

## 5.08 GOLIMUMAB, injection 100 mg/1.0 mL pre-filled syringe, Simponi<sup>®</sup>, Janssen-Cilag Pty Ltd

### 1 Purpose of application

1.1 The submission requested a General Schedule, Authority Required, listing for golimumab for the treatment of moderate to severe ulcerative colitis (MSUC). Golimumab for the treatment of MSUC has not been considered by the PBAC previously. Golimumab is also being considered for an additional indication (non-radiological axial spondyloarthritis) at the November 2017 PBAC meeting.

1.2 The basis for the submission was a cost-minimisation analysis against adalimumab, infliximab and vedolizumab, incorporating an indirect comparison using placebo as the common comparator.

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

Component	Description
Population	Adult patients with moderate to severe ulcerative colitis who have inadequate response to conventional therapy.
Intervention	Golimumab 200 mg at Week 0, 100 mg at Week 2, then 100 mg every 4 weeks.
Comparator	Three clinical comparators were presented: <ul style="list-style-type: none"> <li>• Adalimumab 160 mg at Week 0, 80 mg at Week 2, then 40 mg every two weeks. This was presented as the main comparator for pricing purposes.</li> <li>• Infliximab 5 mg/kg at Week 0, Week 2, Week 6, then every eight weeks.</li> <li>• Vedolizumab 300 mg at Week 0, Week 2, then every eight weeks.</li> </ul>
Outcomes	Remission, response, mucosal healing, and safety.
Clinical claim	In adult patients with moderate to severe ulcerative colitis, golimumab 200 mg/100 mg is: <ul style="list-style-type: none"> <li>• Induction therapy efficacy: <ul style="list-style-type: none"> <li>○ less efficacious than infliximab; and</li> <li>○ no worse than adalimumab and vedolizumab in terms of efficacy.</li> </ul> </li> <li>• Maintenance therapy efficacy: <ul style="list-style-type: none"> <li>○ no worse than infliximab, adalimumab and vedolizumab, in terms of efficacy.</li> </ul> </li> <li>• Safety: no worse than infliximab, adalimumab and vedolizumab, in terms of safety for induction and maintenance therapy.</li> </ul> <p>These claims were supported for induction, and are likely to be supported for maintenance, subject to issues of transitivity between the trials included in the indirect comparison. The submission did not include a formal indirect comparison for safety.</p>

Source: Table 1.1.1 p17 of the submission.

### 2 Requested listing

2.1 The requested restriction is summarised below, and was consistent with the evidence presented and the listings for other biological disease modifying anti-rheumatic drugs (bDMARDs) for the treatment of MSUC.

Suggestions and additions proposed by the Secretariat to the requested listing are added in italics and suggested deletions are crossed out with strikethrough.

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Dispensed Price for Max. Qty	Proprietary Name and Manufacturer
Induction treatment				
GOLIMUMAB 100 mg/1.0 ml injection solution for injection in a pre-filled syringe	1	4	Published Price: \$ [REDACTED] SPA: \$TBD	SIMPONI® Janssen-Cilag Pty Ltd
Continuing treatment				
GOLIMUMAB 100 mg/1.0 mL injection Solution for Injection in a pre-filled syringe	1	5	Published Price: \$ [REDACTED] SPA: \$TBD	SIMPONI® Janssen-Cilag Pty Ltd
Category / Program:	Section 85 Authority Required - GENERAL – General Schedule (Code GE)			
Restriction Level / Method:	<input type="checkbox"/> Restricted benefit <input checked="" type="checkbox"/> Authority Required <input type="checkbox"/> Streamlined			
PBS Indication:	Moderate to Severe Ulcerative Colitis			
Treatment phase:	Induction treatment; and continuing treatment			

- 2.2 The submission proposed that a special pricing arrangement [REDACTED] [REDACTED] for golimumab, be established once PBS listing was recommended. The specific details pertaining to the proposed special pricing arrangement were not discussed in the submission.
- 2.3 In addition to the pre-filled syringe, the Pre-Sub Committee Response (PSCR) requested a listing for a prefilled pen with 100 mg/1.0 mL golimumab (SIMPONI SMARTJECT INJECTOR). A pre-filled pen is defined as an injection device in the Australian Medicines Terminology descriptions.

### 3 Background

#### Registration status

- 3.1 Golimumab was TGA registered in March 2014 for the treatment of moderately to severely active ulcerative colitis in adult patients who have had an inadequate response to conventional therapy.

#### Previous PBAC consideration

- 3.2 Golimumab was previously considered by the PBAC at the March 2010 meeting for the treatment of severe active rheumatoid arthritis, severe psoriatic arthritis and active ankylosing spondylitis in a 50 mg/0.5 mL prefilled syringe, single use pre-filled pen form. The PBAC recommended this form for all three indications.
- 3.3 The PBAC has not previously considered golimumab for the treatment of moderately to severely active ulcerative colitis.

## 4 Population and disease

- 4.1 Ulcerative colitis (UC) is a life-long, chronic relapsing and remitting disease characterised by mucosal inflammation of the colon, which involves the rectum and extends proximally to a variable extent. The symptoms of UC vary between individuals in both duration and intensity. Typical symptoms of UC are cramping abdominal pain, bloody diarrhoea, unpredictable bowel movements, and nocturnal bowel movements. The disease has a significant impact upon patients' quality of life. The goal of treatment is to induce and maintain disease remission, prevent the removal of the bowel, and improve quality of life. Moderate to severe, or more extensive disease, requires therapy with a bDMARD.
- 4.2 Golimumab is proposed as an alternative bDMARD for use in the treatment of MSUC.

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

## 5 Comparator

- 5.1 The submission nominated adalimumab, infliximab, and vedolizumab as the main clinical comparators. These comparators are appropriate for this submission.
- 5.2 The submission nominated adalimumab as the main comparator for pricing purposes. The use of adalimumab as the lowest priced comparator was based on the initial PBS therapeutic relativity for this drug when listed on the basis of a comparison with infliximab. Infliximab will be subject to an 11.73% price reduction from 1<sup>st</sup> October 2017. The PBAC considered that adalimumab, vedolizumab and infliximab were appropriate comparators.
- 5.3 A review of the PBS Therapeutic Relativity Sheets revealed that there are three drugs currently listed for the treatment of MSUC for which a recommendation was made on a cost-minimisation basis. The treatment, comparator and resulting dose relativities are presented in Table 2.

**Table 2: Established therapeutic relativities of MSUC treatments listed on the PBS**

	Treatment	Comparator	
	Infliximab	Adalimumab <sup>a</sup>	Vedolizumab <sup>b</sup>
Induction	5 mg/kg at week 0, week 2, week 6	60 mg at week 0 and 80 mg week 2	-
	5 mg/kg at week 0, week 2, week 6	-	300 mg at week 0, week 2, week 6;
Maintenance	and then 5 mg/kg every 8 weeks	and then 40 mg fortnightly	-
	and then 5 mg/kg every 8 weeks	-	and then 300 mg every 8 weeks

Source: compiled during evaluation. Therapeutic Relativity Sheets - 1 August 2017. available on PBS website.

