

7.03 GOLIMUMAB,

Injection 50 mg in 0.5 mL single use pre-filled syringe and injection 50 mg in 0.5 mL single use pre-filled pen, Simponi® and Simponi Smartject®, Janssen-Cilag Pty Ltd

1 Purpose of application

- 1.1 The resubmission requested Authority Required listing for golimumab for the treatment of non-radiographic axial spondyloarthritis (nr-axSpA).
- 1.2 The requested basis for listing was a cost-utility analysis of golimumab and background non-steroidal anti-inflammatory drugs (NSAIDs) versus conventional care (as represented by placebo plus background NSAIDs). The first submission was considered at the November 2017 PBAC Meeting.
- 1.3 The key components of the clinical issue addressed by the resubmission are presented in Table 1. Changes compared with the previous submission are underlined. The ESC noted that a key change was that the restriction proposed in the resubmission required patients to have both elevated C reactive protein (CRP) and sacroiliitis on magnetic resonance imaging (MRI), rather than only requiring one or the other (as requested by the PBAC in its November 2017 consideration). The ESC noted this would limit use to a much smaller number of patients.

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

Component	Description
Population	Patients with non-radiographic axial spondyloarthritis (nr-axSpA), as defined by Assessment of Spondyloarthritis International Society (ASAS) criteria. Patients must have objective signs of inflammation (OSI) as indicated by <u>elevated C-reactive protein (CRP) and magnetic resonance imaging (MRI) evidence</u> , and have had an inadequate response to, or are intolerant to, at least two nonsteroidal anti-inflammatory drugs (NSAIDs) for a period of 3 months.
Intervention	Golimumab 50 mg, subcutaneous injection once every 4 weeks, on the same date each month. Golimumab may be administered in combination with NSAIDs or as monotherapy.
Comparator	Placebo in combination with conventional care (CC), where CC is defined as 'with NSAID background treatment' (\pm NSAID treatment). The PBAC had previously accepted that the nominated comparator was appropriate (6.04 Golimumab PBAC November 2017 PSD, paragraph 5.1). [The clinical and economic comparison is golimumab + CC versus placebo + CC].
Outcomes	Clinical response (Primary outcome of ASAS 20); change in patient reported outcomes, change in physician's global visual analogue scale, change in safety and tolerability.
Clinical claim	In patients with nr-axSpA, who have OSI as indicated by elevated CRP and MRI evidence, and who have had an inadequate response to, or are intolerant to, NSAIDs, golimumab is superior in effectiveness, with an <u>inferior safety</u> profile compared to placebo + CC..

Source: Table 1.1.1, p22-23 of the resubmission

2 Requested listing

Name, restriction, manner of administration, form	Maximum quantity (packs)	Maximum quantity (units)	No. of repeats	Dispensed price for maximum quantity	Proprietary name and manufacturer	
GOLIMUMAB						
Initial treatment						
50mg/0.5mL pre-filled syringe	1	1	<u>3</u>	\$1,317.93	SIMPONI, Janssen-Cilag Pty Ltd	
50mg/0.5mL pre-filled pen	1	1	<u>3</u>	\$1,317.93		
Continuing treatment						
50mg/0.5mL pre-filled syringe	1	1	5	\$1,317.93		
50mg/0.5mL pre-filled pen	1	1	5	\$1,317.93		

ABBREVIATED VERSION:

Category / Program	General Schedule (Code GE)
Prescriber type:	<input checked="" type="checkbox"/> Medical Practitioners
PBS Indication:	Active non-radiographic axial spondyloarthritis
Treatment phase:	Initial treatment - Initial 1 (new patients)
Restriction:	<input checked="" type="checkbox"/> Authority Required - In Writing
Clinical criteria:	<p>The condition must be non-radiographic axial spondyloarthritis, as defined by Assessment of Spondyloarthritis International Society (ASAS) criteria</p> <p>AND</p> <p>Patient must have chronic lower back pain and stiffness for 3 or more months that is relieved by exercise but not rest,</p> <p>AND</p> <p>Patient must have BASDAI of at least 4</p> <p>AND</p> <p>Patient must have failed to achieve an adequate response following treatment with at least 2 NSAIDs whilst completing an appropriate exercise program, for a total period of 3 months</p> <p>AND</p> <p>Patient must have elevated CRP level of <u>greater than 10mg/L^a</u>.</p> <p>AND</p> <p>The condition must be sacroiliitis with active inflammation and/or oedema that is not visible on a plain X-ray but is visible on MRI;</p> <p>AND</p> <p>The patient must have experienced one or more of the following: (a) <u>Enthesitis (heel)</u>; (b) <u>Uveitis</u>; (c) <u>Dactylitis</u>; (d) <u>Psoriasis</u>; (e) <u>Inflammatory bowel disease</u>; OR (f) <u>HLA-B27^b</u>.</p>
Population criteria	Patient must be an adult over 18 years of age
Treatment criteria	Must be treated by a rheumatologist
Treatment phase:	Initial treatment – initial 2 (initial PBS-subsidised supply for continuing treatment in a patient commenced on non-PBS-subsidised therapy or recommencement in a patient who has had previous PBS-subsidised therapy) and continuing treatment
Clinical criteria:	<p>Patient must have a documented history of non-radiographic axial spondyloarthritis</p> <p>AND</p> <p>Patient must have previously received PBS-subsidised therapy with this drug for this condition</p> <p>AND</p> <p>Patient must have previously demonstrated an adequate response to PBS-subsidised therapy with this drug for this condition based on a reduction in the BASDAI score by 2 or more units</p>

^a elevated CRP was defined as a 'level greater than the upper limit of normal' in the requested restriction in the previous submission.

^b the patient must have experienced one or more of the following: (a) Arthritis; (b) Enthesitis (heel); (c) Uveitis; (d) Dactylitis; (e) Psoriasis; (f) Inflammatory bowel disease; (g) Family history of spondyloarthritis; (h) HLA-B27; or (i) Elevated CRP in the requested restriction in the previous submission

The full version of the requested restriction can be found in Table Att.1.4.1, Attachment 1 of the commentary

- 2.1 The Dispensed Price for Maximum Quantity (DPMQ) proposed in the resubmission was [REDACTED] % lower than the previous submission (revised DPMQ of \$1,317.93 versus \$[REDACTED]). The Pre-Sub-Committee Response (PSCR) stated this was to address “uncertainty issues” with the restriction. The DPMQ requested in the resubmission was the same as the current PBS price for golimumab, which the submission stated is the weighted price across various indications.
- 2.2 No special pricing arrangement was proposed, however the resubmission proposed that the Sponsor would work with the Secretariat and the Department to incorporate the final negotiated price for patients with nr-axSpA into the weighted price calculation that currently exists for golimumab across the PBS listed indications.
- 2.3 In November 2017, the PBAC considered that a number of changes to the restriction would be required in order to better target patients with the highest clinical need and those who would benefit the most, see Table 2 (6.04 Golimumab PBAC November 2017 Public Summary Document (PSD), paragraph 7.4). Table 2 also summarises whether the resubmission incorporated these changes, along with the rationale provided in the resubmission for not incorporating some of the changes.

Table 2: Recommendations based on the previous submission for restricting use to the appropriate patient group

Recommended additions to the requested restriction (6.04 Golimumab November 2017 PBAC Public Summary Document, paragraphs 2.7 and 7.4)	Incorporated?	Rationale in the resubmission for not incorporating
Limit use to patients with <u>elevated CRP and positive MRI</u>	✓	
Initial treatment: “the condition must be sacroiliitis with active inflammation and/or oedema that is not visible on a plain X-ray but is visible on MRI; AND the patient must have experienced one or more of the following: (a) Enthesitis (heel); (b) Uveitis; (c) Dactylitis; (d) Psoriasis; (e) Inflammatory bowel disease; OR (f) HLA-B27.”	✓	In July 2018, the PBAC considered that more work would be required on the definition of changes visible on MRI in the proposed restriction to exclude changes that would be documented to occur in the normal population.
For the elevated CRP, there should be no allowance made for patients currently on corticosteroids with normal inflammatory markers	✓	Though the resubmission argued that some patients have a clinical need for corticosteroids, the resubmission stated that such use is not common, and that this was accounted for in the revised price and RSA. The ESC noted the requested restriction had <u>not</u> included any exceptions to the CRP requirement for patients using concurrent corticosteroids. The ESC considered this was appropriate (i.e. no exceptions). The PBAC considered that 8-10% of patients may be on corticosteroids.
For the positive MRI there should be independent reading and confirmation of sacroiliitis by radiologists who are blinded to the patient’s history, as the diagnosis of sacroiliitis on MRI can be subjective, especially earlier in the course of the disease	x	Insufficient radiologists trained in diagnosis in Australia. The ESC agreed this may be difficult to implement in practice as patients may have insufficient access to radiologists.
Limit use to patients with an age of onset of back pain of 45 years or less, per the GO-AHEAD trial	x	Part of ASAS diagnostic criteria. The ESC further noted this may be difficult to prove as it would be based on patient history.
Limit use to patients with a symptom duration of less than five years, per the GO-AHEAD trial	x	Delayed diagnosis is common; diagnosis may take > 5 years. The ESC noted this would exclude some patients with delayed diagnosis or whose condition has deteriorated.
Include a stopping rule, whereby patients must cease treatment after a certain time period. Patients could re-commence if they relapse. This was based on the lack of long-term data for golimumab, and supported by a study that showed that some patients maintain their response after discontinuing biologic therapy	x	Insufficient evidence for fixed course followed by treatment cessation. The PSCR stated that a continuation rule (based on a reduction from baseline in the BASDAI score by > 2) was included instead of a stopping rule. The ESC noted that the continuation rule differed to the stopping rule proposed by the PBAC where patients would cease regardless of response. The ESC noted there was no evidence for prolonged use in this indication and considered that a stopping rule should have been considered in the requested restriction.

