

7.11 ADALIMUMAB

40 mg/0.8 mL injection, 2 x 0.8 mL cartridges

40 mg/0.8 mL injection, 2 x 0.8 mL syringes

40 mg/0.8 mL injection, 6 x 0.8 mL cartridges

40 mg/0.8 mL injection, 6 x 0.8 mL syringes

Humira®, Abbvie Pty Ltd

1 Purpose of Application

- 1.1 The minor resubmission sought a Section 85 Authority required listing for adalimumab for the treatment of patients with moderate to severe ulcerative colitis (UC). The resubmission offered a price reduction of █% to the current published DPMQ for adalimumab of a pack of 2 syringes or cartridges for induction and maintenance therapy i.e. an effective DPMQ would be \$█.

2 Background

- 2.1 This was the fifth submission for adalimumab in UC. The previous four submissions were considered at November 2013, July 2014, July 2015, and November 2015 PBAC meeting.

Table 1: Summary of the previous two resubmissions and current resubmission for adalimumab in UC

	July 2015: Major resubmission	November 2015: Minor resubmission	March 2016 Current minor resubmission
Requested PBS listing	The restriction was updated to be aligned with infliximab's restriction for moderate to severe UC with the exception that the adalimumab restriction does not include paediatric patients. PBAC comment: The PBAC considered that the exclusion of paediatric patients from the restriction was not adequately justified and should be addressed in any future major resubmission. [Item 7.01, adalimumab Public Summary Document (PSD) July 2015, paragraph 7.2].	Unchanged PBAC comment: The PBAC noted that the proposed restriction was unchanged in the resubmission. The PBAC maintained its previous consideration from the July 2015 meeting that the exclusion of paediatric patients from the adalimumab restriction was not adequately justified and should be addressed in any future submission. [adalimumab PSD November 2015, para 7.2]	The current resubmission agreed to broaden the restriction to include paediatric patients as well as adult patients, as suggested by the PBAC. However, the resubmission maintained that its proposed restriction limiting to adult patients is consistent with the TGA registered indication. The minor submission stated that registration in Australia is currently anticipated for 2019.
Requested price	The DPMQ for: 6 x 40 mg ADA = \$█ 2 x 40 mg ADA = \$█ Specific terms for an RSA were not proposed, however the sponsor was willing to enter into a RSA.	The DPMQ for: 6 x 40 mg ADA = \$█ 2 x 40 mg ADA = same price as infliximab. Sponsor noted there is a Special Pricing Arrangement for infliximab and the price	A price reduction of █% offered to █-pack (maintenance phase). The DPMQ for: 6 x 40 mg ADA = \$█* 2 x 40 mg ADA = \$█#

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	July 2015: Major resubmission	November 2015: Minor resubmission	March 2016 Current minor resubmission
		<p>offer ██████████% ██████████ from the July 2015 resubmission.</p> <p>PBAC Comment: The PBAC noted that the resubmission offered a ██████████% ██████████.</p> <p>Given that inferiority (compared with infliximab) in the maintenance phase is also likely, there is no basis to accept the same price of infliximab. In the absence of a modelled economic evaluation of the cost savings per health outcome foregone, the PBAC considered that a reduction in price of adalimumab of around ██████████% in the maintenance treatment phase is likely to be reasonable given the observed relative treatment effects in both phases and that this about ██████████ of the ██████████.</p> <p>[adalimumab PSD November 2015 , para 7.8]</p>	<p>* ██████████% discount offered in the Nov 15 resubmission</p> <p># ██████████% discount offered in this resubmission, compared with the published DPMQ for the ██████████ pack of adalimumab. In November 2015, the PBAC considered that a reduction in price of adalimumab of around ██████████% in the maintenance treatment phase (in the context of a proposed equivalent price to infliximab) is likely to be reasonable.</p>
Main comparator	Infliximab	unchanged	unchanged
Clinical evidence	<p>An indirect comparison between adalimumab and infliximab was presented. It included the previously presented ULTRA 1 and ULTRA 2 trials plus Suzuki (2014) (n=274) and three Infliximab trials: included: ACT 1 (n=n364), ACT 2 (n=364), Probert (2003) (n=n43)</p> <p>In addition, an indirect comparison to vedolizumab using GEMINI I (n=747, 374 induction and 373 maintenance) was included in an Attachment.</p>	No new clinical evidence presented.	No new clinical evidence presented.
Clinical claim	<p>The breadth of evidence suggests no statistically significant differences in efficacy and considered similar in safety for adalimumab vs infliximab (p152, of the resubmission).</p> <p>PBAC Comment: PBAC considered that the indirect comparisons</p>	Resubmission acknowledged inferiority in the induction phase.	Unchanged from November 2015 minor resubmission.