Notes: a Adalimumab was recommended for an extension to the listing to include the treatment of moderate to severe ulcerative colitis (UC). The PBAC considered that the inferiority should be reflected in the pricing of adalimumab. The equi-effective doses were based on infliximab.

b Vedolizumab was recommended for listing for the treatment of MSUC in adult patients on a cost-minimisation basis with infliximab.

*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 and welcomed the input from individuals (21), healthcare professionals (1) and organisations (2) via the Consumer Comments facility on the PBS website. The comments describe a range of benefits of treatment with golimumab including the ability to self-medicate, avoiding the disruption of trips to hospital, reduction in administration and the potential for a reduction of side effects.

6.3 The PBAC noted the advice received from Crohn’s and Colitis Australia clarifying the likely benefits from use of golimumab. The PBAC specifically noted the advice that the use of golimumab may improve the productivity of patients and decrease the time spent both in hospital and travelling to hospital, which is of particular relevance for patients living in rural and regional Australia. The PBAC noted that this advice was supportive of the evidence provided in the submission.

### Clinical trials

6.4 The submission was based on indirect comparisons of golimumab with infliximab, adalimumab, and vedolizumab, using placebo as the common comparator. The submission presented nine randomised controlled trials (RCTs) as the basis of the indirect treatment comparison as summarised in Table 3.

**Table 3: Summary of source of the main clinical evidence used in the submission**

	Induction Treatment Phase	Maintenance Treatment Phase
Golimumab	PURSUIT-SC: golimumab 200/100 mg vs placebo.	PURSUIT-M: golimumab 200/100 mg vs placebo. PURSUIT-J: golimumab 200/100 mg vs placebo. Supplementary only.
Adalimumab	ULTRA 1 & ULTRA 2: adalimumab 160/80/40 mg vs placebo.  Suzuki 2014: adalimumab 160/80/40 mg vs placebo. Supplementary only.	ULTRA 2: adalimumab 160/80/40 mg vs placebo.  Suzuki 2014: adalimumab 160/80/40 mg vs placebo. Supplementary only.
Infliximab	ACT 1 and ACT 2: infliximab 5 mg/kg vs placebo.	ACT 2: infliximab 5 mg/kg vs placebo.
Vedolizumab	GEMINI 1: vedolizumab 300 mg vs placebo.	

Source: Compiled during the evaluation.

Note: The clinical trials shown may have included treatment groups other than those included in this table. Those shown were the main source of evidence for each of the drugs shown in the respective treatment settings.

6.5 Details of the trials presented in the submission are provided in Table 4.

**Table 4: Trials and associated reports presented in the submission**

Trial ID	Protocol title/ Publication title	Publication citation
<b>Golimumab vs placebo trials</b>		
PURSUIT-SC	A clinical study report C0524T17: A phase 2/3 multicenter,	Janssen Research & Development.

Public Summary Document – November 2017 PBAC Meeting

<b>Trial ID</b>	<b>Protocol title/ Publication title</b>	<b>Publication citation</b>
	randomized, placebo-controlled, double-blind study to evaluate the safety and efficacy of golimumab induction therapy, administered subcutaneously, in subjects with moderately to severely active ulcerative colitis (PURSUIT-SC).	Internal study report, 11 August 2011.
	Sandborn WJ, Feagan BG, Marano C, et al; PURSUIT-SC Study Group. Subcutaneous golimumab induces clinical response and remission in patients with moderate-to-severe ulcerative colitis.	Gastroenterology. 2014; 146:85-95.
	Gibson PR, Feagan BG, Sandborn WJ, et al. 2016. Maintenance of efficacy and continuing safety of golimumab for active ulcerative colitis: PURSUIT-SC maintenance study extension through 1 year.	Clin Transl Gastroenterol 2016; 7 e168
PURSUIT-M	A clinical study report C0524T17: A phase 3 multicenter, randomized, placebo-controlled, double-blind study to evaluate the safety and efficacy of golimumab induction therapy, administered subcutaneously, in subjects with moderately to severely active ulcerative colitis (PURSUIT-Maintenance).	Janssen Research & Development. Internal study report, 12 June 2012.
	Sandborn WJ, Feagan BG, Marano C, et al. Subcutaneous golimumab maintains clinical response in patients with moderate-to-severe ulcerative colitis.	Gastroenterology. 2014; 146:96-109.
PURSUIT-J (Supplementary)	Hibi T, Imai Y, Senoo A, et al. 2017. Efficacy and safety of golimumab 52-week maintenance therapy in Japanese patients with moderate to severely active ulcerative colitis: a phase 3, double-blind, randomized, placebo-controlled study - (PURSUIT-J study).	Journal of Gastroenterology 2017; 1-11.
<b>Infliximab vs placebo trials</b>		
ACT 1	A 30 week clinical study report C0168T37: a phase 3 Randomized, Placebo-controlled, Double-blind Trial to Evaluate the Safety and Efficacy of Infliximab in Patients with Active Ulcerative Colitis (ACT-1).	Centocor (now Janssen). Internal study report, 4 March 2005
	A 54 week clinical study report C0168T37: a phase 3 Randomized, Placebo-controlled, Double-blind Trial to Evaluate the Safety and Efficacy of Infliximab in Patients with Active Ulcerative Colitis (ACT-1).	Centocor (now Janssen). Internal study report, 27 September 2005
	A study extension clinical study report C0168T37: a phase 3 Randomized, Placebo-controlled, Double-blind Trial to Evaluate the Safety and Efficacy of Infliximab in Patients with Active Ulcerative Colitis (ACT-1).	Centocor (now Janssen). Internal study report, 18 August 2008
	Rutgeerts P, Sandborn WJ, Feagan BG, et al. Infliximab for induction and maintenance therapy for ulcerative colitis.	N Engl J Med. 2005; 353:2462-2476.
ACT 2	A 30 week clinical study report C0168T46: a phase 3 Randomized, Placebo-controlled, Double-blind Trial to Evaluate the Safety and Efficacy of Infliximab in Patients with Active Ulcerative Colitis (ACT-2).	Centocor (now Janssen). Internal study report, 23 February 2005.
	A study extension clinical study report C0168T46: a phase 3 Randomized, Placebo-controlled, Double-blind Trial to Evaluate the Safety and Efficacy of Infliximab in Patients with Active Ulcerative Colitis (ACT-2).	Centocor (now Janssen). Internal study report, 12 August 2008.
	Rutgeerts P, Sandborn WJ, Feagan BG, et al. Infliximab for induction and maintenance therapy for ulcerative colitis.	N Engl J Med. 2005; 353:2462-2476.
<b>Adalimumab vs placebo trials</b>		
ULTRA 1	Reinisch W, Sandborn WJ, Hommes DW, et al. Adalimumab for induction of clinical remission in moderately to severely active UC: results of a randomised controlled trial.	Gut. 2011;60(6):780-787