Source: Compiled during the evaluation from section 1 of the resubmission and the 6.04 golimumab November 2017 PBAC Public Summary Document, paragraphs 2.7 and 7.4

2.4 Compared to the requested restriction in the previous submission, the following changes have been made:

- Requesting listing of both the pre-filled syringe and pre-filled pen (only the pre-filled syringe was requested in the previous submission);

- A reduction in the number of repeats from 4 to 3 for initial treatment (as requested by the PBAC in November 2017);
 - The proposed listing for Initial 2 has changed between submissions. Advice received from the Sponsor during the evaluation indicated that the intention for the Initial 2 listing was to cover patients who either re-commence (have had previous PBS-subsidised therapy) or who are grandfathered onto PBS-subsidised therapy (have not had previous PBS-subsidised therapy, though this was not specified in the requested listing provided) and indicated that a further (Initial 3) listing may be required to cover both these patient groups. Amended wording in relation to the recommencing and grandfathering listings was not provided.
- 2.5 The resubmission included requirements for patients to have (i) both elevated CRP and sacroiliitis on MRI; and (ii) the condition must be sacroiliitis with active inflammation and/or oedema that is not visible on a plain X-ray but is visible on MRI; AND the patient must have experienced one or more of the following: (a) Enthesitis (heel); (b) Uveitis; (c) Dactylitis; (d) Psoriasis; (e) Inflammatory bowel disease; OR (f) positive HLA-B27 for eligibility in the initial treatment phase (as requested by the PBAC in November 2017). The PSCR stated that the sponsor was “willing to accept the changes in the Restriction suggested by the PBAC and highlighted in the Commentary, but believes that these changes need careful consideration in terms of the implications for clinicians”.
- 2.6 The ESC considered that there may be practical issues with including some of these criteria, recalling that the PBAC had previously considered that some of these factors would be difficult to address adequately within a PBS restriction (Para 7.4, November 2017 PSD). As such, the ESC considered that alternative methods, such as a Risk Sharing Arrangement (RSA), may be required to address the risk of use outside the intended population (i.e. patients with the highest clinical need and those who would benefit the most). The pre-PBAC response stated that defining an appropriate population through a restriction would be difficult and proposed a revised RSA in order to address the risk of use outside the intended population (see *Financial management – risk sharing arrangements* section).
- 2.7 As noted in Table 2, the PBAC considered more work would be required on the definition of changes visible on MRI in the proposed restriction to exclude changes that would be documented to occur in the normal population.

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

3 Background

Registration status

- 3.1 Golimumab was registered on 2 September 2016 for the treatment of adults with active nr-axSpA with objective signs of inflammation (OSI) as indicated by elevated

CRP and/or MRI evidence, who have had an inadequate response to, or are intolerant to, non-steroidal anti-inflammatory drugs (NSAIDs).

3.2 Table 3 outlines the registration status of biologic agents that are registered for use in nr-axSpA and/or ankylosing spondylitis in Australia and internationally.

Table 3: Summary of biological agents that are registered for use in AS or nr-axSpA in Australia and internationally

Drug	TGA-registration		International registration for nr-axSpA	
	AS	nr-axSpA	FDA ^a	EMA ^b
Adalimumab	✓	x	x	✓
Certolizumab	✓	x	x	✓
Etanercept	✓	✓	x	✓
Etanercept biosimilar	✓	✓	-	-
Golimumab	✓	✓	x	✓
Infliximab	✓	x	x	x
Infliximab biosimilar	✓	x	-	-
Secukinumab	✓	x	x	x

AS = ankylosing spondylitis; EMA = European Medicines Agency; FDA = Food and Drug Administration; nr-axSpA = non-radiographic axial spondyloarthritis; tx = treatment

^a Proft et al stated: “ the US FDA rejected the approval for TNF inhibitors for nr-axSpA, due to questions about the specificity of the ASAS criteria and the natural history of the disease entity, hinting that a significant proportion of these patients may show spontaneous remission and therefore might not require the costly and potentially harmful anti-TNF therapy.”

^b Proft et al stated: “The EMA further demanded a therapy-withdrawal trial design to investigate whether patients with nr-axSpA can achieve a disease state of ‘drug-free remission’ after a treatment cycle like an ‘induction therapy’. These trials are still ongoing.”

Source: Compiled during preparation of ESC advice; Proft F, Poddubnyy D ‘Ankylosing spondylitis and axial spondyloarthritis: recent insights and impact of new classification criteria’, Therapeutic Advances in Musculoskeletal Disease, 2018; 10 (5-6), p. 129 – 139. Accessed at: <http://journals.sagepub.com/doi/full/10.1177/1759720X18773726>

Previous PBAC consideration

3.3 This was the second submission to the PBAC for golimumab for the treatment of patients with nr-axSpA. Matters of outstanding concern from the November 2017 PBAC Meeting are summarised in Table 4.

Table 4: Summary of outstanding matters of concern

Component	Matter of concern	How the resubmission addresses it
Restriction	See Table 2 above	
Clinical issues	The claim of non-inferior comparative safety was not adequately supported by the data (Para 7.6).	A claim of inferior safety was included.
	It was unclear whether the incremental benefit would be sustained long-term (Para 7.5).	A price discount was offered to take into account uncertainty surrounding long-term cost-effectiveness.
Economic model	Lack of long-term data to inform the model (Para 7.7).	Reduced model to a 20 year time horizon (from 30 years) and a discounted DPMQ to account for uncertainty. No additional follow-up data were included (still based on 16 weeks of RCT data plus 32 weeks of open-label follow-up)

Component	Matter of concern	How the resubmission addresses it
	Confine use to patients likely to achieve a very high level of response (Para 7.7).	Although the requested listing was amended to those with elevated CRP and positive MRI, the population in the model was the OSI population from the GO-AHEAD trial; █% of patients in the OSI subgroup met both criteria. The ESC noted that this further limited the applicability of the trial data (i.e. only █% of the total trial population would meet the requirement for elevated CRP and positive MRI; and the trial applicability was further limited due to less stringent requirements around prior NSAIDs and no requirement for to have completed an exercise program in the RCT).
	Inappropriate assumption that all CC responders at Week 16 (28.8%) lose their response (revert to non-responder) by Week 32 (Para 7.7).	All CC responders at Week 16 (28.8%) were assumed to lose their response (revert to non-responder) by Week 52 (rather than 32 weeks in the previous submission). The ESC noted that this was not supported by any RCT data.
	Assumptions around discontinuation rates (█%) may not have been applicable (Para 7.7).	Discontinuation rates: █% per annum and a █% additional discontinuation due to AEs.
	Reasonable for the base case to include transitions to AS, although there was limited reliable data to inform the rate of progression to AS (Para 7.7).	Base case did not include transitions to AS.
	The model should have included costs and disutilities to address the long-term safety of golimumab (Para 7.7).	Increased cost of serious infection management, and disutility added for serious infection for 2 weeks, with serious infection rates of █%/year.
	The transition parameters used in the model were largely fixed over the course of the model; did not appear to represent the clinical course (Para 6.45).	Not addressed.
	Derivation of the regression equation to assign utility scores to health states could not be validated (PBAC Minutes, Table 8).	Additional information provided, although it was unclear whether the same regression equation would be applicable over the longer term. The ESC noted it was not based on Australian data.
	Annual disease costs were based on a regression equation from Tilden (2004) with health care costs linked to BASFI scores. "The original COI study (Tilden 2004) provides no detailed information on the methodology of the study...nor does it provide information on the specific costs included other than specifying 'categories' of costs. As such, the validity of this regression equation in predicting nr-axSpA disease-management costs was unclear." (Golimumab Nov.2017 PBAC PSD, Table 8)	Not addressed.
Financial impact: High and uncertain financial impact	The number of eligible patients was based on studies that were not relevant to the Australian population (Para 7.9)	Same prevalence rate used from US Strand 2013 study: Not addressed.
	Patients 45 years or older who were diagnosed before the age of 45 should have been included in the financial estimates (Para 7.9).	An allowance was made for an additional 5% of the estimated prevalent patient population to be aged over 45 years.
	16 weeks initial treatment in estimates: inconsistent with the requested listing of 20 weeks (Para 7.9).	The requested listing in the resubmission was for 16 weeks of initial treatment. Issue addressed.

Component	Matter of concern	How the resubmission addresses it
	Uptake rates and continuation rates may be higher than estimated due to high unmet clinical need and ease of use (Para 7.9).	The resubmission used higher uptake rates, although continuation rates were not increased. The resubmission used higher discontinuation rates.
	High likelihood of substantial leakage beyond the proposed population (in those with chronic back pain) (Para 7.9).	Not specifically addressed: although a RSA might be negotiated to reduce leakage. Details of an RSA were provided in the PSCR.
	Hospital costs may not represent a real cost-offset (Para 6.52). Estimated cost-offsets to the PBS from nr-axSpA medications were unclear (Para 6.52).	Previously included hospital costs and disease related costs were excluded. The PSCR included hospitalisation costs for treating serious infections. The ESC noted that other hospitalisation costs that were applied in the economic model (i.e. annual disease costs rather than specific adverse event costs) were not based on recent Australian data so may not represent reliable estimates.
Price	Any future submission for a bDMARD for this condition would need to ... propose a lower cost per patient in the context of the lack of long-term outcome data (Para 7.10).	The proposed DPMQ proposed was lowered by approximately █% to \$1,317.93.

Para = paragraph; CC = conventional care; AE = adverse events; MRI = magnetic resonance imaging; CRP = C-reactive protein; RSA = risk sharing arrangement; AS = ankylosing spondylitis; RCT = randomised controlled trial; bDMARD = biological disease-modifying anti-rheumatic drug

Note: All paragraph references refer to the Golimumab PBAC Public Summary Document, November 2017 unless otherwise stated

Source: Compiled during the evaluation.

4 Population and disease

- 4.1 Axial spondyloarthritis (axSpA) is a spectrum of related immune mediated diseases with diverse clinical presentations that all feature axial inflammatory arthritis. Axial spondyloarthritis includes both nr-axSpA and ankylosing spondylitis (AS). Although not well characterised, risk factors for progression from nr-axSpA to AS include elevated CRP, baseline inflammation on MRI and positivity for the HLA-B27 gene (Dougados M, 2017).