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	July 2015: Major resubmission	November 2015: Minor resubmission	March 2016 Current minor resubmission
	presented in the resubmission provided low certainty evidence for the claim on non-inferiority between adalimumab and infliximab, both in the remission phase and in the maintenance phase. [adalimumab PSD July 2015, para 7.7].		
Clinical place	<p>The PBAC considered that non-inferiority between adalimumab and infliximab was not demonstrated, however, the PBAC considered the clinical positioning to be unreasonable and that adalimumab may be more appropriately placed as a subsequent-line biologic, following failure of, or intolerance to, infliximab or vedolizumab [adalimumab PSD July 2015, para 7.3].</p> <p>The PBAC considered that further evidence of non-inferiority against infliximab would need to be provided in any future major re-submission, preferably in the form of a head-to-head randomised trial. Alternatively, the PBAC considered that a way forward could be to position adalimumab as a later-line biologic treatment option following failure of, or intolerance to, infliximab or vedolizumab. [adalimumab PSD July 2015 , para 7.12]</p>	The PBAC reaffirmed its view from the July 2015 meeting that adalimumab may be more appropriately placed as a subsequent-line biologic, following failure of, or intolerance to, infliximab or vedolizumab [adalimumab PSD November 2015, para 7.3]	The current submission maintained adalimumab is appropriate for first line treatment.
Economic evaluation	Cost-minimisation analysis versus infliximab. PBAC Comment: PBAC did not consider that the resubmission had conclusively demonstrated that adalimumab was non-inferior to infliximab, it also did not accept the cost-minimisation analysis. [adalimumab PSD July 2015, para 7.9].	No economic evaluation presented.	No economic evaluation presented.
Number of patients	Less than 10,000 in Year 1 increasing to less than 10,000 in Year 5.	Unchanged	Unchanged
Estimated net cost to PBS and RPBS	Net cost (taking into account cost savings from reduced use of infliximab) of less than \$10 million in Year 1, increasing to less than \$10 million in Year 5.	<p>The resubmission updated the financial estimates to reflect the █% price reduction offer for the █</p> <p>Revised net save of less than \$10 million in Year 1,</p>	<p>The resubmission updated the financial estimates to reflect the █% price reduction offer for the █-pack (maintenance course).</p> <p>Revised net save of less than \$10 million in Year 1,</p>

	July 2015: Major resubmission	November 2015: Minor resubmission	March 2016 Current minor resubmission
		increasing to a net cost of less than \$10 million in Year 5.	increasing to a net cost of less than \$10 million in Year 5.
PBAC decision	The PBAC rejected the request to extend the PBS listing for adalimumab to include the treatment of moderate to severe UC on the basis that the evidence presented did not establish non-inferiority of adalimumab to the nominated comparator (infliximab).	The PBAC rejected the request to extend the PBS listing of adalimumab for the treatment of patients with moderate to severe ulcerative colitis on the basis that the evidence presented in the July 2015 PBAC meeting did not support the non-inferiority claim in the maintenance phase against infliximab. [adalimumab PSD November 2015 , para 7.1]	-

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

3 Requested listing

3.1 The minor resubmission reaffirmed its previous offer of █% price reduction to the █-pack and further offered a █% price reduction to the █ pack of adalimumab. By comparison, the November 2015 resubmission proposed that the 2 pack of adalimumab be the same as the effective price of infliximab. The resubmission also requested a Special Pricing Arrangement.