Public Summary Document – November 2017 PBAC Meeting

Trial ID	Protocol title/ Publication title	Publication citation
	Reinisch W. Sandborn WJ. Panaccione R. Huang B. Pollack PF. Lazar A. Thakkar RB. (2013) 52-week efficacy of adalimumab in patients with moderately to severely active UC who failed corticosteroids and/or immunosuppressants.	Inflammatory Bowel Diseases. 19(8):1700-9, 2013 Jul.
ULTRA 2	Sandborn WJ, van Assche G, Reinisch W, et al. Adalimumab induces and maintains clinical remission in patients with moderate to severe UC.	Gastroenterology. 2012;142(2):257-65[e1-3]
	Sandborn, WJ; Colombel, JF; D'Haens, G; Van Assche, G; Wolf, D; Kron, M; Lazar, A; Robinson, AM; Yang, M; Chao, JD; Thakkar, R (2013).. One-year maintenance outcomes among patients with moderately-to-severely active UC who responded to induction therapy with adalimumab: subgroup analyses from ULTRA 1.	Aliment Pharmacol Ther. 2013 Jan;37(2):204-13
	Wolf, D., G. D'Haens, et al. (2014). Escalation to weekly dosing recaptures response in adalimumab-treated patients with moderately to severely active UC.	Alimentary Pharmacology & Therapeutics 40(5): 486-497.
Suzuki 2014	Suzuki Y, Motoya S, Hanai H, et al. Efficacy and safety of adalimumab in Japanese patients with moderately to severely active ulcerative colitis.	J Gastroenterol. 2014; 49:283-294.
<b>Vedolizumab vs placebo trial</b>		
GEMINI 1	Feagan B, Rutgeerts P, Sands B, et al. Vedolizumab as induction and maintenance therapy for ulcerative colitis.	N Engl J Med. 2013; 369(8):699-710.
<b>Meta-analyses of direct randomised trials</b>		
Archer et al (2014) (NICE Assessment report)	Archer, R., P. Tappenden, S. Ren, M. Martyn-St James, R. Harvey, H. Basarir, J. Stevens, C. Carroll, A. Cantrell, A. Lobo, NHS FoundationTrust and S. Hoque. Infliximab, adalimumab and golimumab for treating moderately to severely active UC after the failure of conventional therapy (including a review of TA140 and TA262): Clinical effectiveness systematic review and economic model.	Health Technol Assess. 2016 May;20(39):1-326.
Cholapranee et al., 2017	Cholapranee A, Hazlewood GS, Kaplan GG, et al. Systematic review with meta-analysis: comparative efficacy of biologics for induction and maintenance of mucosal healing in Crohn's disease and ulcerative colitis controlled trials.	Aliment Pharmacol Ther 45(10): 1291-1302.
Danese, 2014	Danese, S., G. Fiorino, L. Peyrin-Biroulet, E. Lucenteforte, G. Virgili, L. Moja and S. Bonovas. "Biological agents for moderately to severely active UC: a systematic review and network meta-analysis."	Annals of internal medicine 160(10): 704-711.
Galvan-Banqueri et al., 2015	Galvan-Banqueri M, Vega-Coca MD, Castillo-Munoz MA, et al. Indirect comparison for Anti-TNF drugs in moderate to severe ulcerative colitis.	Farm Hosp 2015; 39: 80-91.
Kawalec and Pilc 2016	Kawalec P, Pilc A. An indirect comparison of infliximab versus adalimumab or golimumab for active ulcerative colitis.	Arch Med Sci 2016; 12: 1097-1109.
Mei et al 2015	Mei WQ, Hu HZ, Liu Y, et al. Infliximab is superior to other biological agents for treatment of active ulcerative colitis: A meta-analysis.	World J Gastroenterol 2015; 21: 6044-6051.
Močko et al., 2016	Pharmacotherapy 2016; 36: 870-879.	Pharmacotherapy 2016; 36: 870-879.
Stidham, 2014	Stidham RW, Lee TCH, Higgins PDR, et al. Systematic review with network meta-analysis: the efficacy of anti-tumour necrosis factor-alpha agents for the treatment of UC.	Alimentary Pharmacology and Therapeutics. 2014;39:660-671

<b>Trial ID</b>	<b>Protocol title/ Publication title</b>	<b>Publication citation</b>
Thorlund, 2014	Thorlund K, Druyts E, Mills EJ, et al. Adalimumab versus infliximab for the treatment of moderate to severe UC in adult patients native to anti-TNF therapy: an indirect treatment comparison meta-analysis.	Journal of Crohn's and Colitis. 2014. Available from: dx.doi.org/10.1016/j.crohns.2014.01.010
Vickers, 2015	Vickers, A. D., R. R. Mody, A. Bergman, C. S. Ling, C. Ainsworth, J. Medjedovic and M. Smyth. "P554 Comparative efficacy of biologics in the treatment of moderately to severely active UC (UC): A systematic review and network meta-analysis"	Poster presentations: Clinical: Therapy & observation.
Lopez, 2015	Lopez, A., A. C. Ford, J. F. Colombel, W. Reinisch, W. J. Sandborn and L. Peyrin-Biroulet . "Efficacy of tumour necrosis factor antagonists on remission, colectomy and hospitalisations in UC: Meta-analysis of placebo-controlled trials."	Digestive and Liver Disease 2015; 47 (5):356-364

Source: p44, p51, Table 2.3-4 p51, Table 2.3-5 pp52-53 of the submission.

6.6 The key features of the included randomised trials are summarised in Table 5.

Table 5: Key features of the included evidence – indirect comparison

Trial	N	Design/duration of follow-up	Risk of bias	Patient population	Outcomes
<b>Golimumab vs placebo trials</b>					
PURSUIT-SC	658	R, DB, MC, PC, 8 weeks	Low	MSUC; anti-TNF naïve	W8: remission, response, mucosal healing
PURSUIT-M	310	R, DB, MC, PC, 54 weeks	High	MSUC; anti-TNF naïve	W54: remission, response, mucosal healing
PURSUIT-J	63	R, DB, MC, PC, 54 weeks	High	MSUC; anti-TNF naïve	W54: remission, response, mucosal healing
Meta-analysis		PURSUIT-M and PURSUIT-J were meta-analysed in a sensitivity analysis; assessed remission, response, mucosal healing after Week 54. Exclusion of PURSUIT-J from the main analysis on the basis that it was conducted in Japan was not well justified.			
<b>Infliximab vs placebo trials</b>					
ACT 1	242	R, DB, MC, PC, 54 weeks	High	MSUC; anti-TNF naïve	W6 & W54: Remission, response, mucosal healing, IBDQ response
ACT 2	244	R, DB, MC, PC, 30 weeks	High	MSUC; anti-TNF naïve	W6: Remission, response, mucosal healing, IBDQ response
Meta-analysis		Included ACT 1 and ACT 2; assessed remission, response, mucosal healing after Week 6.			
<b>Adalimumab vs placebo trials</b>					
ULTRA 1	260	R, DB, MC, PC, 8 weeks	Low	MSUC; anti-TNF naïve	W8: remission, response, mucosal healing
ULTRA 2	494	R, DB, MC, PC, 52 weeks	High	MSUC	W8 and W52: remission, response, mucosal healing, IBDQ response
Suzuki (2014)	186	R, DB, MC PC, 52 weeks	High	MSUC; anti-TNF naïve	W52: remission, response, mucosal healing, IBDQ response
Meta-analysis		<p>Assessed remission, response, mucosal healing:</p> <ul style="list-style-type: none"> <li>• after Week 8. <ul style="list-style-type: none"> <li>○ ULTRA 1 and ULTRA 2;</li> <li>○ ULTRA 1, ULTRA 2 and Suzuki 2014 as a sensitivity analysis;</li> <li>○ ULTRA 1 and ULTRA 2 (anti-TNF naïve) as a sensitivity analysis;</li> <li>○ ULTRA 1, ULTRA 2, (anti-TNF naïve) and Suzuki 2014 as a sensitivity analysis;</li> </ul> </li> <li>• After Week 52: <ul style="list-style-type: none"> <li>○ ULTRA 2 (anti-TNF naïve) as a sensitivity analysis</li> </ul> </li> </ul> <p>Inappropriately, the submission did not present sensitivity analyses using meta-analysed results of ULTRA 2 and Suzuki 2014 for the Week 52 outcomes (remission, response, mucosal healing).</p>			
<b>Vedolizumab vs placebo trial</b>					
GEMINI 1	374/373	R, DB, MC, PC, 52 weeks	High	MSUC	W8 and W52: remission, response, mucosal healing, IBDQ response