5 Comparator

- 5.1 The resubmission nominated conventional care (CC), as represented by placebo in the GO-AHEAD trial, plus background NSAIDs (\pm NSAIDs) as the comparator. This was the same comparator as that nominated for the previous submission, which the PBAC considered appropriate.

6 Consideration of the evidence

Sponsor hearing

- 6.1 The sponsor requested a hearing for this item. The sponsor outlined the RSA proposed in the pre-PBAC response and the issues with limiting use to the population requested by PBAC via means of a restriction.

Consumer comments

- 6.2 The PBAC noted and welcomed the input from individuals (4), health care professionals (5) and organisations (1) via the Consumer Comments facility on the PBS website. The comments outlined the impacts of nr-axSpA on patients' ability to work, exercise, study, and maintain family life. The comments described a range of benefits of treatment with golimumab including the early use of a biological disease-modifying anti-rheumatic drug (bDMARD) reducing symptoms and radiographic progress, giving these patients better long term outcomes. Health professionals requested that evidence of change be well described and exclude minor changes or the changes on MRI documented to occur in the normal population. The concern was without sufficient restriction there was potential for a very large market and exposure of patients to unnecessary risks of treatment with a bDMARD.
- 6.3 The PBAC noted the advice received from CreakyJoints Australia clarifying the likely use of golimumab in clinical practice. The PBAC specifically noted the advice that the current treatment options for patients are limited and often less effective than a bDMARD. It was further stated that it is important for patients with nr-axSpA to have access to as many treatment options as possible, to reduce the chance of bone damage and progression of the disease. The PBAC noted that this advice was generally supportive of the evidence provided in the submission, although no long term comparative data was available.

Clinical trials

- 6.4 The resubmission was based on the same head-to-head randomised trial (GO-AHEAD) that was presented in the previous submission. The trial compared golimumab 50 mg once every 4 weeks (n=98) to placebo (n=100) with an assessment at 16 weeks (GO-AHEAD Part I), with patients in both treatment arms being able to receive background NSAID therapy.
- 6.5 The GO-AHEAD trial also included an open-label extension phase in which all patients received golimumab 50 mg from Week 16 up to the final assessment point at Week 52 (GO-AHEAD Part II). A safety assessment was available up to Week 60.
- 6.6 Details of the trial remain unchanged from the previous submission and are provided in Table 5.

Table 5: Trials and associated reports presented in the resubmission

Trial ID	Protocol title/ Publication title	Publication citation
Direct randomised trial		
GO-AHEAD (CSR P006)	A Multicenter, Randomized, Double-blind, Placebo-controlled Study of the Effect of Golimumab (GLM) Administered Subcutaneously (SC) in Subjects with Active Axial Spondyloarthritis (SpA)	02 October 2014 (24-week CSR) 12 November 2015 (60-week CSR)
	Sieper et al. A randomized, double-blind, placebo-controlled, 16-week study of subcutaneous golimumab in patients with active nonradiographic axial spondyloarthritis	Arthritis and Rheumatology 2014; 66:S1283-S1284
	Sieper et al. A randomized, double-blind, placebo-controlled, sixteen-week study of subcutaneous golimumab in patients with active nonradiographic axial spondyloarthritis	Arthritis & rheumatology 2015; 67: (10):2702-2712.
	Sieper et al. Efficacy of golimumab for nonradiographic axial spondyloarthritis (nr-axSpA): Subgroup analysis by baseline MRI and C-reactive protein status	Arthritis and Rheumatology 2016; 68:943-945

Source: Table 2.2.1, p55 of the resubmission

6.7 The key features of the direct randomised trial were identical to those previously presented and are shown in Table 6.

Table 6: Key features of the GO-AHEAD trial

Therapy (N randomised)	Design/duration	Risk of bias	Patient population	Key outcomes	Use in modelled evaluation
Golimumab 50mg (98) Placebo (100)	Part I: R, MC, DB, 16 weeks Part II: OL extension of golimumab only to Week 52	Low in Part I	nr-axSpA	Primary: ASAS 20 Secondary: BASDAI, BASFI, EQ-5D	BASDAI 50 response at Week 16 EQ-5D data used to develop regression model to estimate change in utilities

R = randomised; MC = multi-centre; DB = double-blind; OL = open-label; nr-axSpA = non-radiographic axial spondyloarthritis; ASAS = Ankylosing Spondylitis Activity Score; BASDAI = Bath Ankylosing Spondylitis Disease Activity Index; BASFI = Bath ankylosing spondylitis functional index; EQ-5D = EuroQoL 5D Health Questionnaire

Source: Sections 2.3, 2.4, 2.5 and Section 3 of the resubmission

6.8 The resubmission was based on a pre-specified subgroup of patients with objective signs of inflammation (OSI) in the GO-AHEAD trial. The OSI population (n=158; 80%) consisted of patients with baseline evidence of sacroiliitis (active inflammation) on MRI and/or a screening C-reactive protein (CRP) greater than the upper limit of normal (ULN). This differed to the proposed PBS population who are required to have both an elevated screening CRP level greater than the ULN and evidence of sacroiliitis on MRI. Of the 158 patients with OSI, ■ (■■■%); or ■■■% of the total population) had both an elevated CRP and a positive MRI.

6.9 The ESC noted that this was a relatively small proportion of the total trial population, which may have reduced the applicability of the results. The applicability of the trial was further reduced as patients in the trial: were only required to have trialed one prior NSAID (versus two in the PBS restriction); and were not required to have completed an exercise program (required in the PBS restriction).

Comparative effectiveness

6.10 The results presented for comparative effectiveness in the resubmission were the same as those presented for the previous submission, summarised in Table 7.

Table 7: GO-AHEAD Trial Part I: Proportion of patients achieving ASAS 20 response (primary outcome) and BASDAI 50 endpoints at 16 weeks in the whole (FAS) and OSI and non-OSI populations

Population	Golimumab 50mg n/N (%)	Placebo n/N (%)	Relative risk (95% CI)	Risk difference (%) (95% CI); p-value
ASAS 20 (primary outcome)				
Whole trial (FAS)	69/97 (71.1%)	40/100 (40.0%)	1.78 (1.36, 2.33)	31.2 (17.5, 43.6), p<0.0001
OSI	60/78 (76.9%)	30/80 (37.5%)	2.05 (1.51, 2.79)	39.6 (24.6, 52.6), p<0.0001
Non-OSI	9/19 (47.4%)	10/20 (50.0%)	0.95 (0.50, 1.81)	2.6 (-32.7, 27.9), p<0.8711
Test for interaction (OSI v non-OSI) ^a			p=0.017	p=0.034
BASDAI 50 (relied on in the economic evaluation)				
Whole trial (FAS)	56/97 (57.7%)	30/100 (30.0%)	1.92 (1.36, 2.72)	28.0 (14.4, 40.6), p<0.0001
OSI	46/78 (59.0%)	23/80 (28.8%)	2.05 (1.39, 3.03)	30.5 (15.4, 44.3); p<0.0001
Non-OSI	██████████	██████████	██████████	██████████
Test for interaction (OSI v non-OSI) ^a			██████████	██████████

Source: Table 2.6.1, p127 and Table 2.6.2, p129 of the resubmission

^a Test for interaction conducted during the evaluation

ASAS 20 = Ankylosing Spondylitis Disease Activity Score; BASDAI = Bath Ankylosing Spondylitis Disease Activity Index; CI = confidence interval; FAS = full analysis set; OSI = objective signs of inflammation

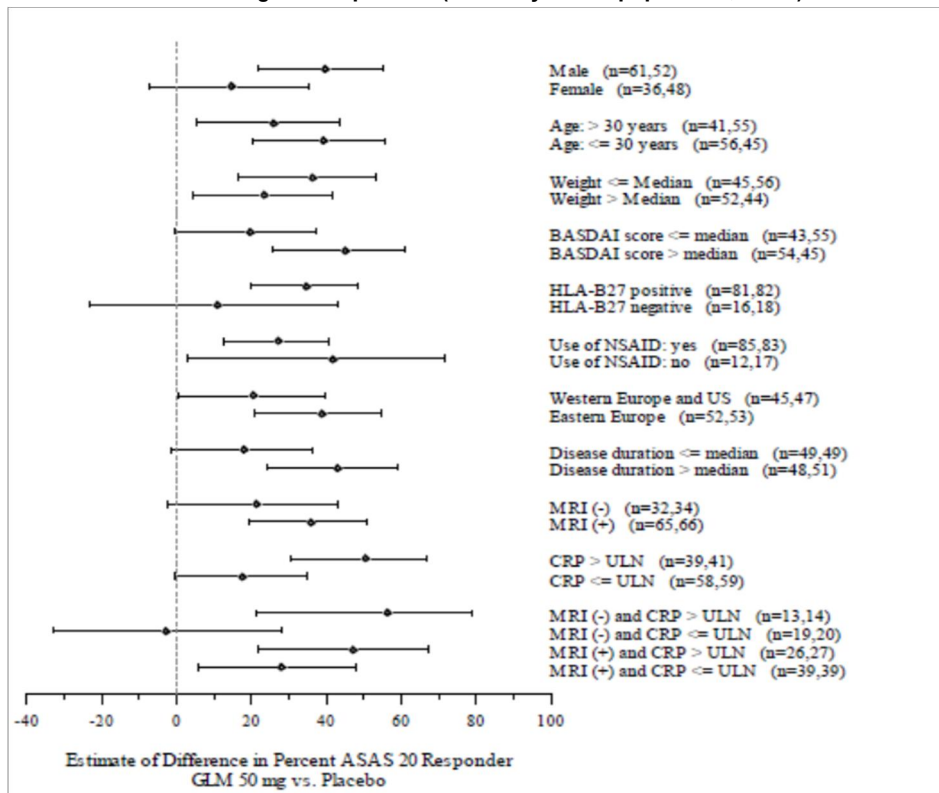
Bold indicates statistically significant differences

6.11 The analyses were not adjusted for multiplicity and it was unclear whether the presence of OSI was a treatment effect modifier given the probable lack of power in the non-OSI population. The proportion of patients who responded at Week 16 and who maintained a BASDAI 50 response to Week 52 remained the same as that previously presented, with ██████% of Week 16 responders maintaining response to Week 52. Based on this data an annual rate of discontinuation due to loss of BASDAI 50 response was applied to golimumab responders in the economic model, which was appropriate.