Name, Restriction, Manner of administration and form	Max. Qty	№.of Rpts	Dispensed Price for Max. Qty	Proprietary Name and Manufacturer
ADALIMUMAB				
<u>Induction</u>				
40 mg in 0.8 mL injection, 6 x 0.8 mL cartridges	1	0	\$ █	Humira AbbVie
40 mg in 0.8 mL injection, 6 x 0.8 mL syringes	1	0	\$ █	
40 mg in 0.8 mL injection, 2 x 0.8 mL cartridges	1	2	*\$ █	
40 mg in 0.8 mL injection, 2 x 0.8 mL syringes	1	2	*\$ █	
<u>Maintenance</u>				
40 mg in 0.8 mL injection, 2 x 0.8 mL cartridges	1	5	*\$ █	
40 mg in 0.8 mL injection, 2 x 0.8 mL syringes	1	5	*\$ █	

*submission has offered a █% price reduction to the █-pack.

3.2 The proposed restriction was the same as for the July 2015 major resubmission.

Section 85, Authority required (Streamlined)

Treatment phase:	Initial treatment (new patient)
Episodicity	For 12 weeks after the first dose
Condition	Moderate to severe UC
Treatment criteria	Must be treated by a gastroenterologist (code 87) or a consultant physician [internal medicine]

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	<p>specialising in gastroenterology (code 81)] or a consultant physician [general medicine specialising in gastroenterology (code 82)].</p> <p>Applications for authorisation of initial treatment must be in writing and must include:</p> <p>(a) two completed authority prescription forms; AND</p> <p>(b) a completed UC PBS Authority Application - Supporting Information Form which includes the following:</p> <p>(i) the completed current Mayo clinic or partial Mayo clinic calculation sheet including the date of assessment of the patient's condition; AND</p> <p>(ii) details of prior systemic drug therapy [dosage, date of commencement and duration of therapy]; AND</p> <p>(iii) the signed patient acknowledgement.</p> <p>A maximum quantity and number of repeats to provide for an initial course of this drug consisting of 6 doses to be administered at weeks 0 (160mg), 2 (80mg), 4 (40mg), 6 (40mg), 8 (40mg) and 10 (40mg) will be authorised.</p> <p>All tests and assessments should be performed preferably whilst still on treatment, but no longer than 1 month following cessation of the most recent prior treatment. The most recent Mayo clinic or partial Mayo clinic score must be no more than 1 month old at the time of application.</p> <p>Patients who fail to achieve a partial Mayo clinic score less than or equal to 2, with no subscore greater than 1, within the first 12 weeks of receiving this drug for UC, or have failed to maintain a partial Mayo clinic score less than or equal to 2, with no subscore greater than 1, with continuing treatment with this drug, will not be eligible to receive further PBS-subsidised treatment with this drug.</p> <p>A partial Mayo clinic assessment of the patient's response to this initial course of treatment must be made up to 12 weeks after the first dose (2 weeks following the sixth dose) so that there is adequate time for a response to be demonstrated.</p> <p>The patient must have signed a patient acknowledgement indicating they understand and acknowledge that the PBS-subsidised treatment will cease if they do not meet the predetermined response criterion for ongoing PBS-subsidised treatment, as outlined in the restriction for continuing treatment.</p> <p>If treatment with any of the above-mentioned drugs is contraindicated according to the relevant TGA-approved Product Information, please provide details at the time of application. If intolerance to treatment develops during the relevant period of use, which is of a severity necessitating permanent treatment withdrawal, please provide details of the degree of this toxicity at the time of application.</p> <p>Patients may qualify for PBS-subsidised treatment under this restriction once only.</p>
Clinical criteria	<p>Patient must have failed to achieve an adequate response to a 5-aminosalicylate oral preparation in a standard dose for induction of remission for 3 or more months or have intolerance necessitating permanent treatment withdrawal, AND</p> <p>Patient must have failed to achieve an adequate response to azathioprine at a dose of at least 2 mg per kg daily for 3 or more months or have intolerance necessitating permanent treatment withdrawal; OR</p> <p>Patient must have failed to achieve an adequate response to 6-mercaptopurine at a dose of at least 1 mg per kg daily for 3 or more months or have intolerance necessitating permanent treatment withdrawal; OR</p> <p>Patient must have failed to achieve an adequate response to a tapered course of oral steroids, starting at a dose of at least 40 mg prednisolone (or equivalent), over a 6 week period or have intolerance necessitating permanent treatment withdrawal, AND</p> <p>Patient must have a Mayo clinic score greater than or equal to 6; OR</p> <p>Patient must have a partial Mayo clinic score greater than or equal to 6, provided the rectal bleeding and stool frequency subscores are both greater than or equal to 2 (endoscopy subscore is not required for a partial Mayo clinic score).</p>
Population criteria	For patients 18 years old and older
Treatment phase: Maintenance treatment	

