inferior to golimumab as the lower bound of the RR 95% CI was greater than 0.43 (RR [95% CI]: 0.85 [0.61, 1.20]). There were no significant differences between upadacitinib and golimumab for ASAS40 and BASDAI50 response rates.
- 6.23 Table 7 presents the efficacy results for the indirect treatment comparison of upadacitinib versus golimumab after 14/16 weeks of treatment for the PBS sub-population (positive MRI and CRP > 9 mg/L).

Table 7: Indirect treatment comparisons of upadacitinib versus golimumab at Week 14/16 via placebo for PBS sub-population (positive MRI and CRP > 9 mg/L)

Trial type or estimate	Trial ID	Intervention n/N (%)	Placebo n/N (%)	RR (95% CI) ^a	OR (95% CI) ^b	RD (95% CI) ^c
ASAS20						
UPA vs PBO	SELECT-AXIS 2	16/19 (84)	8/16 (50)	1.68 (0.99, 2.85)	5.33 (1.10, 25.77)	0.34 (0.05, 0.64)
GLM vs PBO	GO-AHEAD	22/26 (85)	10/27 (37)	2.28 (1.36, 3.84)	9.35 (2.50, 35.04)	0.48 (0.25, 0.70)
Indirect comparison effect UPA vs GLM				0.74 (0.35, 1.54)	0.57 (0.07, 4.46)	-0.13 (-0.51, 0.24)
ASAS40						
UPA vs PBO	SELECT-AXIS 2	12/19 (63)	3/16 (19)	3.37 (1.15, 9.88)	7.43 (1.56, 35.48)	0.44 (0.15, 0.73)
GLM vs PBO	GO-AHEAD	18/26 (69)	7/27 (26)	2.67 (1.34, 5.31)	6.43 (1.94, 21.29)	0.43 (0.19, 0.68)
Indirect comparison effect UPA vs GLM				1.26 (0.35, 4.52)	1.16 (0.16, 8.28)	0.01 (-0.37, 0.39)
BASDAI50						
UPA vs PBO	SELECT-AXIS 2	11/19 (58)	3/16 (19)	3.09 (1.04, 9.18)	5.96 (1.26, 28.10)	0.39 (0.10, 0.68)
GLM vs PBO	GO-AHEAD	18/26 (69)	10/27 (37)	1.87 (1.07, 3.25)	3.83 (1.22, 11.98)	0.32 (0.07, 0.58)
Indirect comparison effect UPA vs GLM				1.65 (0.49, 5.61)	1.56 (0.23, 10.69)	0.07 (-0.32, 0.46)

Source: Table 2.19, p87 of the submission.

ASAS20 = Assessment of Spondyloarthritis International Society 20, ASAS40 = Assessment of Spondyloarthritis International Society 40, BASDAI50 = bath ankylosing spondylitis disease activity index 50, CI = confidence interval, GLM = golimumab, n = number of participants with event, N = total participants in group, OR = odds ratio, PBO = placebo, RD = risk difference, RR = risk ratio, UPA = upadacitinib.

^a RR > 1 favours upadacitinib.

^b OR > 1 favours upadacitinib.

^c RD > 0 favours upadacitinib.

Corrected during evaluation as per Table 2.16, p81 of the submission and Attachment 2.8 of the submission.

- 6.24 The results for ASAS20, ASAS40 and BASDAI50 all showed no statistically significant differences in upadacitinib versus golimumab treatment in the PBS sub-population (ASAS20: RR [95% CI]: 0.74 [0.35, 1.54]; ASAS40: RR [95% CI]: 1.26 [0.35, 4.52]; BASDAI50: RR [95% CI]: 1.65 [0.49, 5.61]). The ASAS20 outcome did not meet the non-inferiority margin as the lower bound of the RR 95% CI was less than 0.43
- 6.25 There were variations in the numerical trends across outcomes. For example, the results observed in the less stringent ASAS20 outcome favoured golimumab, but both the ASAS40 and BASDAI50 outcomes favoured upadacitinib. This variation and the wide 95% CIs are likely driven by the relatively small sample sizes thus lead to uncertainty regarding the non-inferiority claim in the PBS sub-population.
- 6.26 Table 8 presents the efficacy results for the indirect treatment comparison of upadacitinib versus certolizumab pegol, secukinumab and ixekizumab after 12/16 weeks of treatment for the full trial population.

Table 8: Indirect treatment comparisons of upadacitinib versus secondary and near market comparators at Week 12/16 via placebo for full trial population