6.12 In assessing this data on the OSI population previously, “The PBAC considered that the claim of superior comparative effectiveness was reasonable, but the magnitude of the incremental benefit was not well-supported due to: the reliance on data from a subgroup of the total trial population; the short duration of the randomised trial for a long-term treatment; and the lack of applicability to the requested restriction given that only ██████% of the trial population had failed two or more NSAIDs” (6.04 Golimumab November 2017 PSD, paragraph 6.36). Also contributing to the difficulty in determining the degree of incremental effectiveness is the fact that the proposed restriction has narrowed the patient group from the trial that was applicable to the PBS population thereby causing the ESC to note that the applicability of the trial data is reduced. The Pre-PBAC response noted that there will be no further clinical data to address this concern (the open-label follow-up did not continue beyond 60 weeks) and as such the magnitude of incremental effectiveness will remain uncertain.

6.13 The resubmission did not present any new data for patients with OSI who had both an elevated CRP and evidence of sacroiliitis on MRI, reasonably stating that there would be a lack of power for this analysis. The only results presented in the resubmission (and in the previous submission) for this patient population related to the outcome of ASAS 20, and these are presented in Figure 1.

Figure 1: Difference in percent ASAS 20 responder's status at Week 16 by baseline factors – point estimate and 95% confidence interval – GLM 50 mg versus placebo (full analysis set population, Part I)



Source: Figure 2.6.1, p129 of the resubmission

6.14 In relation to this data, the PBAC previously “noted that golimumab appeared to be most efficacious in the subgroups of patients with elevated CRP and MRI changes, which was a subset of the requested PBS population. However, the PBAC acknowledged that the key trial (GO-AHEAD) was not powered for these subgroup analyses” (6.04 Golimumab November 2017 PSD, paragraph 7.3).

6.15 The ESC noted that the effect size (percent of ASAS 20 responders) appeared to be similar in the subgroup of patients who had an elevated CRP n = [redacted] and the subgroup who had both positive MRI and elevated CRP n = [redacted]. The effect size in these two subgroups was larger than in the overall OSI population (not shown in Figure 1, but as outlined in Table 7, is 39.6% (95% CI: 24.6%, 52.6%)), although the ESC acknowledged the limitations of these subgroup analyses.

6.16 The PBAC noted the sub-group analysis showed no benefit in the non-OSI population, however acknowledged patient numbers were small and there were limitations to the sub-group analysis.

Comparative harms

6.17 The resubmission presented the same information on comparative harms; however, in relation to the population with OSI in the GO-AHEAD trial, the resubmission additionally reported that the proportion of patients who experienced serious infections in the golimumab arm was █% (█ of bacterial infection/76 patients in the OSI population). This compared to 1.0% (1/93) of patients treated with golimumab in the full study population. The duration of the episode was █ weeks. An annual rate of serious infection of █% was used in the economic model with the duration assumed to be 2 weeks. This was reasonable as golimumab is associated with increased infections, but it should be noted that the incidence of infection was not statistically significantly different between treatment groups in the GO-AHEAD trial, nor in the OSI populations.

6.18 The GO-AHEAD trial duration was not sufficient to determine the long-term risk of infections in the broader population of patients who would be treated in Australian clinical practice.

Benefits and harms

6.19 A summary of the comparative benefits and harms for golimumab versus placebo is presented in Table 8. These remain unchanged from the previous submission, with the exception of serious infections.

Table 8: Summary of comparative benefits for golimumab 50 mg and placebo

GO-AHEAD trial: OSI population	Golimumab	Placebo	RR (95% CI)	Events/100 patients		RD (95% CI)
				Golimumab	Placebo	
Benefits						
ASAS 20 response at 16 weeks	60/78	30/80	2.05 (1.51, 2.79)	76.9	37.5	0.40 (0.25, 0.53)
BASDAI 50 response at 16 weeks	46/78	23/80	2.05 (1.39, 3.03)	59.0	28.8	0.31 (0.15, 0.44)

RD = risk difference; RR = risk ratio; OSI = objective signs of inflammation

Source: Table 2.6.1 and 2.6.2, p128 and p130 of the resubmission, and Tables 12-3 and 12-9 GO-AHEAD 60-week clinical study report

6.20 On the basis of direct evidence presented by the resubmission, for every 100 patients treated with golimumab in comparison to placebo, in the population with OSI:

- approximately 40 additional patients would have an ASAS 20 response over a maximum duration of exposure of 16 weeks; and
- approximately 31 additional patients would have a BASDAI 50 response over a maximum duration of exposure of 16 weeks.

6.21 The ESC noted there was no statistically significant difference in the risk of serious infection between golimumab and placebo in the GO-AHEAD trial, but re-iterated its previous advice that given GO-AHEAD excluded patients with a history of infections, and its short duration, there was a possibility of an increased risk of infection with golimumab that would not be detected within the trial.

Interpretation of clinical evidence

- 6.22 The resubmission described golimumab as superior in terms of comparative effectiveness and inferior in terms of comparative safety compared to placebo. This differed from the previous submission where a claim of non-inferior safety was presented.
- 6.23 The resubmission's claim was considered adequately supported by the evidence presented although the PBAC considered that the degree of incremental benefit was difficult to determine because:
- The 16-week randomised phase of the GO-AHEAD trial was of insufficient duration to accurately assess the long-term benefits of golimumab.
 - While a statistically significant difference was observed between golimumab and placebo among the pre-specified subgroup of patients with objective signs of inflammation (OSI) in the GO-AHEAD trial, only █████% of the OSI population would be considered representative of the proposed PBS population (those with elevated CRP and evidence of sacroiliitis on MRI). The proportion of the OSI population being representative of the proposed population would further diminish if the criteria for prior failure of two or more NSAIDs, whilst completing an appropriate exercise program for a total period of three months, was also considered.
- 6.24 The pre-PBAC response stated that “no further follow-up for the GO-AHEAD trial or additional golimumab trials in nr-axSpA will be available in the future”
- 6.25 The PBAC considered that the inferior comparative safety was reasonable.

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

Economic analysis

- 6.26 As for the previous submission, the resubmission presented a stepped economic evaluation based on the 16 week direct randomised trial (GO-AHEAD) comparing golimumab 50 mg + conventional care (GLM+CC) versus placebo + conventional care (CC alone), and implemented a modelled economic evaluation based on the 52-week open-label extension of the GO-AHEAD trial. The economic evaluation aimed to quantify the incremental costs and effects associated with GLM+CC versus CC alone in nr-axSpA patients with OSI who are eligible for TNF- α -inhibitor therapy.
- 6.27 The approach and structure of the model presented in the resubmission was unchanged from the previous submission, with trajectories of BASDAI/BASFI scores within health states representing transitions between different levels of health. However, numerous changes to the inputs and assumptions were made. Key changes included: a 20-year time horizon for the model (30 years previously); transition time from responder to non-responder in the CC arm increased from 32 to 52 weeks; a disutility for serious infections of -0.31 was applied to █████% of patients per year for 2 weeks; an increased annual discontinuation rate of █████% was applied (it was previously █████% in Year 1 and █████% thereafter); and equal BASFI progression was

assumed for both golimumab and CC arms (the previous submission assumed a lower rate of BASFI progression for golimumab responders after 4 years).

6.28 The ESC noted that most of these changes were minor and did not address the core underlying concerns raised by the PBAC in its previous consideration (particularly the lack of long-term data and the uncertain utilities). Further, while the time horizon was reduced from 30 years to 20 years, the ESC considered that 20 years may not be appropriate given the uncertain extrapolation from 16 weeks of randomised data and lack of long-term data to inform the model. The pre-PBAC response stated that “When the time horizon is changed to 10 years the resultant ICER is \$ [REDACTED]/QALY compared to 20 year base case of \$ [REDACTED]/QALY, a minimal change despite a halving of the time horizon”.

6.29 Table 9 provides a summary of the model structure and rationale.

Table 9: Summary of model structure and rationale

Component	Summary
Time horizon	20 years in the model base case versus 16 weeks randomised data in the trial
Outcomes	LYs and QALYs, with LYs assumed to be equal in both arms
Methods used to generate results	Markov cohort analysis
Health states	Three golimumab living health states of responder, non-responder and discontinued after golimumab response; two conventional care living health states of responder and non-responder, in the base case, plus a dead health state. As per the previous submission, the model stratified each arm by response status at the beginning of the model as opposed to when response was measured in the GO-AHEAD trial (16 weeks) for the purposes of applying utilities and costs. Additionally, all conventional care responders at Week 16 (28.8%) were assumed to be non-responders by Week 52, thus no potential placebo effect was incorporated in the model beyond 52 weeks.
Utilities	As per the previous submission, utilities were estimated from a regression equation from a separate study that used BASDAI/BASFI terms (from trial and extrapolations) to estimate and assign utilities. The model was demonstrated to be highly sensitive to the utility regression equation applied. An additional disutility was included for serious infections in the resubmission.
Cycle length	Weekly in Year 1, and annually in Years 2-20. Cycle lengths were reasonable; however the lack of half-cycle correction in the annual cycles likely resulted in an inaccurate accrual of costs and benefits.
Transition probabilities	Derived from trial data through to Week 16, from open-label study data to Week 52 for golimumab responders, and from Sponsor assumptions
Annual disease costs	Based on a regression equation from Tilden (2004), with health care costs linked to BASFI scores. This was considered inappropriate in the previous submission with the PBAC Minutes concluding “The original COI study (Tilden 2004) provides no detailed information on the methodology of the study (for example, the healthcare resource-use questions included in the survey, the characteristics of the sample population and whether any eligibility criteria were applied) nor does it provide information on the specific costs included other than specifying ‘categories’ of costs. As such, the validity of this regression equation in predicting nr-axSpA disease-management costs was unclear.” (6.04 Golimumab November 2017 PBAC PSD, Table 8)

Source: Sections 3.1-3.5 of the resubmission

6.30 Key drivers of the model are presented in Table 10.

Table 10: Key drivers of the model

Description	Method/Value	Impact
Utilities/ Extrapolation	Long-term utility values were estimated from a regression equation. While some verification of the regression equation was provided in the resubmission, it was not clear whether the regression equation would be relevant over the 20-year time horizon of the model. As per the previous submission, of the four utility estimation algorithms provided, the submission used the algorithm based on the GO-AHEAD trial. This algorithm resulted in the lowest ICER.	High (base case values favour golimumab)

Source: Compiled during the evaluation

6.31 Table 11 presents the results of the economic evaluation. The base case of the stepped economic evaluation utilised a cost for golimumab of \$ [REDACTED], with the proposed DPMQ of \$1,317.93 used in a scenario analysis. The resubmission stated that the lower price was to mitigate the uncertainty from the lack of longer-term data.