DB=double blind; MC=multi-centre; OL=open label; PC = placebo controlled; R=randomised.

Source: compiled during the evaluation

6.7 The overall risk of bias for each trial in the induction phase (Week 6/8) was low, but was high in the maintenance phase. PURSUIT-M, PURSUIT-J, ACT 2, ULTRA 2, Suzuki 2014 and GEMINI 1 were subject to attribution and reporting bias in the maintenance treatment phase. The PBAC previously considered the risk of bias was high for the maintenance phases in some of these trials (ULTRA 2 and ACT 2) due to

a large number of discontinuations and substantial loss to follow up (Adalimumab PSD July 2015 paragraph 7.6 p16).

- 6.8 The trial design for PURSUIT-M compared golimumab continuation with golimumab cessation (in those randomised to placebo) as only patients responding to golimumab treatment were randomised for maintenance therapy. Patients who were in clinical response at Week 6 in either of the golimumab induction trials (PURSUIT-SC or PURSUIT-IV) were eligible for enrolment. Patients (N=464) were randomised (1:1:1) to golimumab 100 mg q4w, golimumab 50 mg q4w, or placebo through to Week 52. The study also included a non-randomised portion consisting of patients (n=764) that did not have a clinical response to golimumab in either of the induction trials (n=405: continued with GOL 100 mg q4w), patients previously randomised to placebo who achieved a clinical response (n=129, continued with placebo q4w), and patients randomised to placebo who did not respond (n=230, continued with GOL 100 mg q4w). This study design differs from the adalimumab and infliximab trials in that there was an additional re-randomisation step after treatment induction commenced. The study design is similar to GEMINI 1 for vedolizumab.
- 6.9 There were issues identified with regards to the design of these trials that affect the transitivity of the trials included in the indirect treatment comparison:
- The benefit of golimumab in the maintenance phase of PURSUIT-M was for patients who responded to initial treatment with golimumab, and the overall response and remission rates are potentially overestimated when compared with a patient group that includes those who were not responding at week six, or who had been initially allocated to placebo. While the analysis in PURSUIT-M is relevant with respect to the proposed PBS listing, it is inconsistent with the procedures in the trials for adalimumab and infliximab.
  - There was considerable variability in the placebo response rates observed across the trials. The placebo response rates for induction ranged from 26% (GEMINI 1; vedolizumab) to 45% (ULTRA 1; adalimumab) at the end of induction, and from 12% (ULTRA 2; adalimumab) to 31% (PURSUIT-M; golimumab) in the maintenance setting. The higher response rate observed in placebo patients in PURSUIT-M may reflect that placebo patients within that study received golimumab at loss of response (n=76). Potentially, the incremental treatment effect observed for golimumab in PURSUIT-M could have been underestimated relative to the other bDMARD trials.
- 6.10 The submission presented a post-hoc analysis attempting to correct for infliximab and adalimumab responders in ACT1, ACT 2 and ULTRA 2 (as a means of aligning those trial groups with that in PURSUIT-M). It is unclear how this method separates patients in those studies into treatment groups similar to those in PURSUIT-M. An alternative approach of presenting a comparison of all patients that participated in PURSUIT-M (including those non-responding patients who were not randomised to golimumab), would have presented a dataset comparable to those of infliximab and adalimumab, without requiring a post-hoc adjustment of published data, and would be more informative for decision making.

- 6.11 The ESC considered that the submissions claims may be reasonable, particularly as similar transitivity issues were present in the vedolizumab comparison.

### Comparative effectiveness

- 6.12 A summary of the effectiveness for golimumab, infliximab, adalimumab and vedolizumab in patients with MSUC is presented in Table 6 to Table 9.
- 6.13 In induction, golimumab 200/100 mg was superior to placebo in terms of clinical response (OR= [REDACTED], 95% CI [REDACTED]), clinical remission (OR= [REDACTED], 95% CI [REDACTED]) and mucosal healing (OR= [REDACTED], 95% CI [REDACTED]). In maintenance, golimumab 100 mg was superior to placebo in terms of clinical response (OR= [REDACTED], 95% CI [REDACTED]), clinical remission (OR= [REDACTED], 95% CI [REDACTED]), and mucosal healing (OR= [REDACTED], 95% CI [REDACTED]).
- 6.14 The efficacy and safety outcomes after two years (104 weeks) of maintenance treatment for golimumab in PURSUIT-M were reported (Gibson et al (2016) but were not presented in the submission, on the grounds that the reported extension study was not an RCT. This is inappropriate given that this publication reported data on the long-term extension phase of that study and it is intended that golimumab be used as a chronic treatment for patients with MSUC. In the long-term extension study, disease activity was measured using a sub-score of the Mayo score (Physician's Global Assessment (PGA)). The results from that analysis showed that through to week 104, 86% of patients maintained inactive or mild disease activity (Gibson et al 2016).
- 6.15 The results for the comparator trials, as previously reviewed by the PBAC, indicate that all three treatments are superior to placebo in both the induction and maintenance phases with respect to the key clinical outcomes (clinical response, clinical remission and mucosal healing) and achieving sustained response. These results are presented in Table 6 to Table 9 below, along with the corresponding indirect comparisons with golimumab.