Trial type or estimate	Trial ID	Intervention n/N (%)	Placebo n/N (%)	RR (95% CI) ^a	OR (95% CI) ^b	RD (95% CI) ^c
ASAS20						
UPA vs PBO	SELECT-AXIS 2	104/156 (67)	69/157 (44)	1.52 (1.23, 1.87)	2.55 (1.61, 4.03)	0.23 (0.12, 0.33)
CTZ (meta) vs PBO	RAPID-axSpA and C-axSpAnd	131/205 (63.9)	71/208 (34.1)	1.87 (1.51, 2.32)	3.42 (2.28, 5.12)	0.30 (0.21, 0.39)
SEC (LD) vs PBO	PREVENT	105/185 (56.8)	85/186 (45.7)	1.24 (1.02, 1.55)	1.27 (1.04, 1.55)	0.11 (0.01, 0.21)
SEC (NL) vs PBO	PREVENT	107/184 (58.2)	85/186 (45.7)	1.27 (1.04, 1.55)	1.65 (1.10, 2.50)	0.13 (0.02, 0.23)
IXE vs PBO	COAST-X	52/96 (54.2)	41/105 (39.0)	1.39 (1.03, 1.88)	1.84 (1.05, 3.23)	0.15 (0.01, 0.29)
Indirect comparison effect UPA vs CTZ (meta)				0.81 (0.60, 1.09)	0.75 (0.41, 1.38)	-0.07 (-0.21, 0.07)
Indirect comparison effect UPA vs SEC (LD)				1.22 (0.91, 1.63)	1.63 (0.88, 3.02)	0.12 (-0.03, 0.26)
Indirect comparison effect UPA vs SEC (NL)				1.19 (0.89, 1.59)	1.54 (0.83, 2.85)	0.10 (-0.05, 0.25)
Indirect comparison effect UPA vs IXE				1.09 (0.76, 1.58)	1.38 (0.67, 2.85)	0.08 (-0.10, 0.25)
ASAS40						
UPA vs PBO	SELECT-AXIS 2	70/156 (45)	35/157 (22)	2.01 (1.43, 2.83)	2.84 (1.74, 4.63)	0.23 (0.12, 0.33)
CTZ (meta) vs PBO	RAPID-axSpA and C-axSpAnd	NA	NA	-	-	-
SEC (LD) vs PBO	PREVENT	74/185 (40.0)	52/186 (28.0)	1.43 (1.07, 1.91)	1.71 (1.11, 2.65)	0.12 (0.02, 0.22)
SEC (NL) vs PBO	PREVENT	75/184 (40.8)	52/186 (28.0)	1.46 (1.09, 1.95)	1.77 (1.15, 2.74)	0.13 (0.03, 0.22)
IXE vs PBO	COAST-X	34/96 (35.4)	20/105 (19.0)	1.86 (1.15, 3.00)	2.33 (1.23, 4.42)	0.16 (0.04, 0.29)
Indirect comparison effect UPA vs CTZ (meta)				NA	NA	NA
Indirect comparison effect UPA vs SEC (LD)				1.41 (0.90, 2.20)	1.66 (0.86, 3.19)	0.11 (-0.03, 0.25)
Indirect comparison effect UPA vs SEC (NL)				1.38 (0.88, 2.16)	1.60 (0.83, 3.08)	0.10 (-0.04, 0.24)
Indirect comparison effect UPA vs IXE				1.08 (0.60, 1.95)	1.22 (0.54, 2.73)	0.06 (-0.10, 0.22)
BASDAI50						
UPA vs PBO	SELECT-AXIS 2	66/156 (42)	35/157 (22)	1.90 (1.34, 2.68)	2.56 (1.56, 4.18)	0.20 (0.10, 0.30)
CTZ (meta) vs PBO	RAPID-axSpA and C-axSpAnd	80/205 (39.0)	31/208 (14.9)	2.62 (1.81, 3.78)	3.65 (2.28, 5.86)	0.24 (0.16, 0.32)
SEC (LD) vs PBO	PREVENT	69/185 (37.3)	39/186 (21.0)	1.78 (1.27, 2.48)	2.24 (1.41, 3.55)	0.16 (0.07, 0.25)
SEC (NL) vs PBO	PREVENT	69/184 (37.5)	39/186 (21.0)	1.79 (1.28, 2.50)	2.26 (1.42, 3.58)	0.17 (0.07, 0.26)
IXE vs PBO	COAST-X	30/96 (31.3)	15/105 (14.3)	2.19 (1.26, 3.81)	2.72 (1.36, 5.47)	0.17 (0.06, 0.28)

Indirect comparison effect UPA vs CTZ (meta)	0.72 (0.44, 1.20)	0.70 (0.35, 1.38)	-0.04 (-0.17, 0.09)
Indirect comparison effect UPA vs SEC (LD)	1.07 (0.66, 1.73)	1.14 (0.58, 2.24)	0.04 (-0.10, 0.17)
Indirect comparison effect UPA vs SEC (NL)	1.06 (0.66, 1.72)	1.13 (0.58, 2.22)	0.04 (-0.10, 0.17)
Indirect comparison effect UPA vs IXE	0.87 (0.45, 1.67)	0.94 (0.40, 2.20)	0.03 (-0.12, 0.18)

Source: Table 2.20, p88 of the submission.

ASAS20 = Assessment of Spondyloarthritis International Society 20, ASAS40 = Assessment of Spondyloarthritis International Society 40, BASDAI50 = bath ankylosing spondylitis disease activity index 50, CI = confidence interval, CTZ = certolizumab pegol, IXE = ixekizumab, LD = loading dose, meta = meta-analysed, n = number of participants with event, N = total participants in group, NA = not applicable, NL = no loading dose, OR = odds ratio, PBO = placebo, RD = risk difference, RR = risk ratio, SEC = secukinumab, UPA = upadacitinib.

^a RR > 1 favours upadacitinib.

^b OR > 1 favours upadacitinib.

^c RD > 0 favours upadacitinib.

Corrected during evaluation as per Attachment 2.8 of the submission.

- 6.27 There were no significant differences in response rates between upadacitinib and certolizumab pegol, secukinumab and ixekizumab for any outcomes after 12/16 weeks of treatment in the full trial population. Applying the non-inferiority margin to the risk ratio for ASAS20 upadacitinib was non-inferior to all comparators as the lower bound of the RR 95% CI was greater than 0.43 (upadacitinib vs certolizumab pegol RR [95% CI]: 0.81 [0.60, 1.09]; upadacitinib vs secukinumab [loading dose] RR [95% CI]: 1.22 [0.91, 1.63]; upadacitinib vs secukinumab [no loading dose] RR [95% CI]: 1.19 [0.89, 1.59]; upadacitinib vs ixekizumab RR [95% CI]: 1.09 [0.76, 1.58]). There were no significant differences between upadacitinib and certolizumab pegol, secukinumab and ixekizumab for ASAS40 or BASDAI50 response rates.
- 6.28 The efficacy results for the indirect treatment comparison of upadacitinib versus certolizumab pegol, secukinumab and ixekizumab after 12/16 weeks of treatment for the PBS sub-population were presented in the submission. To account for discrepancies for the ULN between trials that were used to inform the analysis, the PBS sub-populations were either patients with a positive MRI and an elevated CRP level > ULN of 9 mg/L at baseline or patients with a positive MRI and an elevated CRP level > ULN of 5 mg/L at baseline. The indirect treatment comparisons in the PBS sub-population did not meet the ASAS20 non-inferiority margin.
- 6.29 The PSCR acknowledged the limitations of the post-hoc subgroup analysis of the PBS population, and argued the trials were not powered to support the claim in the PBS population and the wide 95% confidence intervals observed were likely driven by the small sample sizes. The ESC agreed with the evaluation and PSCR and considered the claim of non-inferior comparative effectiveness to certolizumab pegol, secukinumab and ixekizumab was likely to be reasonable.

Comparative harms

- 6.30 The submission presented the longer-term safety data from the SELECT-AXIS 2 trial. The submission reported no statistically significant differences in safety outcomes between upadacitinib and placebo. However, the treatment emergent adverse events (TEAE) of special interest had higher rates in upadacitinib versus placebo for any serious infection (1.3% vs 0.6%), herpes zoster (2.6% vs 0.6%) and neutropenia (4.5%

vs 0.6%) based on Week 52 trial data. These TEAE are consistent with known safety profile of upadacitinib, as described in the proposed PI.