Table 11: Results of the stepped economic evaluation

Step and component	Golimumab + conventional care	Conventional care	Increment
Step 1: Trial-based analysis [16 weeks; costs and outcomes undiscounted] using DPMQ of \$ [REDACTED]			
Costs = golimumab, administration, treatment initiation, non-serious infection management	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]
Outcome = BASDAI 50 responder rate	59.0%	28.8%	30.2%
Incremental cost/additional responder			\$ [REDACTED]
Step 2a: Base case model-based analysis [20 years; discounted at 5% per annum] using DPMQ of \$ [REDACTED]			
Costs = all extrapolated costs	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]
Outcome = QALYs	[REDACTED]	[REDACTED]	[REDACTED]
Incremental cost//QALY			\$ [REDACTED]
Step 2b: Scenario of model-based analysis with new requested DPMQ of \$1,317.93 [20 years; discounted at 5% per annum]			
Costs = all extrapolated costs	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]
Outcome = QALYs	[REDACTED]	[REDACTED]	[REDACTED]
Incremental cost//QALY			\$ [REDACTED]

The economic evaluation's base case used the previously requested DPMQ of \$1 [REDACTED]

Source: Table 3.8.1, p199 of the resubmission

6.32 The trial-based analysis was identical to that presented in the previous submission, with both analyses assuming 16 weeks of golimumab treatment prior to assessment of response and resulting in an ICER of \$15,000/QALY - \$45,000/QALY per additional responder over 16 weeks (using the previously requested DPMQ of \$ [REDACTED]). Using the proposed DPMQ of \$1,317.93, the ICER becomes 15,000/QALY - \$45,000/QALY per additional responder over 16 weeks.

6.33 The base case model-based analysis over 20 years estimated the ICER to be 15,000/QALY - \$45,000/QALY per QALY gained; this compared to 15,000/QALY - \$45,000/QALY over 30 years (or 15,000/QALY - \$45,000/QALY over 20 years) in the previous submission (all using a DPMQ of \$ [REDACTED]). Using the discounted DPMQ of \$1,317.93, the ICER reduced to \$15,000/QALY - \$45,000/QALY per QALY gained.

- 6.34 The modelled ICER was associated with uncertainty due to the extrapolation of 16/52 week trial/open-label data to 20 years, the regression equations used to estimate the utilities and the disease management costs.
- 6.35 The ESC noted that the model was structured in the following way:
- At the outset of the model (Week 0) patients are designated as either a responder or non-responder (based on their BASDAI 50 response at 16 weeks) and continued in this health state until Week 16 (conventional care) or Week 52 (golimumab);
 - At Week 16, all conventional care responders were assumed to lose their placebo response and become “conventional care non-responders” by Week 52, and remained conventional care non-responders thereafter;
 - BASFI and BASDAI scores underpin each of the health states. After 16 weeks, the assumptions related to BASFI and BASDAI score progression differed by group:
 - golimumab responders: after 16 weeks, BASFI and BASDAI scores were kept constant through to 52 weeks; thereafter, BASFI scores increased (i.e. worsened) based on a long-term progression rate while BASDAI scores remained constant at a score of 1.2.
 - conventional care responders: as outlined above, after 16 weeks, BASFI and BASDAI scores rebounded (i.e. worsened) to their respective baseline score by Week 52; thereafter, conventional care responders were immediately transitioned to the non-responder health state.
 - conventional care and golimumab non-responders: after 16 weeks, BASFI and BASDAI scores immediately rebound (i.e. worsen) to their respective baseline scores; thereafter, BASFI scores increase (i.e. worsen) using a long-term rate of progression and BASDAI scores remain constant at a score of 7.0.
- 6.36 The ESC noted that the algorithm for determining the utility value in each cycle was largely driven by the change in BASDAI and BASFI score over that cycle (with BASDAI scores having almost double the impact of BASFI scores).¹ Thus a key driver of the model was the assumption that BASDAI scores would remain constant (at a score of 1.2) in the “golimumab responders” arm.
- 6.37 The utility estimation algorithm applied in the resubmission was produced for a submission to the Scottish Medical Consortium based on individual patient data from the GO-AHEAD trial. The ESC noted the algorithm only explained █████% of the variation in EQ-5D change, and omitted baseline EQ-5D as an independent variable despite the model’s dependant variable being EQ-5D change. The ESC also noted that three other algorithms had been identified in the resubmission’s literature search (one was developed from a nr-axSpA population while the other two were developed from AS populations). The ESC noted that the ICER was very sensitive to the algorithm chosen (and the one selected in the base case, which was based on the GO-AHEAD trial, resulted in the lowest ICER) as shown in sensitivity analyses below. The ESC

¹ The algorithm applied in the base case (to estimate the EQ-5D score for every cycle) was: $Utility = Baseline\ utility + (0.10034 - 0.05735 \times BASDAI^* - 0.03120 \times BASFI^* + 0.00126 \times MALE - 0.00440 \times AGE)$

* Per 1-unit change in the BASDAI and BASFI

considered that, while some verification of the regression equation was provided in the resubmission, it remained unclear whether the regression equation would be relevant over the 20-year time horizon of the model.

- 6.38 The pre-PBAC response stated that the main uncertainty with the utility mapping method was whether responders will continue to have a similar utility gain over time, because when patients lose BASDAI-50 response, the utility gain ceases. The pre-PBAC response attempted to evaluate this through two sensitivity analyses. Firstly, by reducing the time horizon which limits the duration of the 'constancy' in utility gain for responders versus non-responders: the ICER at 10 years (20 year base case result) is \$15,000/QALY - \$45,000/QALY which as discussed above is a minimal change from the base case (\$15,000/QALY - \$45,000/QALY. Second, by reducing the rate of long-term responders, which limits the application of the utility gain to much smaller cohorts; using high rates of annual discontinuation at 15% and 20% per year (base case discontinuation was ■% per year), provide ICERS of \$15,000/QALY - \$45,000/QALY , both lower than the base-case ICER.
- 6.39 Table 12 summarises the key model parameters and the costs and QALYs estimated for each treatment group in the model.

Table 12: Key model parameters

	Golimumab			Conventional care		
	Total	Responder	Non-responder	Total	Responder	Non-responder
Costs (discounted over 20 years)						
Total	\$████	-	-	\$████	-	-
% at Week 16	100%	59%	41%	100%	29%	71%
Transition to non-responder						
- at Week 52		████% ^a			████% at Week 52 ^b	
- subsequent years		████% ^a				
Avg. no. injections per patient	████	████ ^c	█	-	-	-
Levels of health within the model (impacts utility and disease management costs)						
Baseline utility ^h	████	████ ^d	████	████	████	████
Mean change in utility at Week 16	████	████	████	████	████	████
Baseline BASFI score		4.9	████		████	████
Annual progression of BASFI score		████ ^e	████		████	████
Utility gains in model (based on undiscounted results)^f						
Life years	████	████	████	████	████	████
QALYs	████	████	████	████	████	████
Average utility	████	████	████	████	████	████
Previous model (November 2017)^g						
Average utility	████	████	████	████	████	████

^a Of this, █████% was due to loss of response and █████% was due to adverse events. In the previous submission, this was █████% in Year 1 and 6% in subsequent years.

^b This was 100% at Week 32 in the previous submission.

^c This was 152 injections in the previous submission. The change was primarily due to the reduced time horizon (rather than the increased discontinuation/transition to non-responder rate).

^d A disutility of -0.31 was also applied to the proportion of patients with serious infection for two weeks, and applied on an annual recurring base.

^e The previous submission had assumed a slower rate of BASFI progression for golimumab responders after 4 years (████ after 4 years).

^f Differs from Table 9 due to the presentation of undiscounted results. Calculated during the evaluation.

^g Calculated during the previous evaluation.

^h Based on EQ-5D data from the GO-AHEAD trial

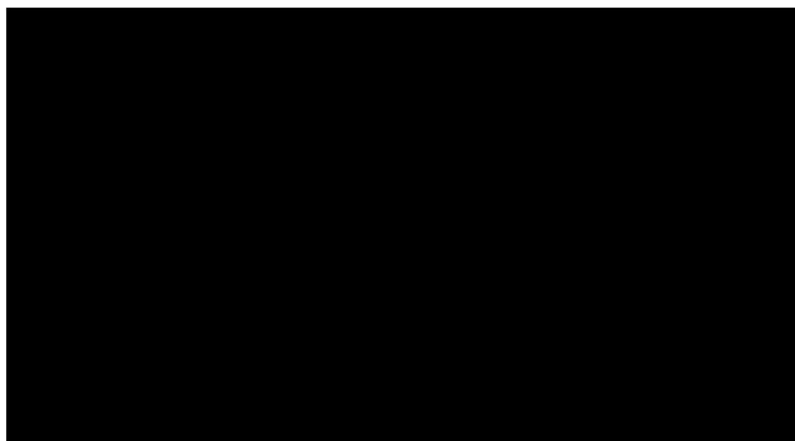
Source: Compiled during the evaluation from Sections 2 and 3 of the resubmission and from the Section 18 workbook in the previous submission

6.40 As shown in Table 12, golimumab responders in the model had a much higher average utility score compared to golimumab non-responders █████ versus █████. The model assumed that 59% of patients in the golimumab arm were responders, and that there would be a high level of continued response with patients who are responders staying on golimumab for an average of nine years. On the other hand, the model assumed that there would be no CC responders after Year 1. While the transition time from responder to non-responder in the CC arm increased from 32 weeks in the previous model to 52 weeks, this amendment may not have adequately addressed the PBAC's

concerns about the lack of a placebo response after 32 weeks (6.04 Golimumab November 2017 PSD, paragraph 7.7).