**Table 6: Summary of results of the indirect comparison for remission (induction)**

Comparison	Trial ID	GOL/IFX/ADA/VDZ n/N (%)	Placebo n/N (%)	Treatment effect
				OR <sup>b</sup> (95% CI)
GOL vs PBO	PURSUIT-SC	██████████	██████████	██████████
IFX vs PBO	ACT 1	47/121 (38.8)	18/121 (14.9)	██████████
	ACT 2	41/121 (33.9)	7/123 (5.7)	██████████
Meta-analysis	ACT 1, ACT 2			██████████
ADA vs PBO	ULTRA 1	██████████ (18.5)	██████████ (9.2)	██████████
	ULTRA 2	██████████ (16.5)	██████████ (9.3)	██████████
	ULTRA 2 (anti-TNF naïve)	██████████ (21.3)	██████████ (11.0)	██████████
	Suzuki 2014	██████████ (10.0) <sup>b</sup>	██████████ (11.5)	██████████
Meta-analysis	ULTRA 1, ULTRA 2			██████████
	ULTRA 1, ULTRA 2 (anti-TNF naïve)			██████████
	ULTRA 1, ULTRA 2, Suzuki 2014			██████████
	ULTRA 1, ULTRA 2 (anti-TNF naïve), Suzuki 2014			██████████
VDZ vs PBO	GEMINI 1	38/225 (16.9)	8/149 (5.4)	██████████
Indirect estimate of effect adjusted for the common reference (GOL vs IFX)				
Using trial results: PURSUIT-SC, ACT1, ACT 2				██████████
Indirect estimate of effect adjusted for the common reference (GOL vs ADA)				
Using trial results: PURSUIT-SC, ULTRA 1, ULTRA 2				██████████
Using trial results: PURSUIT-SC, ULTRA 1, ULTRA 2 (anti-TNF naïve)				██████████
Using trial results: PURSUIT-SC, ULTRA 1, ULTRA 2, Suzuki 2014				██████████
Using trial results: PURSUIT-SC, ULTRA 1, ULTRA 2 (anti-TNF naïve), Suzuki 2014				██████████
Indirect estimate of effect adjusted for the common reference (GOL vs VDZ)				
Using trial results PURSUIT-SC, GEMINI 1				██████████

Abbreviations: ADA, adalimumab; CI, Confidence interval; GOL, golimumab; IFX, infliximab; n, number of participants with event; N, total number of participants in group; OR, Odds ratio; PBO, placebo; VDZ, vedolizumab.

Notes: Figures in bold are statistically significant.

a Submission did not report (95% CI).

b The RR (95% CI) is denoted in Table 2.6-1 of the submission, however, the treatment effect presented in Table 2.6-1 was actually the OR (95% CI) as reported in the source documentation.

Source: Table 2.6.1 p117 of the submission; Attachment 07-ITC\_Analyses\_0.1\_10 of the submission; Attachment 06 of the submission.

**Table 7: Summary of results of the indirect comparison for response (induction)**

Comparison	Trial ID	GOL/IFX/ADA/VDZ n/N (%)	Placebo n/N (%)	Treatment effect
				OR <sup>d</sup> (95% CI)
GOL vs PBO	PURSUIT-SC	██████████	██████████	██████████
IFX vs PBO	ACT 1	84/121 (69.4)	45/121 (37.2)	██████████
	ACT 2	78/121 (64.5)	36/123 (29.3)	██████████
Meta-analysis	ACT 1, ACT 2			██████████
ADA vs PBO	ULTRA 1	██████████ (54.6)	██████████ (44.6)	██████████
	ULTRA 2	125/248 (50.4) <sup>b</sup>	85/246 (34.6) <sup>c</sup>	██████████
	ULTRA 2 (anti-TNF naïve)	89/150 (59.3)	56/145 (38.6)	██████████
	Suzuki 2014	██████████ (50.0)	██████████ (35.4)	██████████
Meta-analysis	ULTRA 1, ULTRA 2			██████████
	ULTRA 1, ULTRA 2 (anti-TNF naïve)			██████████
	ULTRA 1, ULTRA 2, Suzuki 2014			██████████
	ULTRA 1, ULTRA 2 (anti-TNF naïve), Suzuki 2014			██████████
VDZ vs PBO	GEMINI 1	106/225 (47.1)	38/149 (25.5)	██████████
Indirect estimate of effect adjusted for the common reference (GOL vs IFX)				
Using trial results: PURSUIT-SC, ACT1, ACT 2				██████████
Indirect estimate of effect adjusted for the common reference (GOL vs ADA)				
Using trial results: PURSUIT-SC, ULTRA 1, ULTRA 2				██████████
Using trial results: PURSUIT-SC, ULTRA 1, ULTRA 2 (anti-TNF naïve)				██████████
Using trial results: PURSUIT-SC, ULTRA 1, ULTRA 2, Suzuki 2014				██████████
Using trial results: PURSUIT-SC, ULTRA 1, ULTRA 2 (anti-TNF naïve), Suzuki 2014				██████████
Indirect estimate of effect adjusted for the common reference (GOL vs VDZ)				
Using trial results PURSUIT-SC, GEMINI 1				██████████

Abbreviations: ADA, adalimumab; CI, Confidence interval; GOL, golimumab; IFX, infliximab; n, number of participants with event; N, total number of participants in group; OR, Odds ratio; PBO, placebo; VDZ, vedolizumab.

Notes: Figures in bold are statistically significant.

a Submission did not report (95% CI).

b Reported as 125/248 (50.4) in Sandborn 2012 p259. Submission reported this as ██████████ (██████████%) in Attachment 07; and ██████████ (██████████%) in Table 2.6.1.

c Reported as 85/246 (34.6) in Sandborn 2012 p259. Submission reported this as ██████████ (██████████%) in Attachment 07 in Table 2.6.1.

d The RR (95% CI) is denoted in Table 2.6-1 of the submission, however the treatment effect was actually the OR (95% CI) as reported in the source documentation.

Source: Table 2.6.1 p117 of the submission; Attachment 07-ITC\_Analyses\_0.1\_10 of the submission; Attachment 06 of the submission.

**Table 8: Summary of results of the indirect comparison for remission (maintenance)**

Comparison	Trial ID	GOL/IFX/ADA/VDZ n/N (%)	Placebo n/N (%)	Treatment effect
				OR (95% CI)
GOL vs PBO	PURSUIT-M			
	PURSUIT-J	16/32 (50.0)	2/31 (6.5)	
Meta-analysis	PURSUIT-M, PURSUIT-J			
IFX vs PBO	ACT 1			
	ACT 1 (Induction responders) <sup>b</sup>			
ADA vs PBO	ULTRA 2	(17.3)	(8.5)	
	ULTRA 2 (Induction responders) <sup>c</sup>			
	ULTRA 2 (anti-TNF naïve)	33/150 (22.0)	18/145 (12.4)	
	ULTRA 2 (anti-TNF naïve, induction responders) <sup>c</sup>	33/89 (37.1)	18/56 (32.1)	
	Suzuki 2014	41/177	7/96	
Meta-analysis	ULTRA 2, Suzuki 2014			
VDZ vs PBO	GEMINI 1	51/122 (41.8)	20/126 (15.9)	
Indirect estimate of effect adjusted for the common reference (GOL vs IFX)				
Using trial results: PURSUIT-M, ACT 1				
Using trial results: PURSUIT-M, ACT 1 (Induction responders)				
Using trial results: PURSUIT-M, PURSUIT-J, ACT 1				
Using trial results: PURSUIT-M, PURSUIT-J, ACT 1 (Induction responders)				
Indirect estimate of effect adjusted for the common reference (GOL vs ADA)				
Using trial results: PURSUIT-M, ULTRA 2				
Using trial results: PURSUIT-M, ULTRA 2 (Induction responders)				
Using trial results: PURSUIT-M, ULTRA 2 (anti-TNF naïve)				
Using trial results: PURSUIT-M, ULTRA 2 (anti-TNF naïve, induction responders)				
Using trial results: PURSUIT-M, PURSUIT-J, ULTRA 2,				
Using trial results: PURSUIT-M, PURSUIT-J, ULTRA 2 (Induction responders)				
Using trial results: PURSUIT-M, PURSUIT-J, ULTRA 2 (anti-TNF naïve)				
Using trial results: PURSUIT-M, PURSUIT-J, ULTRA 2 (anti-TNF naïve, induction responders)				
Using trial results: PURSUIT-M, PURSUIT-J, ULTRA 2, Suzuki 2014				
Indirect estimate of effect adjusted for the common reference (GOL vs VDZ)				
Using all trial results PURSUIT-M, GEMINI 1				
Using all trial results PURSUIT-M, PURSUIT-J, GEMINI 1				

Abbreviations: ADA, adalimumab; CI, Confidence interval; GOL, golimumab; IFX, infliximab; n, number of participants with event; N, total number of participants in group; OR, Odds ratio; PBO, placebo; VDZ, vedolizumab.