- 6.31 Several serious AE were identified in the clinical study report (CSR) of the SELECT-AXIS 2 trial by Week 52 including COVID-19 pneumonia, pyelonephritis, foot fracture, osteoarthritis, ureterolithiasis, and nasal polyps. However, the number of patient events were small.
- 6.32 Table 9 presents the safety results for the indirect treatment comparison of upadacitinib versus golimumab after 14/16 weeks of treatment for the full trial population.

Table 9: Summary of the safety indirect comparison: upadacitinib versus golimumab at Week 14/16 full trial population

Treatment	Trial ID	UPA n/N (%)	PBO n/N (%)	RR (95% CI) ^a	OR (95% CI) ^b	RD (95% CI) ^c
Any AE						
UPA	SELECT-AXIS 2	75/156 (48)	72/157 (46)	1.05 (0.83, 1.33)	1.09 (0.70, 1.70)	0.02 (-0.09, 0.13)
GLM	GO-AHEAD	40/97 (41)	47/100 (47)	0.88 (0.64, 1.20)	0.79 (0.45, 1.39)	-0.06 (-0.20, 0.08)
Indirect comparison effect UPA vs GLM				1.19 (0.81, 1.77)	1.38 (0.67, 2.83)	0.08 (-0.10, 0.26)
Serious AE						
UPA	SELECT-AXIS 2	4/156 (2.6)	2/157 (1.3)	2.01 (0.37, 10.83)	2.04 (0.37, 11.30)	0.01 (-0.02, 0.04)
GLM	GO-AHEAD	1/97 (1.0)	2/100 (2.0)	0.52 (0.05, 5.59)	0.51 (0.05, 5.72)	-0.01 (-0.04, 0.02)
Indirect comparison effect UPA vs GLM				3.90 (0.21, 72.28)	4.00 (0.21, 77.26)	0.02 (-0.02, 0.07)
Any AE with reasonable possibility of being related to study treatment						
UPA	SELECT-AXIS 2	29/156 (18.6)	30/157 (19.1)	0.97 (0.61, 1.54)	0.97 (0.55, 1.70)	-0.01 (-0.09, 0.08)
GLM	GO-AHEAD	13/97 (13)	17/100 (17)	0.79 (0.41, 1.53)	0.76 (0.35, 1.65)	-0.04 (-0.14, 0.06)
Indirect comparison effect UPA vs GLM				1.23 (0.55, 2.77)	1.28 (0.49, 3.36)	0.03 (-0.10, 0.16)
AE leading to withdrawal of study treatment						
UPA	SELECT-AXIS 2	4/156 (2.6)	2/157 (1.3)	2.01 (0.37, 10.83)	2.04 (0.37, 11.30)	0.01 (-0.02, 0.04)
GLM	GO-AHEAD	2/97 (2.1)	1/100 (1.0)	2.06 (0.19, 22.37)	2.08 (0.19, 22.37)	0.01 (-0.02, 0.04)
Indirect comparison effect UPA vs GLM				0.98 (0.05, 18.07)	0.98 (0.05, 18.92)	0.00 (-0.04, 0.05)

Source: Table 2.12, p75 of the submission, Table 2.13, p76 of the submission and Attachment 2.8.

AE = adverse events, CI = confidence interval, COVID-19 = coronavirus disease of 2019, GLM = golimumab, n = number of participants reporting data, N = total participants in group, PBO = placebo, RD = risk difference, RR = relative risk, UPA = upadacitinib.

^a RR < 1 favours upadacitinib.

^b OR < 1 favours upadacitinib.

^c RD < 0 favours upadacitinib.

- 6.33 The submission claimed that upadacitinib is non-inferior with respect to all safety outcomes based on the indirect treatment comparison safety results for upadacitinib versus golimumab after 14/16 weeks of treatment in the full trial population. There were higher numbers of serious AE for upadacitinib compared to golimumab in the indirect treatment comparison.

- 6.34 The submission stated that it did not present the long-term safety results for the indirect treatment comparison of upadacitinib versus golimumab due to differences in reporting, methodology and time periods of the long-term safety data.
- 6.35 The safety results for the indirect treatment comparison of upadacitinib versus certolizumab pegol, secukinumab and ixekizumab after 14 to 52 weeks of treatment for the full trial population was presented in the submission.
- 6.36 The submission claimed that upadacitinib is non-inferior to certolizumab pegol, secukinumab and ixekizumab with respect to safety outcomes. Upadacitinib had numerically lower rates of 'any AE' in comparison to its comparators across all analyses, with no statistically significant differences. There were no statistically significant differences for drug-related AE except for upadacitinib (Week 14) versus certolizumab pegol (Week 52). This analysis favoured upadacitinib, but the submission stated that significance is likely attributable to differences in the reported time periods between trials. The ESC considered the evidence presented likely supported a conclusion of non-inferior comparative safety between upadacitinib and certolizumab pegol, secukinumab and ixekizumab.

Clinical claim

- 6.37 The submission described upadacitinib as non-inferior in terms of effectiveness and safety compared to golimumab and the secondary comparators. The evaluation and ESC considered the claim was likely adequately supported by the evidence from the submission, however the key issues were:
- Differences in age and prior medication exposure between trials may limit the exchangeability of studies as well as generalisability to the Australian setting.
 - Despite no significant differences in ASAS20, ASAS40 and BASDAI50 response rates between upadacitinib and golimumab in the PBS sub-population, the ASAS20 outcome did not meet the previously accepted non-inferiority margin for RR of 0.43. Although this treatment comparison in the PBS sub-population was limited by small patient samples.
 - Higher numbers of serious AE for upadacitinib compared to golimumab was observed in the submission, and the safety comparison in the full trial population was limited by small number of patient events.
- 6.38 The PBAC considered that the claim of non-inferior comparative effectiveness was, on balance, likely to be reasonable.
- 6.39 The PBAC considered that the claim of non-inferior safety was reasonable.

Economic analysis

- 6.40 The submission presented a cost-minimisation approach comparing upadacitinib and golimumab, based on the clinical claim that upadacitinib is non-inferior in terms of

effectiveness and safety compared with golimumab. The claim of non-inferior effectiveness and safety appears adequately supported by the evidence presented in the clinical effectiveness section. Based on the available evidence, the evaluation and ESC considered the cost minimisation approach taken by the submission was reasonable.