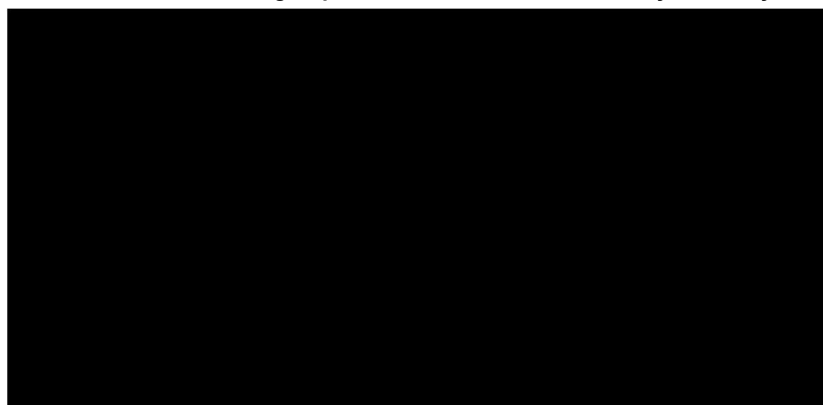
- 6.41 The model continued to assume that patients who achieved a BASDAI 50 response experienced a greater incremental utility gain (from baseline to Week 16) in the golimumab arm than the CC arm (utility gain of [REDACTED] versus [REDACTED] respectively). The PBAC had previously considered that this would only be reasonable if the PBS restriction could confine use to patients who were likely to achieve a very high level of response (6.04 Golimumab November 2017 PSD, paragraph 7.7).
- 6.42 The average utility difference in the resubmission's model was calculated to be [REDACTED], compared to [REDACTED] for the previous submission (based on undiscounted outcomes, refer to Table 12: Key model parameters). This compared to an average utility difference in the GO-AHEAD trial of 0.16.
- 6.43 QALYs accrued in each health state every week in the first year of the model and every year in years 2-20 of the model are depicted in Figure 2 and Figure 3.

Figure 2: QALYs accrued in each treatment group and in each health state in each week over the first year



Source: Attachment 20 CUA Model Revised_Final 2
GLM = golimumab; CC = conventional care; R = responder; NR = non-responder

Figure 3: QALYs accrued in each treatment group and in each health state, each year over years 2-20 of the model



Source: Attachment 20 CUA Model Revised_Final 2
Note all QALYs in the CC arm are derived from the non-responder health state
GLM = golimumab; CC = conventional care; R = responder; NR = non-responder; DC = discontinued

6.44 Table 13 outlines univariate sensitivity analyses presented by the resubmission. The ICER (using the proposed DPMQ of \$1,317.93) was sensitive to the utility regression equation used (ICER range: \$15,000/QALY - \$45,000/QALY in the base case model, up to \$15,000/QALY - \$45,000/QALY using alternative utility regression models) and to the annual disease cost estimation (ICER range: less than \$15,000 per QALY when using BASFI-based exponential model to \$15,000/QALY - \$45,000/QALY when disease-related costs assumed in the base case were reduced by 75%). The multivariate sensitivity analyses were conducted after ESC at the request of the PBAC.

Table 13: Results of sensitivity analyses

Model setting	Scenario setting	Incremental		ICER
		Costs	QALYs	
Step 2a model with DPMQ of \$1,317.93 (base case)		\$ [REDACTED]	[REDACTED]	\$ [REDACTED]
Utility estimation algorithm: MSD-GOAHEAD	Model 2 [AbbVie]	\$ [REDACTED]	[REDACTED]	\$ [REDACTED]
	Model 3 [MSD-AS]	\$ [REDACTED]	[REDACTED]	\$ [REDACTED]
	Model 4 [Ara 2007]	\$ [REDACTED]	[REDACTED]	\$ [REDACTED]
Annual disease cost estimation: BASFI-based exponential model (Tilden 2004)	Disease-related costs reduced by 75%	\$ [REDACTED]	[REDACTED]	\$ [REDACTED]
	Disease-related costs reduced by 50%	\$ [REDACTED]	[REDACTED]	\$ [REDACTED]
	BASFI-based exponential model constant inflated to calculate costs in 2017 AUD	\$ [REDACTED]	[REDACTED]	\$ [REDACTED]
Time horizon: 20 years	10 years	\$ [REDACTED]	[REDACTED]	\$ [REDACTED]
Discontinuation rates: : [REDACTED]% per year (CHECK)*	15% per year	xx	xx	\$ [REDACTED]
	20% per year	xx	xx	\$ [REDACTED]
Multivariate sensitivity analyses				
10 year time horizon plus variations to the utility estimation algorithm	Model 2 [AbbVie]	\$ [REDACTED]	[REDACTED]	\$ [REDACTED]
	Model 3 [MSD-AS]	\$ [REDACTED]	[REDACTED]	\$ [REDACTED]
	Model 4 [Ara 2007]	\$ [REDACTED]	[REDACTED]	\$ [REDACTED]

AS = Ankylosing spondylitis; BASFI = Bath ankylosing spondylitis functional index; GLM = golimumab; ICER = Incremental cost effectiveness ratio; QALY = Quality adjusted life-year

Source: Table 3.9.1, pp208-209 of the resubmission, *p2 pre-PBAC response, "Attachment 20 CUA model Revised_Final 2.xlsx"

6.45 The PBAC noted that multivariate sensitivity analyses with both a ten-year time horizon and alternative utility estimation equations resulted in ICERs between \$15,000/QALY - \$75,000/QALY. The PBAC noted these additional analyses in the context of other optimistic assumptions in the model including the higher utilities applied to responders in the golimumab arm than the conventional care arm (and reliance on only 16 weeks of randomised trial data).

Drug cost/patient/year: \$15,816.16 (for responders)

6.46 Based on a DPMQ of \$1,317.93 and 12 scripts per year (dosing on the same date each month). This compared to \$ [REDACTED] in the previous submission, with the lower cost in the resubmission being due to the reduced DPMQ.

Estimated PBS usage & financial implications

6.47 This resubmission was not considered by DUSC. The resubmission appropriately used an epidemiological approach to estimate the financial implications of listing

golimumab on the PBS for patients with nr-axSpA. The new proposed DPMQ of \$1,317.93 was used in the financial estimates.

6.48 Numerous changes were made to the financial estimates provided in the resubmission:

- increased the estimated prevalent population with nr-axSpA in Australia by 5% in acknowledgement that some patients treated with golimumab may be aged over 45 years
- estimated the eligibility of the prevalent patient pool for golimumab from the OSI population in the GO-AHEAD trial who had elevated CRP, positive evidence of sacroiliitis on MRI, one or more SPA features (other than arthritis and family history), and who were positive for the HLA-B27 gene
- removed the previous subtraction of patients from the prevalent patient pool who had progressed to AS
- based the estimated continuation rate of golimumab on estimates from the GO-AHEAD trial rather than from Wang 2016
- increased the market uptake rate due to the more specific at risk population requested in the PBS listing, and removed the previous 'patients electing to receive treatment rate' based on the Sieper 2016 study
- removed the cost savings associated with changes in the use of other PBS medicines assumed in the previous submission (based on Tilden 2004)
- no longer subtracted the cost of conventional care (in regard to 'other PBS' or MBS items) from the financial estimates
- did not include any costs for inpatient hospital costs for golimumab or conventional care
- included an annual Group A GP consultation MBS fee for women
- used the reduced DPMQ of \$1,317.93 and an updated weighted average co-payment to calculate revised financial estimates
- no longer specifically requested a special pricing arrangement, although in Section 1 the resubmission stated that the Sponsor proposed to work with the Department to incorporate the final negotiated price for patients with nr-axSpA into the weighted price calculation that currently exists for golimumab across the PBS listed indications.

6.49 Table 14 summarises the estimated use and financial implications presented in the resubmission, and the comparable estimates provided in the previous submission (shaded cells). These reflect revised estimates provided in the PSCR, which were updated to correct a number of minor errors identified in the commentary (i.e. calculation of weighted co-payments, and use of the correct MBS benefit fee). Further,

to address issues raised in the commentary, the revised estimates provided in the PSCR also included:

- MBS item 10997, Nurse Practitioner for Chronic Disease service (\$12, applied once per initiating patient) to replicate the self-administration advice provided by site personnel in the GO-AHEAD study; and
- Hospitalisation costs for managing serious adverse reactions, based on the incidence of infections in the GO-AHEAD trial.