Notes: Figures in bold are statistically significant.

a Submission did not report (95% CI).

b The denominator of the comparison of 'Induction responders' was not verified during the evaluation. It was unclear from the source provided whether the patients in clinical remission counted at Week 6 were the same subjects that were counted at Week 54.

c The denominator of the comparison of 'Induction responders' was not verified during the evaluation. The submission did not provide the method of calculation from Sandborn 2012 Table 3 p262. It was unclear from the source provided whether the patients in clinical remission counted at Week 8 were the same subjects that were counted at Week 52.

d The submission did not conduct an analysis on this comparison.

Source: Table 2.6-3 p119, Table 2.7-3 p132-134 of the submission; Attachment 07-ITC\_Analyses\_0.1\_10 of the submission; Attachment 6 of the submission; Sandborn 2012 Table 3 p262.

**Table 9: Summary of results of the indirect comparison for sustained response (maintenance)**

Comparison	Trial ID	GOL/IFX/ADA/VDZ n/N (%)	Placebo n/N (%)	Treatment effect
				OR (95% CI)
GOL vs PBO	PURSUIT-M			
	PURSUIT-J			
Meta-analysis	PURSUIT-M, PURSUIT-J			
IFX vs PBO	ACT 1	(38.8)	(14.0)	
	ACT 1 (Induction responders) <sup>b</sup>			
ADA vs PBO	ULTRA 2	59/248 (23.8)	30/246 (12.2)	
	ULTRA 2 (Induction responders) <sup>c</sup>			
	ULTRA 2 (anti-TNF naïve)	44/150 (29.3)	24/145 (16.6)	
	ULTRA 2 (anti-TNF naïve, Induction responders) <sup>c</sup>			
VDZ vs PBO	GEMINI 1	69/122 (56.6)	30/126 (23.8)	
Indirect estimate of effect adjusted for the common reference (GOL vs IFX)				
Using trial results: PURSUIT-M, ACT 1				
Using trial results: PURSUIT-M, ACT 1 (Induction responders)				
Using trial results: PURSUIT-M, PURSUIT-J, ACT 1				
Using trial results: PURSUIT-M, PURSUIT-J, ACT 1 (Induction responders)				
Indirect estimate of effect adjusted for the common reference (GOL vs ADA)				
Using trial results: PURSUIT-M, ULTRA 2				
Using trial results: PURSUIT-M, ULTRA 2 (Induction responders)				
Using trial results: PURSUIT-M, ULTRA 2 (anti-TNF naïve)				
Using trial results: PURSUIT-M, ULTRA 2 (anti-TNF naïve, induction responders)				
Using trial results: PURSUIT-M, PURSUIT-J, ULTRA 2				
Using trial results: PURSUIT-M, PURSUIT-J, ULTRA 2 (Induction responders)				
Using trial results: PURSUIT-M, PURSUIT-J, ULTRA 2 (anti-TNF naïve)				
Using trial results: PURSUIT-M, PURSUIT-J, ULTRA 2 (anti-TNF naïve, induction responders)				
Indirect estimate of effect adjusted for the common reference (GOL vs VDZ)				
Using all trial results PURSUIT-M, GEMINI 1				

Abbreviations: ADA, adalimumab; CI, Confidence interval; GOL, golimumab; IFX, infliximab; n, number of participants with event; N, total number of participants in group; OR, Odds ratio; PBO, placebo; VDZ, vedolizumab.

Notes:

Figures in bold are statistically significant.

a Submission did not report (95% CI).

b The denominator of the comparison of 'Induction responders' was not verified during the evaluation. It was unclear from the source provided whether the patients in clinical remission counted at Week 6 were the same subjects that were counted at Week 54.

c The denominator of the comparison of 'Induction responders' was not verified during the evaluation. The submission did not provide the method of calculation from Sandborn 2012 Table 3 p262. It was unclear from the source provided whether the patients in clinical remission.

d Sustained response was defined in the PURSUIT trials as response at Week 30 and Week 54.

Source: Table 2.6-3 p119 of the submission; Attachment 07-ITC\_Analyses\_0.1\_10, Attachment 07-ITC\_Analyses\_11\_12, Attachment 07-ITC\_Analyses\_13\_16 of the submission; Sandborn 2012 Table 3 p262.

6.16 The PBAC considered that golimumab was most likely non inferior in efficacy to adalimumab and vedolizumab for both induction and maintenance and inferior to infliximab for induction and non-inferior for maintenance.

## Comparative harms

6.17 A summary of the adverse events for golimumab, infliximab, adalimumab and vedolizumab in patients with MSUC is presented in Table 10 (induction) and Table 11 (maintenance). Data presented in the submission were obtained from the trials included in the indirect comparison, the golimumab PSUR, and the long term extension of PURSUIT-M (Gibson et al 2016).

**Table 10: Summary of adverse events in the induction phase for trials**

AEs	Golimumab		Infliximab				Adalimumab				Vedolizumab	
	PURSUIT-SC		ACT I*		ACT II*		ULTRA 1		Suzuki 2014†		GEMINI I	
	PBO	GOL	PBO	IFX	PBO	IFX	PBO	ADA	PBO	ADA	PBO	VDZ
N	330	331	121	121	123	121	223	223	96	90	149	225
Any AEs	126 (38.2)	124 (37.5)	98 (81.0)	103 (85.1)	90 (73.2)	99 (81.8)	108 (48.4)	112 (50.2)	45 (46.9)	40 (44.4)	69 (46.3)	90 (40.0)
SAEs	15 (4.5)	9 (2.7)	24 (19.8)	17 (14.0)	24 (19.5)	13 (10.7)	17 (17.6)	9 (4.0)	7 (7.3)	4 (4.4)	10 (6.7)	5 (2.2)
Infections	40 (12.1)	39 (11.8)	20 (16.5) <sup>a</sup>	28 (23.5) <sup>a</sup>	15 (12.2) <sup>a</sup>	18 (14.9) <sup>a</sup>	35 (15.7)	32 (14.3)	15 (15.6)	17 (18.9)	22 (14.7)	31 (13.8)
Serious infectious	6 (1.8)	1 (0.3)	2 (1.7)	1 (0.8)	1 (0.8)	2 (1.7)	3 (1.3)	0	0	3 (3.3)	3 (2.0)	1 (0.4)

Source: Table 2.6-4 of the submission.