- 6.41 The equi-effective doses were estimated as upadacitinib 15 mg modified release oral tablet once daily over 2 years and golimumab 50 mg subcutaneous injection once monthly over 2 years. The equi-effective doses are aligned with the proposed (upadacitinib) and approved (golimumab) doses in TGA product information (PI). They are consistent with the dosing and frequency of use in the trial arms in the clinical effectiveness section that provide the evidence to support the clinical claims.
- 6.42 The submission assumed that 10% of patients will require injection assistance associated with treatment with golimumab and MBS item code #23 was used. Other potential resource utilisation was assumed to occur equally with each treatment. This is reasonable and leads to an injection assistance cost per dose from golimumab of \$3.91.
- 6.43 The results of the cost-minimisation approach using published prices are presented in Table 10.

Table 10: Results of the cost-minimisation approach

Component	Upadacitinib	Golimumab
Cost per pack (AEMP)	\$965.05	\$1,044.43
Cost per administration	\$0	\$3.91
Dose duration	Two years	Two years
Doses over two years	730 doses (26.08 packs)	24
Total medicine cost over two years	\$25,160	\$25,160
Difference in cost	\$0	-

Source: Table 3.4, p102 of the submission
AEMP = approved ex-manufacturer price.

- 6.44 On the basis of equivalence of cost over two years, the requested ex-manufacturer price for upadacitinib was calculated at \$965.05 in the submission. Based on the proposed price, the sponsor calculated that the corresponding dispensed price for upadacitinib was \$1,077.23.
- 6.45 The submission listed the current published AEMP (\$1,149.97) for upadacitinib in ankylosing spondylitis, calculated the corresponding DPMQ (\$1,271.4), and carried these prices forward for calculations in the utilisation and financial estimates. This was inappropriate; however the evaluation noted the effective price of upadacitinib for nr-axSpA would require confirmation following a PBAC recommendation.

Drug cost/patient/year

- 6.46 Based on the published DPMQ of \$1,077.29 (corrected using the July 2022 price calculator) and 13.04 scripts per patient per year, the drug cost is \$14,042 per patient per year.

Estimated PBS usage & financial implications

- 6.47 This submission was not considered by DUSC. A market share approach was used to estimate the financial impact of the proposed listing on the PBS, based on the substitution of golimumab, certolizumab pegol, secukinumab. The market share approach is justified given the proposed medicine is expected to represent a direct substitution of golimumab, certolizumab pegol and secukinumab. The assumption of equal substitution rate across all comparators is reasonable. The financial estimates do not consider the impact on the market share from ixekizumab which was recommended for listing in November 2021.
- 6.48 Table 11 summarises the key inputs in the financial estimates.

Table 11: Key inputs for financial estimates

Data	Value and source			Comment
Script equivalence / substitution rate		Scripts / year	Script equivalence vs UPA	<p>The calculation for SEC scripts is inaccurate. Based on the current PBS restrictions for SEC, the number of scripts is 12.5 per year for secukinumab with loading dose and 13 per year without loading. Even though there is currently no clinical evidence on utilisation of loading versus no loading dose, it is more appropriate to assume a 70:30 weighting for with and without loading doses respectively (paragraph 7.7, secukinumab, PSD, November 2020). The weighted scripts/year for SEC should be 12.65. The PSCR accepted the updated script equivalence with SEC calculated in the evaluation.</p> <p>These discrepancies are likely to affect the growth rate in subsequent calculations and result in an overestimate in the financial implications for other affected medications on the PBS.</p>
	GLM	12	1.09	
	CZP	14	0.93	
	SEC LD	16.5	0.79	
	SEC NL	14	0.93	
	SEC	15.25	0.85	
	UPA	13.04	-	
Market growth (without UPA)	Yr1: █%; Yr2: █%; Yr3: █%; Yr4: █%; Yr5: █%; Yr6: █%; Source: Calculated based on patient treatment years estimated from the logarithmic growth curve.			The extrapolation of growth rates is uncertain given it was based on 3 years of data (2019-21).
Market growth due to UPA listing (additional growth)	0% Source: Upadacitinib is assumed to only displace the existing PBS listed bDMARDs/tsDMARDs, and not grow the market.			This assumption appears reasonable, although there is possibility of additional market growth as a result of patients who are refractory or intolerant to other classes of bDMARDs/tsDMARDs returning for treatment. UPA may also have some potential to grow the market as the first oral therapy for this indication.
Market share displacement	Yr1: █%; Yr2: █%; Yr3: █%; Yr4: █%; Yr5: █%; Yr6: █%; Source: Assumption			The submission did not justify the values of market share displacement due to UPA listing but provided sensitivity of displacement with 25% higher or lower uptake.
MBS item	The submission assumed 10% of patients will require injection assistance for all current PBS bDMARD listings in nr-axSpA that are administered via subcutaneous injection. MBS item code #23 was applied.			This is appropriate.

Source: Constructed during the evaluation from pp104-116 of the submission, and parameters in the excel spreadsheet (Attachment 4 - Section 4 Workbook nr-axSpA.xlsx).

bDMARD = biological disease-modifying anti-rheumatic drug, CZP = certolizumab pegol, DPMQ = dispensed price for maximum quantity, GLM = golimumab, LD = loading dose, NL = no loading dose, nr-axSpA = non-radiographic axial spondyloarthritis, PBS = Pharmaceutical Benefits Scheme, PSCR = Pre-Sub-Committee Response, PSD = Public summary document, RPBS = Repatriation Schedule of Pharmaceutical Benefits, SEC = secukinumab, UPA = upadacitinib.

6.49 The submission assumed that upadacitinib will displace the existing market through substitution of all reimbursed bDMARDs/tsDMARDs in equal proportions. Based on the 2019-2021 usage statistics, the full PBS market for nr-axSpA including all three

comparator treatments (golimumab, certolizumab pegol and secukinumab) has been projected for 6 years post-listing (2023 - 2028), with the assumption that market share would not change over time.