Table 14: Estimated use and financial implications (corrected for errors acknowledged in the PSCR)

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Estimated extent of use						
Number of patients treated	█	█	█	█	█	█
Number of scripts dispensed ^a	█	█	█	█	█	█
Number of scripts dispensed ^b (previous submission)	█	█	█	█	█	█
Estimated financial implications of listing golimumab on the PBS/RPBS and Net financial implications						
Cost to PBS/RPBS	\$█	\$█	\$█	\$█	\$█	\$█
Co-payments	-\$█	-\$█	-\$█	-\$█	-\$█	-\$█
Cost to PBS/RPBS less co-payments	\$█	\$█	\$█	\$█	\$█	\$█
Cost to PBS/RPBS less co-payments (previous submission)	\$█	\$█	\$█	\$█	\$█	\$█
MBS (Net cost)	\$█	\$█	\$█	\$█	\$█	\$█
MBS (Net cost; previous submission)	\$█	-\$█	-\$█	-\$█	-\$█	-\$█
Net cost PBS/RPBS/MBS	\$█	\$█	\$█	\$█	\$█	\$█
Net cost PBS/RPBS/MBS (previous submission)	\$█	\$█	\$█	\$█	\$█	\$█
Hospital costs ^c	\$█	\$█	\$█	\$█	\$█	\$█

^a Assuming 12.17 scripts per year (calculated as 365 days/30 days) for non-discontinuing responders as estimated by the resubmission, with an average of █ scripts per year in Year 1, and █, █, █, █ and █ scripts per year in Years 2-6 respectively (taking into account discontinuations). It was noted that an assumption of 12.17 scripts per year was higher than the 12 scripts per year used in the economic model and that while this assumption would have overestimated the proposed cost to the PBS

^b Assuming █, █, █, █, █, █ scripts per year in Years 1-6, respectively as estimated by the submission. These script numbers account for proportion of responders each year and discontinuation from treatment. Discrepancy between Year 2 script numbers between submissions was due to the resubmission accounting for grand-fathered patients in Year 1, whereas the previous submission did not account for grand-fathered patients

^c Cost of managing serious infections based on a rate of █% (based on Go-AHEAD trial) and a cost per hospitalisation of \$16,127 based on AR-DRG codes T60A and T60B (weighted).

Source: Table 4.2.5, 4.2.9, pp218-219, 221 of the resubmission; Table 11, 6.04.COM.16, PSCR attachment titled "7.03 Attachment 21 Simponi nr-AxSpA Section 4_v2.1.xlsx" with 10% "buffer" removed from cell G7 of "3b. Impact – PUB" worksheet.

6.50 The estimated cost to the PBS/RPBS was \$30 - \$60 million in Year 1 and more than \$100 million over the first five years of listing. However, the proposed RSA would reduce this cost by capping scripts at 50% of that predicted in the financial estimates (see *Financial management – risk sharing arrangements*).

- 6.51 As for the previous submission, there was considerable uncertainty surrounding: (i) the prevalence of patients with nr-axSpA given the lack of Australian data; and (ii) the estimated market-uptake, which was based on assumptions by the Sponsor.
- 6.52 The resubmission also underestimated the number of patients who would be eligible for treatment under the proposed restriction by assuming that all eligible patients must have the HLA-B27 gene. That is, the eligible patient population was calculated from the GO-AHEAD trial by estimating the proportion of patients in the OSI population who had elevated CRP, positive sacroiliitis on MRI, one or more SPA features (excluding family history and arthritis) and HLA-B27 gene positivity. The evaluation considered that the resubmission's approach was inappropriate, as positivity for the gene was not an absolute requirement under the proposed restriction. This reduced the proportion of OSI patients eligible for golimumab from ■■■% to ■■■.
- 6.53 The resubmission stated that it anticipated that around ■■■ patients would be enrolled in a patient familiarisation program and that these patients were expected to continue golimumab should it be listed on the PBS. The resubmission stated that grandfathered patients were assumed to be part of the Year 1 initiating cohort estimated through the epidemiological approach, and thus were not separately added into the number of treated patients.
- 6.54 Overall, the financial estimates were considered to be highly uncertain given the lack of certainty surrounding the prevalence of nr-axSpA and the likely uptake of golimumab. The ESC considered that the estimated patient numbers and prescription volumes were overestimated compared with the population intended by the PBAC in its November 2017 consideration (i.e. patients with the highest clinical need and those who would benefit the most, which would rely on incorporation of all the elements outlined in Table 2) and if a stopping rule were applied.
- 6.55 Further, the ESC noted the significant opportunity cost that would be associated with listing golimumab for nr-axSpA at the price proposed in the resubmission (cost to PBS/RPBS of more than \$100 million over five years). This estimated cost excludes the proposed RSA.
- 6.56 The ESC considered there to be a continued risk of golimumab use beyond the proposed population in patients with chronic back pain. While the proposed restriction narrowed the patient population compared to the previously proposed restriction, it may not sufficiently restrict use to the patient population likely to benefit the most.
- 6.57 The pre-PBAC response acknowledged that there was uncertainty in the financial estimates given the lack of reliable data to estimate the size of the patient population intended by the PBAC in its previous consideration. To address this, the pre-PBAC response proposed an RSA (outlined below).

- 6.58 The PBAC noted that the financial estimates did not include the increased number of MRIs that would be required to determine patient eligibility for PBS subsidy (PBS eligibility).
- 6.59 The PBAC noted the DUSC report for ankylosing spondylitis (AS)² showed an increase in the number of scripts for bDMARD for AS, and that there may already be usage across indications.
- 6.60 The resubmission proposed a patient education program to support self-administration of golimumab, however this appeared to rely on MBS item 10997, Nurse Practitioner for Chronic Disease service (refer to financial estimates).

Financial management – risk sharing arrangements

- 6.61 PBS utilisation was likely overestimated compared with the population intended by the PBAC in its November 2017 consideration (i.e. patients with the highest clinical need and those who would benefit the most) and if a stopping rule were applied. The ESC considered that neither the proposed restriction nor the RSA proposed in the PSCR had adequately addressed these issues. In light of potential difficulties implementing the PBAC's intended restriction, the ESC advised that an RSA based on substantially lower patient numbers would be required to address the risks associated with the uncertain and poorly defined patient population.
- 6.62 The pre-PBAC response proposed an RSA based on:
- capping the number of golimumab scripts for nr-axSpA at ■■■% of that predicted in the financial estimates (per Table 14) in Year 1 of PBS listing; with the cap (proportion of predicted) increasing by a ■■■% increment each year to ■■■% in Year 5; and
 - An ■■■% rebate on Commonwealth expenditure for all scripts above the cap. The pre-PBAC response stated that an ■■■% rebate was proposed (rather than a hard cap) because the GO-AHEAD trial demonstrated benefits in the nr-axSpA patient population broader than that proposed by the PBAC (i.e. “it is probable that the patients included in the trial who are outside of the PBAC-intended patient population will also benefit from golimumab therapy”).

- 6.63 The RSA proposed in the pre-PBAC response is summarised in Table 15.

² <http://www.pbs.gov.au/info/industry/listing/participants/public-release-docs/2016-02/bdmards-for-ankylosing-spondylitis2016-02>

Table 15: RSA proposed in pre-PBAC response

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
No. of scripts in estimated in resubmission	█	█	█	█	█	█
% of scripts within the cap	█%	█%	█%	█%	█%	█% ^d
No. of scripts within cap	█	█	█	█	█	█ ^d
Rebate on scripts above the cap	█%	█%	█%	█%	█%	█%
Cost to PBS/RPBS (before RSA) ^b	\$█	\$█	\$█	\$█	\$█	\$█
Estimated rebate ^c	\$█	\$█	\$█	\$█	\$█	\$█
Cost to PBS/RPBS (with RSA)	\$█	\$█	\$█	\$█	\$█	\$█

Source: Pre-PBAC response: "RSA proposal" worksheet of "Item 7.03 Pre-PBAC Response for Golimumab – SIMPONI – Janssen – RSA proposal.xlsx"

^a The pre-PBAC response assumed that the Year 5 subsidisation cap would roll-over to Year 6

^b Reported as per Table 14 above for consistency. Does not align exactly with worksheet due to minor differences in co-payments (weighting between RPBS and PBS)

^c If scripts are as estimated in Row 1

^d Based on the number of scripts in the Year 5 cap rolling over to Year 6 (i.e. the number of scripts included in the cap remains the same at █ scripts. The proportion of estimated scripts increases because the estimated number of scripts decreases in Year 6).

6.64 The pre-PBAC response stated that the proposed RSA, the estimated net cost to the PBS/RPBS for golimumab in nr-axSpA was expected to reduce the estimated net cost to the PBS/RPBS for golimumab in nr-axSpA \$60 - \$100 million over five years, representing a █% reduction.

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

7 PBAC Outcome

7.1 The PBAC recommended extending the PBS-listing of golimumab to include the treatment of patients with non-radiographic axial spondyloarthritis (nr-axSpA) as a Section 85 Authority Required (written) listing. The PBAC is satisfied that golimumab provides, for some patients, a significant improvement in efficacy over conventional care. The PBAC considered that the cost-effectiveness of golimumab was acceptable at the price applied in the economic model. The PBAC considered that effective controls would be needed to ensure that cost-effective treatment was realised and to limit the financial costs to the PBS to the intended patient group.

7.2 The PBAC reiterated there was a clinical need in certain patients with inflammatory back pain associated with nr-axSpA. However, PBAC remained concerned about the risk of over-treating patients with lower back pain (ie the inappropriate use in misdiagnosed patients). The PBAC noted the consumer comments shared this concern and the PBAC considered that the restriction would require further work with expert advice around the definition of MRI changes — the Committee noted the *Consensus statements on the imaging of axial spondyloarthritis in Australia and New Zealand*³

³ Truong SL, Saad NF, Robinson PC, Cowderoy G, Lim I, Schachna L, Stebbings S, Stuckey S, Taylor AL, Whittle SL, Zochling J, Bird P, Brown MA. J Med Imaging Radiat Oncol. 2017 Feb;61(1):58-69.

Statement 9: The recommended MRI technique for imaging axial SpA is the combination of Short Tau Inversion Recovery (STIR) and T1 without gadolinium. The recommended planes for MRI are axial and oblique coronal planes for the SIJ and the sagittal plane for the spine. The PBAC considered expert advice from the Australian Rheumatology Association (ARA) and the Royal Australian and New Zealand College of Radiologists (RANZCR) should be sought to inform the PBS restriction. The PBAC also considered the restriction needed a criterion that on plain x-ray there was no evidence of bilateral grade II sacroiliitis or unilateral grade III sacroiliitis.