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Episodicity	Maximum 5 repeats, 12 weeks after the initial course (maximum 24 weeks)
Condition	Moderate to severe UC
Treatment criteria	<p>Must be treated by a gastroenterologist (code 87) or a consultant physician [internal medicine specialising in gastroenterology (code 81)] or a consultant physician [general medicine specialising in gastroenterology (code 82)].</p> <p>Patients who have failed to maintain a partial Mayo clinic score less than or equal to 2, with no subscore greater than 1, with continuing treatment with this drug, will not be eligible to receive further PBS-subsidised treatment with this drug.</p> <p>Patients are eligible to receive continuing treatment with this drug in courses of up to 24 weeks providing they continue to sustain the response.</p> <p>Up to a maximum of 5 repeats will be authorised. No applications for increased repeats will be authorised.</p>
Clinical criteria	<p>Patient must have previously been issued with an authority prescription for this drug for this condition, AND</p> <p>Patient must have demonstrated or sustained an adequate response to treatment by having a partial Mayo clinic score less than or equal to 2, with no subscore greater than 1 while receiving treatment with this drug.</p>
Population criteria	For patients 18 years old and older

Treatment Phase: Initial PBS-subsidised treatment of moderate to severe ulcerative colitis in a patient who has previously received non-PBS-subsidised therapy with this drug (Grandfather).	
Episodicity	Maximum 5 repeats, 12 weeks after the initial course (maximum 24 weeks)
Condition	Moderate to severe UC
Treatment criteria	<p>Must be treated by a gastroenterologist (code 87) or a consultant physician [internal medicine specialising in gastroenterology (code 81)] or a consultant physician [general medicine specialising in gastroenterology (code 82)].</p> <p>Applications for authorisation of initial treatment must be in writing and must include:</p> <p>(a) a completed authority prescription form; AND</p> <p>(b) a completed Ulcerative Colitis PBS Authority Application - Supporting Information Form which includes the following:</p> <p>(i) the completed current and baseline Mayo clinic or partial Mayo clinic calculation sheet including the date of assessment of the patient's condition; AND</p> <p>(ii) the date of commencement of this drug; AND</p> <p>(iii) the signed patient acknowledgement.</p> <p>The current Mayo clinic or partial Mayo clinic assessment must be no more than 1 month old at the time of application. The baseline assessment must be from immediately prior to commencing treatment with this drug.</p> <p>Patients are eligible to receive continuing treatment with this drug in courses of up to 24 weeks providing they continue to sustain the response.</p> <p>Up to a maximum of 5 repeats will be authorised. No applications for increased repeats will be authorised.</p> <p>The patient must have signed a patient acknowledgement indicating they understand and acknowledge that the PBS-subsidised treatment will cease if they do not meet the predetermined response criterion for ongoing PBS-subsidised treatment, as outlined in the restriction for continuing treatment.</p> <p>Patients may qualify for PBS-subsidised treatment under this restriction once only. For continuing PBS-subsidised treatment, a Grandfathered patient must qualify under the Continuing treatment criteria.</p>
Clinical criteria	<p>Patient must have been receiving treatment with this drug prior to [DATE OF PBS LISTING], AND</p> <p>Patient must have had a Mayo clinic score greater than or equal to 6 prior to commencing treatment with this drug; OR</p> <p>Patient must have had a partial Mayo clinic score greater than or equal to 6, provided the rectal bleeding and stool frequency subscores were both greater than or equal to 2</p>