6.50 Table 12 summarises the estimated net financial implications of listing upadacitinib based on published prices.

Table 12: Estimated use and financial implications (using published prices)

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Estimated extent of use						
Number of patients treated	■ ¹	■ ¹	■ ¹	■ ¹	■ ¹	■ ¹
Number of scripts dispensed ^a	■ ¹	■ ¹	■ ²	■ ²	■ ²	■ ²
Estimated financial implications of upadacitinib						
Cost to PBS/RPBS less copayments ^b (\$)	■ ³	■ ³	■ ³	■ ³	■ ³	■ ³
Estimated financial implications for golimumab, certolizumab pegol and secukinumab						
Cost to PBS/RPBS less copayments (\$)	■ ⁴	■ ⁴	■ ⁴	■ ⁴	■ ⁴	■ ⁴
Net financial implications						
Net cost to PBS/RPBS (\$)	■ ⁴	■ ⁴	■ ⁴	■ ⁴	■ ⁴	■ ⁴
Net cost to MBS (\$)	■ ⁴	■ ⁴	■ ⁴	■ ⁴	■ ⁴	■ ⁴
Total net cost to PBS/RPBS/MBS (\$)	■ ⁴	■ ⁴	■ ⁴	■ ⁴	■ ⁴	■ ⁴

Source: Calculated during evaluation using July 2022 PBS price calculator.

PBS, Pharmaceutical Benefits Scheme; RPBS, Repatriation Pharmaceutical Benefits Scheme. MBS, Medical Benefits Schedule.

^a Assuming 13.04 per year as estimated by the submission.

^b Based on the published price of upadacitinib for nr-axSpA

The redacted values correspond to the following ranges:

¹ < 500

² 500 to < 5,000

³ \$0 to < \$10 million

⁴ net cost saving

6.51 The submission calculated the patient years of each medicine by multiplying the total number of patients per year with the market share of each medicine. Market share is derived from the number of scripts, this is applied to the total number of patients to calculate the number of patients who would receive each drug.

6.52 The script volume of each drug in 2022 was taken from the 2021 data. It appears that extrapolation is inconsistent with assumptions for 2021-22. Without considering growth of scripts, this will lead to an underestimate of the scripts displaced, and a subsequent underestimate of the financial impact.

6.53 The script volume in future years was calculated based on the script volume from the previous year, adjusted by the growth rate of patient years. Rather than applying the growth rate in scripts to the script volume, the submission applied patient growth rate. This is inappropriate as different numbers of scripts are required for each drug. The

submission assumed the same displacement rates for initial and continuing scripts. Whether these will lead to an over or underestimate is uncertain.

- 6.54 The submission considered that < 500 grandfathered patients had already displaced patients on current bDMARD/tsDMARD each year and are not growing the market.

Quality Use of Medicines

- 6.55 The sponsor has a risk management plan, including an Australian-specific annex that has been submitted to the TGA as part of the dossier. The sponsor will be extending the AbbVie Care patient support program to provide support to prescribers and patients with regards to the use of upadacitinib. No post-marketing surveillance study was proposed in the submission.

Financial Management – Risk Sharing Arrangements

- 6.56 The sponsor stated that a risk sharing arrangement is in place for the nr-axSpA market and will be willing to discuss joining it upon a recommendation on upadacitinib.

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

7 PBAC Outcome

- 7.1 The PBAC deferred making a recommendation to list upadacitinib (UPA) for the treatment of non-radiographic axial spondyloarthritis (nr-axSpA), as the TGA Delegate's Overview was not available at time of PBAC consideration. However, the PBAC was of a mind to recommend listing on the basis that, among other matters, its assessment that the cost-effectiveness of UPA would be acceptable if it were cost-minimised to the least costly alternative treatment.
- 7.2 The PBAC considered the equi-effective doses of UPA and the alternative therapies were:
- UPA 15 mg once daily;
 - Ixekizumab (IXE) 80 mg once every four weeks;
 - Golimumab (GLM) 50 mg once every four weeks;
 - Secukinumab (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, at a 70:30 weighting for loading dose versus no loading dose (as outlined in paragraph 7.7 of the SEC November 2020 PSD); and
 - Certolizumab pegol (CZP): 400 mg at Week 0, 2, 4, then 200 mg every 2 weeks; or CZP 400 mg every 4 weeks.
- 7.3 The PBAC considered it was reasonable for the listing of UPA to be consistent with other biological or targeted synthetic disease modifying anti-rheumatic drugs (bDMARDs/tsDMARDs) for nr-axSpA, with prescribing limited to medical practitioners

and an initial treatment period of 16 weeks, followed by maintenance therapy with re-assessment at 24-week intervals. The PBAC noted the Secretariat request to consider whether it was appropriate to increase maximum number of therapies a patient can use as part of a treatment cycle for nr-axSpA and whether the current '3 strikes' rule should continue or be amended to a '4 strike' rule. The PBAC considered it may be reasonable to review the design of treatment cycle requirements for bDMARDs/tsDMARDs broadly given the range of available treatments with different mechanisms of action since these requirements were originally devised. The PBAC noted such a review was broader than the scope of its consideration of UPA and considered listing could progress (when the Committee is in a position to make a recommendation) under current arrangements (i.e. 3 treatment failures).

- 7.4 The PBAC considered the nominated primary comparator of GOL, as currently the most-prescribed alternative bDMARD/tsDMARD for nr-axSpA was reasonable, and also considered the nominated secondary comparators of CZP, SEC and IXE were reasonable.
- 7.5 The PBAC noted no direct trials comparing UPA to GOL or any of the secondary comparators were available, and the submission relied on indirect treatment comparisons with placebo as the common comparator to support the clinical claims. The PBAC noted the requested PBS listing was narrower than the populations recruited into the trials and the submission presented analyses based on the intention to treat (ITT) population and PBS subgroups from the clinical trial data. The Committee considered the analyses presented for the outcomes of Assessment of Spondylo-Arthritis International Society 20 or 40 (ASAS20/ASAS40) and Bath Ankylosing Spondylitis Disease Activity Index 50 (BASDAI50) were consistent with previous bDMARD/tsDMARD submissions for nr-axSpA.
- 7.6 The PBAC noted the results for the ITT population analyses found no statistically significant differences between UPA and GOL for any of these outcomes and noted the 95% CIs for the relative risk (RR) comparison of ASAS20 did not exceed the non-inferiority margin (NIM) of 0.43 it had previously accepted in nr-axSpA. The PBAC noted the lower bound of the 95% CI for the comparison of UPA and GOL for ASAS20 in the PBS population analysis exceeded the NIM, however agreed with the ESC and Pre-Sub-Committee Response (PSCR) that the results were likely driven by the small sample sizes of the PBS subpopulations, leading to wide 95% CIs (paragraph 6.27). Furthermore, the PBAC noted there were no statistically significant differences between UPA and GOL or UPA and the secondary comparators for the PBS population analyses and considered, on balance, that the claim of non-inferior comparative effectiveness to the alternative therapies was likely to be reasonable.
- 7.7 The Committee noted the PSCR presented additional evidence for UPA out to week 52, which supported a conclusion the treatment effect is sustained beyond the 14/16 week treatment period used in the indirect comparisons to the alternative therapies.