- 7.3 The PBAC remained concerned about the applicability of the trial data (as highlighted in section 6 above) and that there was only 16-weeks randomised trial data with an open-label extension phase out to 52 weeks supportive of a sustained treatment response out to one year. The PBAC further noted the pre-PBAC response which suggested that uncertainty with longer-term response could be managed with the proposed continuation rule which required that patients “must have demonstrated an adequate response to PBS-subsidised therapy with this drug based on a reduction from baseline in the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score by 2 or more units (on a scale of 1 -1 0)”. Hence, after the initial 16 weeks assessment, patients will need to demonstrate an ongoing adequate response every 24 weeks to access further PBS subsidized treatment. The PBAC recalled in November 2017 it was suggested a stopping rule may be worth considering; however as no relevant evidence from a withdrawal trial was forthcoming, it was considered that the proposed continuation criteria combined with a suitable RSA would be adequate to contain usage and overall expenditure to the population most likely to receive a sustained benefit.
- 7.4 PBAC remained concerned about the economic model given the uncertain extrapolation of short-term randomised trial data and utilities — the whole model is based on utilities that were from a trial that only had a randomised phase of 16 weeks. The PBAC considered the ICER was more likely to be in the range of the multivariate sensitivity analyses conducted after ESC, however was reassured that these remained within a reasonable range.
- 7.5 The PBAC considered that the utilisation remained highly uncertain, with a high risk of use beyond the intended population and requested a predicted versus actual DUSC utilisation analysis after two years of listing.
- 7.6 The PBAC noted that the RSA proposed in the pre-PBAC response was based on a cap with increasing proportions of estimated scripts over time (i.e. ■■■% increasing by ■■■% per year up to ■■■% in Year 5). The PBAC considered that there was no rationale for the increasing cap proportion and considered that a cap based on ■■■% of scripts in the financial estimates was appropriate over the 5 years of the RSA, with an ■■■% rebate for any expenditure incurred above the cap. The PBAC did not consider there would be a benefit to patients that were non-OSI, and considered that to manage the risk of leakage further, a second tier cap set at the level of the financial estimates, should

result in a rebate of █% to the Commonwealth for expenditure above the second cap.

- 7.7 Financial estimates should account for the increased number of MRIs required to determine eligibility.
- 7.8 The PBAC recommended that a grandfather restriction be included for this indication for the same population with associated restriction criteria consistent with the initial and continuing restrictions.
- 7.9 The PBAC advised that golimumab is not suitable for prescribing by nurse practitioners.
- 7.10 The PBAC recommended that the Early Supply Rule should apply.
- 7.11 The PBAC noted that this submission is not eligible for an Independent Review because the PBAC has made a positive recommendation.

Outcome:

Recommended

8 Recommended listing

- 8.1 Add new item: *restriction to be finalised following expert advice on MRI imaging from ARA and RANZCR.*

Initial 1: new patients (to be finalised)

Name, restriction, manner of administration, form	Maximum quantity (packs)	Maximum quantity (units)	No. of repeats	Proprietary name and manufacturer	
GOLIMUMAB					
Initial treatment					
50mg/0.5mL pre-filled syringe	1	1	3	SIMPONI, Janssen-Cilag Pty Ltd	
50mg/0.5mL <u>pre-filled pen</u>	1	1	3		
Continuing treatment					
50mg/0.5mL pre-filled syringe	1	1	5		
50mg/0.5mL <u>pre-filled pen</u>	1	1	5		

Category / Program	General Schedule (Code GE)
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
Condition:	Active non-radiographic axial spondyloarthritis
PBS Indication:	Active non-radiographic axial spondyloarthritis
Treatment phase:	Initial treatment – initial 1 (new patients)
Restriction Level / Method:	<input checked="" type="checkbox"/> Authority Required - In Writing
Clinical criteria:	The condition must be non-radiographic axial spondyloarthritis, as defined by Assessment of Spondyloarthritis International Society (ASAS) criteria; AND

	<p>Patient must have chronic lower back pain and stiffness for 3 or more months that is relieved by exercise but not rest,</p> <p>AND</p> <p>Patient must have severe disease based on a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) of at least 4;</p> <p>AND</p> <p>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;</p> <p>AND</p> <p>Patient must have elevated C-reactive protein (CRP) level of greater than 10mg/L;</p> <p>AND</p> <p>The condition must be sacroiliitis with active inflammation and/or oedema on Magnetic Resonance Imaging (MRI);</p> <p>AND</p> <p>Patient must have no evidence on plain x-ray of bilateral Grade II sacroiliitis or unilateral Grade III or IV sacroiliitis;</p> <p>AND</p> <p>Patient must have experienced one or more of the following: (a) Enthesitis (heel); (b) Uveitis; (c) Dactylitis; (d) Psoriasis; (e) Inflammatory bowel disease; OR (f) positive Human Leukocyte Antigen B27 (HLA-B27).</p>
Population criteria	Patient must be aged 18 years or older
Treatment criteria	Must be treated by a rheumatologist.
Prescriber Instructions	<p>The application must include details of the NSAIDs trialed, their doses and duration of treatment. If the NSAID dose is less than the maximum recommended dose in the relevant TGA-approved Product Information, the application must include the reason a higher dose cannot be used.</p> <p>If treatment with NSAIDs is contraindicated according to the relevant TGA-approved Product Information, the application must provide details of the contraindication.</p> <p>If intolerance to NSAID treatment develops during the relevant period of use which is of a severity to necessitate permanent treatment withdrawal, the application must provide details of the nature and severity of this intolerance.</p> <p>The following criteria indicate failure to achieve an adequate response to NSAIDs and must be demonstrated at the time of the initial application:</p> <p>(a) a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) of at least 4 on a 0-10 scale and less than a 2 unit change in BASDAI since treatment initiation; AND</p> <p>(b) C-reactive protein (CRP) level greater than 10 mg per L.</p> <p>The BASDAI must be determined at the completion of the 3-month NSAID and exercise trial, but prior to ceasing NSAID treatment. The BASDAI must be no more than 1 month old at the time of</p>

	<p>initial application.</p> <p>CRP measures should be provided with the initial treatment application and both must be no more than 1 month old.</p> <p>The assessment of the patient's response to the initial course of treatment must be made following a minimum of 12 weeks of treatment and submitted no later than 4 weeks from the cessation of that treatment course. If the response assessment is not submitted within these timeframes, the patient will be deemed to have failed this course of treatment.</p> <p>A maximum of 16 weeks of treatment with this drug will be approved under this criterion.</p> <p>The authority application must be made in writing and must include:</p> <p>(a) a completed authority prescription form; and</p> <p>(b) a completed Ankylosing Spondylitis PBS Authority Application - Supporting Information Form which must include the following:</p> <ul style="list-style-type: none"> (i) a copy of the radiological report confirming the absence of Grade II bilateral sacroiliitis or Grade III unilateral sacroiliitis; and (ii) a completed BASDAI Assessment Form; and (iii) a completed Exercise Program Self Certification Form included in the supporting information form; and (iv) a copy of the MRI report and xray report
Administrative advice	<p>Details of the toxicities, including severity, which will be accepted for the purposes of administering this restriction can be found on the Department of Human Services website at www.humanservices.gov.au.</p> <p>For details on the appropriate minimum exercise program that will be accepted for the purposes of administering this restriction, please refer to the Department of Human Services website at www.humanservices.gov.au.</p> <p>No increase in the maximum quantity or number of units may be authorised.</p> <p>No increase in the maximum number of repeats may be authorised.</p>

Initial 2 – recommencement of treatment – to be drafted. This restriction will only be included in the listing if a patient can trial and fail golimumab for this indication more than once.

Category / Program	General Schedule (Code GE)
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
Condition:	Active non-radiographic axial spondyloarthritis
PBS Indication:	Active non-radiographic axial spondyloarthritis
Treatment phase:	Initial treatment – initial 2 (re-commencement of treatment) This restriction will only be included in the listing if a patient can trial and fail golimumab for this indication more than once.
Restriction Level / Method:	<input checked="" type="checkbox"/> Authority Required - In Writing
Clinical criteria:	<p>Patient must have received prior PBS-subsidised treatment with a biological medicine for this condition;</p> <p>AND</p> <p>Patient must not have failed PBS-subsidised treatment with this drug for this condition more than once.</p>

Population criteria	Patient must be aged 18 years or older
Treatment criteria	Must be treated by a rheumatologist
Prescriber Instructions	To be drafted.
Administrative Advice	

Initial 3 – grandfather treatment (to be drafted)

Initial 1, 2 and 3 – balance of supply (to be drafted)

Continuing treatment – to be drafted

Treatment phase:	Continuing treatment
Clinical criteria:	Patient must have previously received PBS-subsidised therapy with this drug for this condition AND Patient must have demonstrated an adequate response to PBS-subsidised therapy with this drug based on a reduction from baseline in the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score by 2 or more units (on a scale of 1 -1 0).
Population criteria	Patient must be aged 18 years or older
Treatment criteria	Must be treated by a rheumatologist Patients who do not achieve a reduction from the baseline assessment in the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score by 2 or more units (on a scale of 1 -1 0) with continuing treatment with this drug will not be eligible to receive further PBS-subsidised treatment with this drug. Patient must not receive more than 24 weeks of therapy under this restriction
Note	The authority application must be made in writing and must include: (a) a completed authority prescription form; and (b) a completed Ankylosing Spondylitis PBS Authority Application - Supporting Information Form which must include the following: (i) a copy of the radiological report confirming the absence of Grade II bilateral sacroiliitis or Grade III unilateral sacroiliitis; and (ii) a completed BASDAI Assessment Form; and (iii) a completed Exercise Program Self Certification Form included in the supporting information form;

Continuing treatment – balance of supply (to be drafted)

9 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised in Australia. It considers submissions in this context. A PBAC decision not to recommend listing or not to recommend changing a listing does not represent a final PBAC view about the merits of the medicine. A company can resubmit to the PBAC or seek independent review of the PBAC decision.

10 Sponsor's Comment

The sponsor had no comment.