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	(endoscopy subscore is not required for a partial Mayo score) prior to commencing treatment with this drug; OR Patient must have a documented history of moderate to severe refractory ulcerative colitis prior to having commenced treatment with this drug where a Mayo clinic or partial Mayo clinic baseline assessment is not available, AND Patient must have demonstrated or sustained an adequate response to treatment by having a partial Mayo clinic score less than or equal to 2, with no subscore greater than 1 while receiving treatment with this drug.
Population criteria	Patient must be 18 years of age or older.

Treatment Phase: Balance of supply	
Episodicity	Maximum 5 repeats, 12 weeks after the initial course (maximum 24 weeks)
Condition	Moderate to severe UC
Treatment criteria	Must be treated by a gastroenterologist (code 87) or a consultant physician [internal medicine specialising in gastroenterology (code 81)] or a consultant physician [general medicine specialising in gastroenterology (code 82)].
Clinical criteria	Patient must have received insufficient therapy with this drug under the Initial treatment (new patient) restriction to complete the 6 doses (i.e. the initial infusion regimen at weeks 0, 2, 4, 6, 8 and 10 weeks); OR Patient must have received insufficient therapy with this drug under the Continuing treatment restriction to complete 24 weeks of treatment; OR Patient must have received insufficient therapy with this drug to complete 24 weeks of treatment under the Initial PBS-subsidised treatment restriction for patients who had previously received non-PBS subsidised treatment (Grandfathered patient), AND The treatment must provide no more than the balance of up to 6 doses (new patients) or 5 repeats (Continuing patients or Grandfathered patients).
Population criteria	Patient must be 18 years of age or older

Source: July 2015 resubmission

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

4 Clinical place for the proposed therapy

- 4.1 The minor resubmission maintained its view that adalimumab would provide an alternate treatment to infliximab or vedolizumab for moderate to severe UC patients; and that the availability of subcutaneously administered adalimumab would allow equity of access to UC patients, who may not be able to access an infusion clinic either for reasons of disruption of work and other activities or due to location outside a major city. The resubmission stated that positioning adalimumab as a second-line treatment in UC would not address the above-mentioned issue and may create additional barriers for patients who are forced to decline treatment with either of the available infusions, therefore denying them access to effective treatment.
- 4.2 The resubmission further provided correspondence from the [REDACTED] of AIBDA, [REDACTED] of AIBDA, and [REDACTED] from Liverpool Hospital in supporting adalimumab's clinical place as first-line treatment.

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

5 Comparator

- 5.1 No change made to the nominated comparator, infliximab. The PBAC previously accepted that infliximab was the appropriate comparator.

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 as it was a minor submission.

Consumer comments

- 6.2 The PBAC noted and welcomed the input from individuals (3) and health care professionals (3) via the Consumer Comments facility on the PBS website. The comments described a range of benefits of treatment with adalimumab related to the different mode of administration compared with infliximab and vedolizumab, including the ability to self-inject for better adherence to treatment, reduction in time spent travelling and in hospital for infusions and reduction in absence from employment.

Clinical trials

- 6.3 The minor resubmission did not present new clinical trials. The resubmission reproduced a summary of results of the indirect comparisons between adalimumab vs infliximab and adalimumab vs vedolizumab as below.