- 7.8 The PBAC noted the submission reported no statistically significant differences in safety outcomes between upadacitinib and placebo. In addition, the PBAC also noted treatment emergent adverse events (TEAE) of special interest appeared to be numerically higher in upadacitinib than placebo for any serious infection (1.3% vs 0.6%), herpes zoster (2.6% vs 0.6%) and neutropenia (4.5% vs 0.6%), based on Week 52 trial data, however considered these events were consistent with the known safety profile of UPA. The PBAC noted the safety ITCs to GOL and the secondary comparators and considered overall the claim of non-inferior comparative safety was likely to be reasonable.
- 7.9 The PBAC noted that the submission inappropriately used the current published price of UPA for ankylosing spondylitis as a placeholder price in the cost minimisation approach (paragraph 6.45), however also noted the effective prices of alternative bDMARDs/tsDMARDs were not available to the sponsor and therefore the price of UPA would require recalculation following a recommendation. Based on its conclusion that the claim of non-inferior effectiveness and safety to the alternative therapies was adequately supported, the PBAC considered that a listing based on a cost minimisation approach with costs over two years, consistent with the approach previously used for bDMARDs/tsDMARDs was appropriate to determine the cost minimised price of UPA and was of the view the cost of UPA should be no greater than the alternative therapies.
- 7.10 With regards to the utilisation and financial estimates, the PBAC noted the submission incorrectly calculated script equivalences with SEC due to the way loading doses are provided for under the PBS restriction and noted this revision was accepted in the PSCR. Accounting for this, the PBAC considered that, under the parameters of its consideration that listing on a cost minimisation basis with the least costly of GOL, SEC, CZP and IXE, the listing of UPA would likely be cost neutral or result in a modest save to the PBS as it would only replace therapies that are either of equivalent cost or more expensive. The PBAC noted a Risk Sharing Arrangement (RSA) was currently in place for bDMARDs/tsDMARDs for the treatment of nr-axSpA and considered it would be appropriate for the listing of UPA to join the existing arrangement.

Outcome:

Deferred

8 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised through the Pharmaceutical Benefits Scheme (PBS) in Australia. It considers applications regarding the listing of medicines on the PBS and provides advice about other matters relating to the operation of the PBS in this context. A PBAC decision in relation to PBS listings does not necessarily represent a final PBAC view about the merits of the medicine or the circumstances in which it should be made available

through the PBS. The PBAC welcomes applications containing new information at any time.

9 Sponsor's Comment

The sponsor had no comment.

Addendum to the November 2022 PBAC PSD:

**4.01 UPADACITINIB,
Tablet 15 mg
Rinvoq[®],
AbbVie Pty Ltd.**

10 Background

10.1 At its November 2022 meeting, the PBAC deferred making a recommendation for a General Schedule Authority Required (Written) listing for the treatment of non-radiographic axial spondyloarthritis (nr-axSpA) as the TGA Delegate's Overview was not available at the time of PBAC consideration. The PBAC was of a mind to recommend the General Schedule, Authority Required (in writing) listing of UPA for nr-axSpA on the basis the cost-effectiveness of UPA would likely be acceptable if it were cost minimised to the least costly alternative therapy out of ixekizumab (IXE) (recommended in November 2021 but not yet listed), golimumab (GLM), secukinumab (SEC) and certolizumab pegol (CZP). The PBAC considered, based on the evidence presented, that UPA is likely to be of non-inferior comparative effectiveness and safety to these agents in nr-axSpA.

10.2 The TGA Delegate's Overview, ACM advice and finalised TGA registration were provided prior to the March 2023 PBAC meeting. The finalised TGA indication for UPA for nr-axSpA is as follows:

'RINVOQ is indicated for the treatment of adults with active non-radiographic axial spondyloarthritis with objective signs of inflammation as indicated by elevated C-reactive protein (CRP) and/or magnetic resonance imaging (MRI) change, who have responded inadequately to, or are intolerant to nonsteroidal anti-inflammatory drugs (NSAIDs).'

11 PBAC Outcome

11.1 The PBAC recommended the General Schedule listing of upadacitinib (UPA) 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 UPA would be acceptable if it were cost minimised to the least costly alternative therapy out of ixekizumab (IXE) (recommended but not yet listed), golimumab (GLM), secukinumab (SEC) and certolizumab pegol (CZP).

11.2 The PBAC reaffirmed its view, based on the evidence presented, that UPA is likely to be of non-inferior comparative effectiveness and safety to these agents in nr-axSpA (paragraphs 7.1 and 7.6 refer).

- 11.3 The Committee also reaffirmed its view that based on its conclusion that the claim of non-inferior effectiveness and safety to the alternative therapies was adequately supported, that a listing based on a cost minimisation approach with costs over two years, consistent with the approach previously used for bDMARDs/tsDMARDs was appropriate to determine the cost minimised price of UPA and was of the view the cost of UPA should be no greater than the alternative therapies.
- 11.4 The PBAC reaffirmed its view the equi-effective doses of UPA and the alternative therapies were as-outlined in paragraph 7.2.
- 11.5 The PBAC noted that its recommendation was on a cost-minimisation basis and advised that, because UPA is not expected to provide a substantial and clinically relevant improvement in efficacy, or reduction of toxicity over the alternative therapies, or not expected to address a high and urgent unmet clinical need given the presence of alternative therapies, the criteria prescribed by the National Health (Pharmaceuticals and Vaccines – Cost Recovery) Regulations 2022 for Pricing Pathway A were not met.
- 11.6 The PBAC noted that this submission is not eligible for an Independent Review, as it received a positive recommendation.