Abbreviations: AE = adverse event; ADA = adalimumab; GLM = golimumab; IFX = infliximab; NR = not reported; PBO = placebo; VDZ = vedolizumab

Note: a Reported as infections requiring antimicrobial treatment.

**Table 11: Summary of adverse events in the maintenance phase for trials**

Adverse event	Golimumab				Infliximab		Adalimumab		Vedolizumab	
	PURSUIT-M		PURSUIT-J		ACT I		ULTRA II		GEMINI I	
	PBO	GOL	PBO	GOL	PBO	IFX	PBO	ADA	PBO	VDZ
N	156	154	31	32	121	121	260	257	275	620
Any adverse event	103 (66.0)	113 (73.4)	22 (71.0)	31 (96.9)	103 (85.1)	106 (87.6)	218 (83.8)	213 (82.9)	220 (80)	497 (80)
Serious adverse event	13 (8.3)	22 (14.3)	4 (12.9)	1 (3.1)	31 (25.6)	26 (21.5)	32 (12.3)	31 (12.1)	37 (13.5)	77 (12.4)
Infections	44 (28.2)	60 (39.0)	11 (35.5)	21 (65.6)	37 (38.8)	53 (43.8)	103 (39.6)	116 (45.1)	155 (56)	371 (60)
Serious infectious	3 (1.9)	5 (3.2)	NR	NR	5 (4.1)	3 (2.5)	5 (1.9)	4 (1.6)	8 (2.9)	12 (1.9)
Deaths	0	2 (1.3) <sup>‡</sup>	0	0	0	0	0	0	NR	NR

Source: Source: Table 2.6-5 p124 of the submission.

Abbreviations: AE = adverse event; ADA = adalimumab; GLM = golimumab; IFX = infliximab; NR = not reported; PBO = placebo; VDZ = vedolizumab

Note: For Suzuki 2014, values were reported in events per 100 patient years, therefore they are not included in this table

a Includes a patient who died during the long-term study extension

6.18 The submission did not conduct an indirect comparison of safety for golimumab with any of the comparators (infliximab, adalimumab or vedolizumab).

6.19 Three publications (a systematic review, meta-analysis and indirect comparison) of the safety of golimumab, infliximab, adalimumab and vedolizumab noted that these drugs have generally similar AE profiles (Mocko et al. 2016, Danese et al. 2014 and Mei et al. 2015). A fourth publication (Kawalec and Pilc 2016) reported a higher risk

of SAEs with golimumab compared with infliximab (RR 0.41, 95% CI 0.19-0.87, p=0.0205).

## Interpretation of clinical evidence

- 6.20 The submission described golimumab as:
- Use in induction therapy:
    - less effective (efficacy) for induction therapy compared with infliximab; and
    - non-inferior (efficacy) to adalimumab and vedolizumab.
  - Use in maintenance therapy: non-inferior (efficacy) compared with infliximab, adalimumab and vedolizumab.
  - Non-inferior in terms of safety for induction compared with infliximab, adalimumab and vedolizumab.
- 6.21 The PBAC considered the efficacy and safety claims to be reasonable for the induction phase of treatment, when comparing golimumab with all three comparators.
- 6.22 In the maintenance phase, differences between the study designs (largely due to PURSUIT-M enrolling golimumab responders only) mean that the non-inferiority claim is uncertain, but likely to be supported. However, the efficacy results for PURSUIT-SC and PURSUIT-J presented in the submission are for a maximum of 54 weeks of treatment. The submission did not present the longer term efficacy data for PURSUIT-M published by Gibson et al (2016).
- 6.23 On balance, the PBAC considered that the claim of non-inferior comparative effectiveness in the maintenance phase was reasonable.
- 6.24 The PBAC considered that the claim of non-inferior comparative safety was reasonable.

## Economic analysis

- 6.25 The submission nominated adalimumab as the comparator for pricing purposes on the basis that it was the lowest priced drug in this indication. The ESC and PBAC considered that the least expensive of adalimumab, infliximab and vedolizumab was the appropriate comparator for pricing purposes.
- 6.26 The equi-effective doses in the submission were golimumab 100 mg monthly and two doses of adalimumab 40 mg given every other week (i.e. 28 days' supply). This estimation was based on the indirect comparison of golimumab (PURSUIT-M) and adalimumab (ULTRA 2) in the maintenance phase of treatment. The estimation of the equi-effective dose excluded treatment in the induction period, and assumed golimumab dosing was on a monthly rather than four weekly basis.
- 6.27 The exclusion of induction dosing was inconsistent with the method used to estimate the equi-effective doses for adalimumab and vedolizumab where the equi-effective doses included the induction and maintenance treatment phases:

- “The equi-effective doses are based on the following: adalimumab 160 mg at week 0 and 80 mg week 2, then 40 mg fortnightly thereafter and infliximab 5 mg/kg (weeks 0, 2, and 6 then every 8 weeks thereafter).”
- “The equi-effective doses are: Vedolizumab – 300 mg administered at week 0, week 2, week 6 and then every 8 weeks thereafter; and Infliximab – 5 mg/kg administered at week 0, week 2, week 6 and then every 8 weeks thereafter.”

The ESC noted that the PSCR acknowledged (p3) that equi-effective dosing of golimumab should include the doses given for induction.

6.28 Assuming monthly rather than four weekly dosing for golimumab results in one less administration of drug per 12 month period.

- The ESC noted that the PSCR argued (p3) that the dosing of golimumab would likely be monthly and not every 28 days, thereby increasing adherence and effectiveness.
- The ESC noted that in this submission the dosing in the PI and associated trial was every 28 days and considered that treatment every 4 weeks was appropriate for the purposes of the economic analysis. The ESC further noted that the PBAC had previously considered that the pricing of golimumab for other indications should be based on administration once every four weeks, consistent with the trials presented in their respective submissions.

6.29 The PBAC noted the pre-PBAC response that claimed that “clinicians (and patients) are most likely to administer golimumab on a monthly basis” however it considered that the economic analysis should be conducted on the basis of 4 weekly dosing as used in the clinical trial and reported in the PI.

6.30 The submission considered that there would be additional administration costs for a proportion of patients who are unable to self-inject treatment and factored the cost-offset (associated with less frequent dosing) into the requested price of golimumab. The cost offset used for administration was consistent with previous submissions considered for golimumab in the indications for the treatment of ankylosing spondylitis, psoriatic arthritis and rheumatoid arthritis. The submission’s estimate of a reduction of \$ [REDACTED] per injection was based on the assumption that golimumab is administered monthly. A revised estimated cost offset of \$ [REDACTED] per injection over one year was calculated during the evaluation based on golimumab dosing every four weeks. Including dosing given during the induction period and adjusting for dosing over two years, the estimated cost offset decreased to \$ [REDACTED] per injection.

6.31 During the evaluation the DPMQ based on the published prices was re-calculated using the equi-effective doses (induction and maintenance) based on the dosing schedule used in the trials. The revised price cost-minimised to adalimumab over a two year treatment period was \$ [REDACTED]. When factoring the price premium requested to include the cost-offset proposed, the revised price was \$ [REDACTED].