Table 2: Summary of results of the indirect comparisons (adalimumab vs infliximab) and (adalimumab vs vedolizumab)

	Induction Phase, Indirect RR (95% CI)	Maintenance Phase Indirect RR (95% CI)	Conclusion for adalimumab
ITT population, adalimumab vs infliximab			
Clinical remission	() ^a	() ^{a,c,d}	Non-inferior
Clinical response	() ^a	() ^{a,c,d}	Inferior in IP/Non-inferior in MP
TNFα antagonist naïve patients, adalimumab vs infliximab			
Clinical remission	() ^a	() ^{a,c,d}	Non-inferior
Clinical response	() ^a	() ^{a,c,d}	Inferior in IP/Non-inferior in MP
ITT population, adalimumab vs vedolizumab			
Clinical remission	() ^b	() ^{a,c}	Non-inferior
Clinical response	() ^b	NR	Non-inferior

IP = induction phase; ITT = intention to treat; MP = maintenance phase; RR= relative risk; NR = not reported. a: excludes Probert (2003), b: excludes Suzuki (2013); c: excludes ULTRA 1; d: excludes ACT2 **Bold** indicates statistically significant.

Source: Table 5, Public Summary Document – July 2015 (and Table B-23 pp118 – 119 and Table B-24 pp123 -124 of the re-submission; tables A-18 and A-19, pp34-35 in the Attachment A, of the re-submission. b: ULTRA 1, ULTRA 2, Suzuki (2013), GEMINI I trials).

Clinical claim

- 6.4 The current resubmission stated that, according to the July 2015 submission, the evaluators and the ESC had concluded adalimumab is non-inferior to infliximab and

vedolizumab in the maintenance of remission, which the submission argued is the most relevant clinical outcome in UC.

- 6.5 The resubmission also stated that non-inferiority was conducted for all remission endpoints and for clinical response in the maintenance phase. The same conclusion applied when a subgroup of biologic naïve patients was analysed. Non-inferiority was also concluded for the comparison of adalimumab and vedolizumab.
- 6.6 Regarding the claims above, the PBAC previously considered that the indirect comparison presented in the submission provided low certainty evidence for the claim of non-inferiority between adalimumab and infliximab, both in the remission phase and in the maintenance phase. The PBAC noted that an indirect comparison of adalimumab and vedolizumab resulted in a non-significant point estimate that favoured vedolizumab (RR [REDACTED], 95% CI: [REDACTED], [REDACTED]) (July 2015 PSD, paragraph 7.7).
- 6.7 At its November 2015 meeting, the PBAC maintained its view that the indirect comparison provided low certainty evidence for the claim on non-inferiority between adalimumab and infliximab, both in the remission phase and in the maintenance phase (November 2015 PSD, paragraph 7.5).

Economic analysis

- 6.8 There was no new economic comparison presented.
- 6.9 The PBAC noted the current minor re-submission offered a [REDACTED]% reduction to the published DPMQ for [REDACTED]-pack adalimumab 40 mg.
- 6.10 The PBAC further noted the current minor re-submission offered a [REDACTED]% reduction to the published DPMQ for [REDACTED]-pack adalimumab 40 mg while the previous submission offered the same price as infliximab. Given that inferiority (compared with infliximab) in the maintenance phase is also likely, there is no basis to accept the same price of infliximab. In the absence of a modelled economic evaluation of the cost savings per health outcome foregone, the PBAC considered that a reduction in price of adalimumab of around [REDACTED]% in the maintenance treatment phase (compared with infliximab) is likely to be reasonable.

Estimated PBS usage & financial implications

- 6.11 The minor resubmission provided a comparison table of net cost to PBS/RPBS between the July 15, November 15 and March 16 submissions.

Table 3: Estimated use and financial implications

	Year 1	Year 2	Year 3	Year 4	Year 5
Number treated	█	█	█	█	█
Major Re-submission July 2015					
Total cost to PBS/RPBS (excluding co-payments)	\$█	\$█	\$█	\$█	\$█
Net cost PBS/RPBS (excluding co-payments)	\$█	\$█	\$█	\$█	\$█
Minor Re-submission November 2015					
Total cost to PBS/RPBS (excluding co-payments)	\$█	\$█	\$█	\$█	\$█
Net cost PBS/RPBS (excluding co-payments)	-\$█	\$█	\$█	\$█	\$█
Minor Re-submission March 2016					
Total cost to PBS/RPBS (excluding co-payments)	\$█	\$█	\$█	\$█	\$█
Net cost PBS/RPBS (excluding co-payments)	-\$█	-\$█	\$█	\$█	\$█

Source: Table 5 of the re-submission p12 and Section E attachment of the minor re-submission

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

- 6.12 The resubmission acknowledged that these financial implications only assumed a reduced use of infliximab and did not factor the market share of adalimumab with the recent listing of vedolizumab. The resubmission stated that, to date, vedolizumab still cannot be appropriately estimated due to the lag in the availability of the PBS item data.