Outcome:

Recommended

12 Recommended listing

- 12.1 Add indication (Non-radiographic axial spondyloarthritis) as follows:

Category / Program: GENERAL – General Schedule (Code GE)					
MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
UPADACITINIB					
upadacitinib 15 mg modified release tablet, 28	NEW (Do not add to 12625L) MP	1	28	3	Rinvoq
Add Restriction Summary [New] / Treatment of Concept: [New] Authority Required (in writing only) (modelled of golimumab – PBS item codes 11538G & 11560K, Restriction Summary 11484 as at 1 February 2023; shaded area indicates difference with golimumab):					
	Administrative Advice: insert updated concept 27999 here (see end of document)				
	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: Special Pricing Arrangements apply.				
	Indication: Non-radiographic axial spondyloarthritis				

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	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
	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:
	The treatment must not exceed a maximum of 16 weeks with this drug under this restriction.
	Population criteria:
	Patient must be at least 18 years of age
	Treatment criteria:
	Must be treated by rheumatologist; or
	Must be treated by a clinical immunologist with expertise in the management of non-radiographic axial spondyloarthritis.

	<p>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.</p>
	<p>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) score of at least 4 on a 0-10 scale; and (b) C-reactive protein (CRP) level greater than 10 mg per L.</p> <p>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.</p>
	<p>Prescribing 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>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 authority application must be made in writing and must include: (a) a completed authority prescription form(s); and (b) a completed authority application form relevant to the indication and treatment phase (the latest version is located on the website specified in the Administrative Advice).</p>
	<p>Prescribing 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. 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>
	<p>Add Restriction Summary [New] / Treatment of Concept: [New]: Authority Required (telephone/online PBS Authorities system) (modelled of golimumab – PBS item codes 11538G & 11560K, Restriction Summary 11483 as at 1February 2023; shaded area indicates difference with golimumab):</p>
	<p>Indication: Non-radiographic axial spondyloarthritis</p>
	<p>Treatment Phase: Initial treatment - Initial 2 (Change or re-commencement of treatment after a break in biological medicine of less than 5 years)</p>
	<p>Clinical criteria:</p>

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	Patient must have received prior PBS-subsidised treatment with a biological medicine for this condition in this treatment cycle
	AND
	Clinical criteria:
	The condition must not have responded inadequately to biological medicine on 4 occasions within the same treatment cycle
	AND
	Clinical criteria:
	Patient must not have failed PBS-subsidised therapy with this biological medicine for this PBS indication more than once in the current treatment cycle
	AND
	Clinical criteria:
	The treatment must not exceed a maximum of 16 weeks with this drug under this restriction.
	Population criteria:
	Patient must be at least 18 years of age
	Treatment criteria:
	Must be treated by rheumatologist; or
	Must be treated by a clinical immunologist with expertise in the management of non-radiographic axial spondyloarthritis.
	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., 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.
	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: (a) a CRP measurement no greater than 10 mg per L; or, (b) a CRP measurement reduced by at least 20% from baseline.
	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.
	Prescribing Instructions: BASDAI scores and CRP levels must be documented in the patient's medical records.
	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.
	Prescribing Instructions: The following must be provided at the time of application and documented in the patient's medical records: (a) the BASDAI score; and, (b) the C-reactive protein (CRP) level.
	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. Monday to Friday).
<p>Add Restriction Summary [New] / Treatment of Concept: [New]: Authority Required (telephone/online PBS Authorities system) (modelled of golimumab – PBS item codes 11538G & 11560K, Restriction Summary 10525 as at 1 February 2023; shaded area indicates difference with golimumab):</p>	

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	Indication: Non-radiographic axial spondyloarthritis
	Treatment Phase: Initial treatment - Initial 3 (Resumption 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:
	Patient must have had 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:
	The treatment must not exceed a maximum of 16 weeks with this drug under this restriction.
	Population criteria:
	Patient must be at least 18 years of age
	Treatment criteria:
	Must be treated by rheumatologist; or
	Must be treated by a clinical immunologist with expertise in the management of non-radiographic axial spondyloarthritis.

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	<p>Prescribing 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.</p>
	<p>Prescribing Instructions: The BASDAI score and CRP level must be no more than 4 weeks old at the time of this application.</p>
	<p>Prescribing 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>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>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. Monday to Friday).</p>
<p>Add Restriction Summary / Treatment of Concept:: Authority Required (telephone/online PBS Authorities system); (copy from golimumab – PBS item codes 11538G & 11560K as at 1 February 2023; shaded area indicates difference with golimumab):</p>	
	<p>Indication: Non-radiographic axial spondyloarthritis</p>
	<p>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</p>
	<p>Clinical criteria:</p>
	<p>Patient must have received insufficient therapy with this drug for this condition under the Initial 1 (new patient) restriction to complete 16 weeks treatment; or</p>
	<p>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 16 weeks treatment; or</p>
	<p>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 16 weeks treatment</p>
	<p>AND</p>
	<p>Clinical criteria:</p>
	<p>The treatment must provide no more than the balance of up to 16 weeks treatment.</p>
	<p>Treatment criteria:</p>
	<p>Must be treated by rheumatologist; or</p>
	<p>Must be treated by a clinical immunologist with expertise in the management of non-radiographic axial spondyloarthritis.</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. Monday to Friday).</p>

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Category / Program: GENERAL – General Schedule (Code GE)					
MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
UPADACITINIB					
upadacitinib 15 mg modified release tablet, 28	NEW (Do not add to 12621G) MP	1	28	5	Rinvoq
Add Restriction Summary [New] / Treatment of Concept [New]: Authority Required (telephone online PBS Authorities system); (modelled of golimumab – PBS item codes 11521J & 11516D, Restriction Summary 10630 as at 1February 2023; shaded area indicates difference with golimumab):					
	Administrative Advice: insert updated concept 27999 here (see end of document)				
	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: Special Pricing Arrangements apply.				
	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 biological 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				
	Population criteria:				
	Patient must be at least 18 years of age				
	Treatment criteria:				
	Must be treated by rheumatologist; or				
	Must be treated by a clinical immunologist with expertise in the management of non-radiographic axial spondyloarthritis.				
	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: (a) a CRP measurement no greater than 10 mg per L; or (b) a CRP measurement reduced by at least 20% from baseline.				
	Prescribing 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.				