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

6.32 Using the published price requested in the submission, the cost per pack of golimumab (28 days treatment) was \$ [REDACTED]. Assuming 13 packs per patient per year are dispensed in the maintenance treatment phase the cost would be \$ [REDACTED] per patient. Treatment is ongoing for the lifetime of the patient. Using the re-estimated cost-minimising price of \$ [REDACTED], the resulting cost per year of maintenance treatment was \$ [REDACTED] per patient.

**Estimated PBS usage & financial implications**

6.33 This submission was not considered by DUSC.

6.34 The submission adopted a market share approach in estimating the potential utilisation of golimumab on the PBS. A summary of the estimated use and financial implications for listing golimumab for the treatment of MSUC to the PBS is presented in Table 12. The submission assumed that golimumab was administered monthly (rather than every four weeks). Based on the requested published price, once dosing for golimumab was adjusted to every four weeks, listing of golimumab was no longer cost saving to the PBS. The cost of listing golimumab on the PBS increased to less than \$10 million per year in year 1, up to less than \$10 million per year in year 6. A summary of the estimated use and financial implications for listing golimumab on the PBS, assuming 13 units of golimumab are dispensed per patient per year, is presented in Table 13.

**Table 12: Estimated use and financial implications (submission)**

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
<b>Total market bDMARDs (infliximab, adalimumab and vedolizumab) for MSUC</b>						
Net cost to PBS	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]
<b>Estimated extent of use of golimumab</b>						
Number of scripts dispensed <sup>a</sup>	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
<b>Estimated financial implications of golimumab</b>						
Cost to PBS/RPBS	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]
Copayments	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]
Cost to PBS/RPBS less copayments	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]
<b>Estimated financial implications for infliximab, adalimumab and vedolizumab if golimumab is listed</b>						
Cost to PBS/RPBS	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]
Copayments	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]
Cost to PBS/RPBS less copayments	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]
<b>Net financial implications</b>						
Net reduction in cost to PBS	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]

<sup>a</sup> Assuming 12 administrations per year.

Source: Table 4.2.2, Table 4.2.3, Table 4.3.2, and Table 4.4.1 of the Commentary.

The redacted table shows that at year 5, the estimated number of scripts was less than 10,000 per year and the net reduction in cost to the PBS would be less than \$10 million per

year.

**Table 13: Estimated use and financial implications: Commentary**

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
<b>Total market bDMARDs (infliximab, adalimumab and vedolizumab) for MSUC</b>						
Net cost to PBS	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]
<b>Estimated extent of use of golimumab</b>						
Number of scripts dispensed <sup>a</sup>	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
<b>Estimated financial implications of golimumab</b>						
Cost to PBS/RPBS	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]
Copayments	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]
Cost to PBS/RPBS less copayments	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]
<b>Estimated financial implications for infliximab, adalimumab and vedolizumab if golimumab is listed</b>						
Cost to PBS/RPBS	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]
Copayments	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]
Cost to PBS/RPBS less copayments	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]
<b>Net financial implications</b>						
<b>Net increase in cost to PBS</b>	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]

<sup>a</sup> Assuming 13 rather than 12 administrations per year.

Source: Table 4.2.2, Table 4.2.3, Table 4.3.2, and Table 4.4.2 of the Commentary.

The redacted table shows that at year 5, the estimated number of scripts was less than 10,000 per year and the net increase in cost to the PBS would be less than \$10 million per year.

## Quality use of medicines

6.35 No quality use of medicines information was provided in the submission. There is the potential for confusion between monthly and four weekly dosing.

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

## 7 PBAC Outcome

7.1 The PBAC recommended the Authority Required, listing of golimumab for the treatment of moderate to severe ulcerative colitis.

7.2 The PBAC accepted that the clinical place for therapy of golimumab would be as an alternative treatment option to the currently PBS listed bDMARDs: adalimumab, infliximab and vedolizumab.

7.3 The PBAC considered that any of the currently PBS listed bDMARDs could be an appropriate comparator. The PBAC accepted that golimumab was non-inferior in efficacy and safety to vedolizumab and adalimumab in both induction and maintenance therapy; and inferior to infliximab for efficacy for induction, but non-inferior to infliximab for safety and for efficacy in maintenance therapy.

7.4 The PBAC considered that in the absence of demonstrated superior comparative

effectiveness or safety over these alternative bDMARDs, golimumab should be listed on the basis of a cost-minimisation analysis against the least expensive bDMARD, but it must also be less expensive than infliximab to account for its inferiority in induction therapy.

- 7.5 The PBAC noted that the Pre-Sub Committee Response (PSCR) (p3) and the pre-PBAC response (p2) acknowledged that equi-effective dosing of golimumab should include the doses given for induction.
- 7.6 The PBAC considered that the equi-effective doses were:
- Golimumab - 200 mg at Week 0, 100 mg at Week 2, then 100 mg every 4 weeks
  - Adalimumab - 160 mg at week 0 and 80 mg week 2, then 40 mg fortnightly thereafter
  - Vedolizumab – 300 mg administered at week 0, week 2, week 6 and then every 8 weeks thereafter; and
  - Infliximab – 5 mg/kg administered at week 0, week 2, week 6 and then every 8 weeks thereafter.
- 7.7 The PBAC recommended that the Early Supply Rule should apply to golimumab.
- 7.8 The PBAC advised that golimumab was not suitable for prescribing by nurse practitioners as antineoplastic and immunomodulating agents are currently outside of the scope for prescribing by nurse practitioners.
- 7.9 The PBAC did not recommend that golimumab should be treated as interchangeable on an individual patient basis with any other drug.
- 7.10 The PBAC noted that this submission is not eligible for an Independent Review because it has received a positive recommendation.

**Outcome:**

Recommended

## 8 Recommended listing

Add new items:

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Name and Manufacturer	
Induction treatment				
GOLIMUMAB 100 mg/1.0 ml injection solution for injection in a pre-filled syringe	1	4	SIMPONI ®	Janssen-Cilag Pty Ltd
Continuing treatment				
GOLIMUMAB 100 mg/1.0 mL injection Solution for Injection in a pre-filled syringe	1	5	SIMPONI ®	Janssen-Cilag Pty Ltd
Category / Program:	GENERAL – General Schedule (Code GE)			
Restriction Level / Method:	<input type="checkbox"/> Restricted benefit <input checked="" type="checkbox"/> Authority Required <input type="checkbox"/> Streamlined			
PBS Indication:	Moderate to Severe Ulcerative Colitis			
Treatment phase:	Induction treatment; and continuing treatment			

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Name and Manufacturer	
Induction treatment				
GOLIMUMAB 100 mg/1.0 ml injection, 1 mL injection device	1	4	SIMPONI Smartject	Janssen-Cilag Pty Ltd
Continuing treatment				
GOLIMUMAB 100 mg/1.0 mL injection, 1 mL injection device	1	5	SIMPONI Smartject	Janssen-Cilag Pty Ltd
Category / Program:	GENERAL – General Schedule (Code GE)			
Restriction Level / Method:	<input type="checkbox"/> Restricted benefit <input checked="" type="checkbox"/> Authority Required <input type="checkbox"/> Streamlined			
PBS Indication:	Moderate to Severe Ulcerative Colitis			
Treatment phase:	Induction treatment; and continuing treatment			

## 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.