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

7 PBAC Outcome

- 7.1 The PBAC recommended the listing of adalimumab on the General Schedule for the treatment of moderate to severe ulcerative colitis (UC) on the basis of a clinical need for subcutaneous therapy for this condition. In making this recommendation, the PBAC considered that while adalimumab is inferior to infliximab for this indication, listing will allow clinicians to choose from a range of bDMARDs with different modes of administration for the treatment of individual patients. The PBAC considered that the inferiority should be reflected in the pricing of adalimumab.
- 7.2 The PBAC therefore recommended extending the current listing based on the offered █% price reduction of the █-pack and that the price of the █-pack is reduced by around █% compared to the equi-effective dose of infliximab.
- 7.3 The PBAC recommendation was based the following comparable doses: 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).

- 7.4 The PBAC recalled that it previously considered that MBS item 14245 (\$97.95) was the most appropriate cost to use to account for the avoided administration cost of infliximab infusions.
- 7.5 The PBAC noted that there were no new data presented in the minor re-submission. The PBAC therefore reaffirmed its view on the indirect comparison presented in the July 2015 submission, which was based on the three RCTs comparing adalimumab with placebo (ULTRA1, ULTRA2 and Suzuki 2004) and the three RCTs comparing infliximab with placebo (ACT1, ACT2 and Probert); specifically, that the comparison provided low certainty evidence for the claim on non-inferiority between adalimumab and infliximab, in the maintenance phase. The PBAC noted that the November 2015 re-submission acknowledged that adalimumab is inferior to infliximab in the induction phase.
- 7.6 The PBAC noted that infliximab and vedolizumab are currently PBS-listed for the treatment of UC, and that both drugs are administered by intravenous infusions. The PBAC acknowledged there is a clinical need for subcutaneous therapies for ease of administration for the condition. The PBAC welcomed the input received from three individuals and three Health Professionals in support of the listing.
- 7.7 The PBAC recommended that the listing and restriction wording for adalimumab should be aligned with that of infliximab and vedolizumab in the treatment of UC, where appropriate. The PBAC recommended that the adalimumab listing for ulcerative colitis be silent on the age of the patient.
- 7.8 The PBAC also recommended a flow on change to the current Note for treatment of adult patients with moderate to severe ulcerative to reflect the addition of adalimumab to the PBS-subsidised therapies for this condition. Currently, within the same treatment cycle a patient cannot trial and fail, or cease to respond to, the same PBS-subsidised infliximab or vedolizumab more than twice. As a consequence of the listing of adalimumab, it should be read as 'Within the same treatment cycle, a patient cannot trial and fail, or cease to respond to, the same PBS-subsidised infliximab, vedolizumab or *adalimumab* more than *once*'.
- 7.9 The PBAC recommended that the Early Supply Rule should apply to adalimumab for the treatment of UC.
- 7.10 The PBAC advised that adalimumab is not suitable for prescribing by nurse practitioners.
- 7.11 Advice to the Minister under subsection 101(3BA) of the Act
In accordance with subsection 101(3BA) of the Act the PBAC advised that it is of the opinion that, on the basis of the material available to it at its November 2014 meeting, adalimumab should not be treated as interchangeable on an individual patient basis with any other drugs.

Outcome:

Recommended

8 Recommended listing

- 8.1 Amend existing listing with the new indication. Restriction to be finalised.

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

AbbVie welcomes the PBAC decision to recommend Humira for first line treatment in UC and as the first subcutaneous option, offering patients an effective and convenient treatment.