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	Prescribing 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.
	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. Monday to Friday).
Add Restriction Summary / Treatment of Concept:: Authority Required (<i>telephone/online PBS authorities system</i>); (<i>copied from golimumab</i>)	
	Indication: Non-radiographic axial spondyloarthritis
	Treatment Phase: Continuing treatment - balance of supply
	Clinical criteria: Patient must have received insufficient therapy with this drug under the Continuing treatment restriction to complete 24 weeks of treatment
	AND
	Clinical criteria: The treatment must provide no more than the balance of up to 24 weeks of treatment.
	Treatment criteria: Must be treated by 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. Monday to Friday).
Add Restriction Summary [NEW] / Treatment of Concept: [NEW]: Authority Required (<i>in writing only</i>)	
	Indication: Non-radiographic axial spondyloarthritis
	Treatment Phase: Transitioning from non-PBS to PBS-subsidised supply – ‘Grandfather’ arrangements
	Clinical criteria: Patient must have commenced treatment with this biological medicine for this condition prior to [insert listing date here].
	AND
	Clinical criteria: The condition must not have responded inadequately to biological medicine on 4 occasions within the same treatment cycle
	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,

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	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:
	The treatment must not exceed a maximum of 24 weeks with this drug per authorised course under this restriction
	Population criteria:
	Patient must be at least 18 years of age
	Treatment criteria:
	Must be treated by rheumatologist; or
	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.
	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) score 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.
	Prescribing 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>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 authority application must be made in writing and must include: (a) a completed authority prescription form(s); and (b) a completed authority application form relevant to the indication and treatment phase (the latest version is located on the website specified in the Administrative Advice).</p>
	<p>Prescribing 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. 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>

<p>Administrative Advice: TREATMENT OF ADULT PATIENTS WITH NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS – TREATMENT CYCLES AND TREATMENT PHASES</p> <p>The following information applies to the prescribing under the Pharmaceutical Benefits Scheme (PBS) of secukinumab, 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 secukinumab, certolizumab pegol, and golimumab only pharmaceutical benefits listed specifically for the indication of: non-radiographic axial spondyloarthritis. Some listed pharmaceutical benefits are technically not biological medicines (e.g. Janus-kinase inhibitors), but for practical purposes, have been included under the broad term of 'biological medicine'.</p> <p>A patient is eligible for PBS-subsidised treatment with only 1 of the 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>Treatment cycles:</p> <p>A treatment cycle commences when the authority application for first PBS-subsidised biological medicine is approved for a given patient under the 'Initial 1' treatment phase. The treatment cycle continues until a third fourth biological medicine number fails to provide the patient with an adequate response. A new treatment cycle begins each time PBS-subsidy is obtained through the 'Initial 3' treatment phase.</p> <p>Within the same a treatment cycle, a patient cannot trial and fail, or cease to respond to, the same PBS-subsidised biological medicine <i>must not be subsidised more than once where it has failed to provide the patient with an adequate response on any occasion that a response assessment is conducted.</i></p> <p>Once a patient has either failed or ceased to respond to treatment biological medicines have failed to provide a patient with an adequate response 3 4 times (once with any biological medicine) within the same treatment cycle, they are deemed to have completed a treatment cycle <i>has been completed</i> and they patient 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><i>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 completed treatment attempt.</i></p> <p>A patient who has failed Where there has been fewer than 3 trials 4 inadequate responses with of biological medicine therapy in a treatment cycle and who has there has been a break in therapy of less than 5 years, the patient may commence a further course of continue treatment within the same treatment cycle.</p> <p>A patient who has had 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 <i>with up to 4 treatment attempts.</i></p> <p>There is no limit to the number of treatment cycles a patient may undertake in their lifetime.</p> <p>Treatment phases: How to prescribe PBS-subsidised biological medicine treatment with secukinumab, certolizumab pegol, upadacitinib and golimumab:</p> <p>(1) 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 <i>has been prescribed – apply through the ('Initial 1 - New patient')-treatment phase</i></p>

	<p>(ii) a patient has received prior PBS-subsidised (initial or continuing) biological medicine therapy, and wishes to but is not prescribed an alternate agent biological medicine - apply through the (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 is recommencing treatment with a specific biological medicine following a break in PBS-subsidised therapy of less than 5 years with the same agent - apply through the (Initial 2 - Change or Recommencement of treatment after a break in therapy of less than 5 years) <i>treatment phase (note that where there is both a change and recommencement after less than 5 years occurring simultaneously, Initial 2 is the correct treatment phase to apply through)</i>; or</p> <p>(iv) a patient wishes to is recommencing treatment with a biological medicine following a break in PBS-subsidised therapy of more than 5 years – apply through the (Initial 3 - Recommencement of treatment after a break in biological medicine of more than 5 years) <i>treatment phase</i>.</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>(2) Continuing treatment.</p> <p>For continuing courses of PBS-subsidised <i>of biological medicine</i> it is recommended that a patient be reviewed the month prior to completing their current course when the continuing dose is due 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 Continuing PBS subsidy is available in quantities/repeats that provide up to 24 weeks of continuing treatment with that biological medicine provided they have demonstrated where an adequate response to the immediately preceding supply of treatment has been experienced. 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-treatment will be deemed to have failed to respond to treatment with that biological medicine provide an adequate response, unless the patient has experienced a serious adverse reaction requiring permanent treatment withdrawal.</p> <p>(3) Swapping therapy <i>Changing the prescribed biological medicine.</i></p> <p>Once initial treatment with the first PBS-subsidised biological medicine is approved, a patient may swap to an alternate biological medicine <i>may be prescribed</i> 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. <i>An authority application must be made under the 'Initial 2' treatment phase and must indicate the response to the preceding biological medicine in terms of whether the response was adequate or not. The prescription for the discontinued biological medicine must be marked as cancelled by the prescriber.</i></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.</p> <p>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 untreated with biological medicines, 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>
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	<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.</p> <p>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 <i>occur through</i> 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> <p>(6) Balance of Supply Where the full number of repeat prescriptions have not been requested under any initial or continuing listing, apply for the balance of the supply of the repeats under any treatment phase listing containing the words "balance of supply".</p>
<p>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</p> <p>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</p> <p>12321L / secukinumab 150 mg/mL injection, 1 mL pen device 12297F / secukinumab 150 mg/mL injection, 1 mL pen device 12307R / secukinumab 150 mg/mL injection, 1 mL pen device</p>	

Flow-on changes:

Update the treatment attempts per treatment cycle with the following new words:

MEDICINAL PRODUCT - PBS item code(s)	Restriction Summary number (as at 1February 2023)
CERTOLIZUMAB PEGOL – 12027B & 12063X	11462
GOLIMUMAB – 11538G & 11560K	11483
SECUKINUMAB – 12321L	11463
<i>Current concept/text to remove:</i>	
	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
<i>New concept/text to insert:</i>	
Insert	Clinical criteria:
	The condition must not have responded inadequately to biological medicine on 4 occasions within the same treatment cycle

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

13 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.

14 Sponsor's Comment

The sponsor had no comment.