

**7.01 ADALIMUMAB,
injection 40 mg in 0.8 mL pre-filled pen, injection 40 mg in 0.8
mL pre-filled syringe,
Humira[®],
AbbVie Pty Ltd.**

1 Purpose of Application

1.1 Resubmission to request Authority Required listing for adalimumab for initial treatment and Authority Required (Streamlined) listing for continuation of adalimumab for the treatment of moderate to severe hidradenitis suppurativa (HS). The first submission was considered at the March 2016 PBAC Meeting and a minor resubmission was considered at the July 2016 PBAC Meeting.

2 Requested listing

2.1 An abbreviated version of the requested restriction is below. 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	№.of Rpts	Dispensed Price for Max. Qty (effective)	Proprietary Name and Manufacturer
ADALIMUMAB				Humira® Abbvie
40 MG/0.8 ML INJECTION, 6 X 0.8 ML SYRINGES	1	0	\$ [REDACTED]	
40 MG/0.8 ML INJECTION, 2 X 0.8 ML SYRINGES	2	2	\$ [REDACTED]	
40 MG/0.8 ML INJECTION, 6 X 0.8 ML CARTRIDGES	1	0	\$ [REDACTED]	
40 MG/0.8 ML INJECTION, 2 X 0.8 ML CARTRIDGES	2	2	\$ [REDACTED]	

Category / Program	GENERAL – 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
PBS Indication:	Moderate to severe hidradenitis suppurativa
Treatment phase:	Initial treatment (new patients)
Restriction Level / Method:	<input checked="" type="checkbox"/> Authority Required - In Writing
Treatment criteria:	Must be treated by a dermatologist

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Clinical criteria:	<p>Patient must have confirmed hidradenitis suppurativa, with the diagnosis confirmed by a dermatologist; AND Patient must have failed to achieve an adequate response to 2 courses of different antibiotics each for 3 months; OR Patient must have a documented intolerance to antibiotics of a severity necessitating permanent treatment withdrawal or a medical contraindication to such therapy with 2 different courses of antibiotics each for 3 months; AND Patient must have, at the time of application, disease severity considered to be moderate to severe as demonstrated by a Hurley stage II or III grading with an AN count ≥ 3 preferably whilst still on treatment. Assessment must be no longer than 1 month following cessation of the most recent prior conventional treatment. AND Patient must not have previously received PBS-subsidised treatment with this biological agent for this condition.</p>
Prescriber Instructions	<p>A maximum of 16 weeks treatment will be authorised under this criterion.</p> <p>Assessment of disease severity must be no longer more than 1 month old at the time of application following cessation of the most recent prior conventional treatment. An adequate response to antibiotic treatment is defined as: Achieving HiSCR (50% reduction in AN count as compared to baseline with no increase in abscesses or draining fistulae)</p> <p>An assessment of the patient's response to this initial course of treatment must be made following a minimum of 12 weeks of therapy. so that there is adequate time for a response to be demonstrated.</p>

Treatment phase:	Re-initiation treatment of PBS-subsidised treatment of hidradenitis suppurativa by a dermatologist
Restriction Level / Method:	<input checked="" type="checkbox"/> Authority Required - In Writing
Treatment criteria:	Must be treated by a dermatologist
Clinical criteria:	<p>Patient must have a documented history of moderate to severe hidradenitis suppurativa and an AN count ≥ 3; AND Patient must have received prior PBS-subsidised treatment with this biological agent for this condition in this treatment cycle; AND Patient must not have already failed, or ceased to respond to, PBS-subsidised treatment with this biological agent within this treatment cycle; AND Patient must not receive more than 16 weeks of treatment under this restriction</p>

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Dispensed for Max. (effective)	Price Max. Qty	Proprietary Name and Manufacturer
ADALIMUMAB					Humira® Abbvie
40 MG/0.8 ML INJECTION, 2 x 0.8 ML SYRINGES	2	5	\$ [REDACTED]		
40 MG/0.8 ML INJECTION, 2 x 0.8 ML CARTRIDGES	2	5	\$ [REDACTED]		

Treatment phase:	Continuing treatment (subsequent)
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Restriction Level / Method:	<input checked="" type="checkbox"/> Authority Required - In Writing <input checked="" type="checkbox"/> Streamlined
Treatment criteria:	Must be treated by a dermatologist
Clinical criteria:	Patient must have a documented history of moderate to severe hidradenitis suppurativa; AND Patient must have previously been issued with a prescription for this drug for this condition; AND Patient must have demonstrated an adequate response to treatment with this drug. Response is defined as achieving HiSCR (50% reduction in AN count compared to baseline, with no increase in abscesses or draining fistulae) with the assessment being no more than 1 month old at the time of application.
Prescriber Instructions	An adequate response to treatment is defined as: Achieving HiSCR (50% reduction in AN count as compared to baseline with no increase in abscesses or draining fistulae)

Treatment phase:	Initial PBS-subsidised treatment of moderate to severe hidradenitis suppurativa in a patient who has previously received non-PBS-subsidised therapy with this drug (grandfather)
Restriction Level / Method:	<input checked="" type="checkbox"/> Authority Required - In Writing
Treatment criteria:	Must be treated by a dermatologist
Clinical criteria:	Patient must have been receiving treatment with this drug prior to 1 April 2017 [listing date to be determined], AND Patient must have had a disease severity considered to be moderate to severe as demonstrated by a Hurley stage II or III with an AN count ≥ 3 prior to starting treatment with this drug, OR Patient must have a documented history of moderate to severe hidradenitis suppurativa prior to having commenced treatment with this drug where a Hurley stage or AN count baseline assessment is not available, AND Patient must have demonstrated or sustained an adequate a response to treatment by achieving HiSCR after 12 weeks of treatment.

- 2.2 The requested basis for listing is cost-effectiveness of adalimumab compared with best supportive care (BSC).
- 2.3 The ESC noted that the resubmission no longer requested recommencement for non-responders to the initial course of treatment (compared with the March and July 2016 submissions). Therefore, retreatment was included only for those patients who were previous responders and required a treatment break.

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

3 Background

- 3.1 TGA status at the time of PBAC consideration: Adalimumab was registered on the ARTG on 26 July 2016 for the treatment of active moderate to severe hidradenitis

suppurativa (acne inversa) in adult patients with an inadequate response to conventional systemic hidradenitis suppurativa therapy.

- 3.2 The ESC noted that while the TGA Clinical Evaluation Report recommended approval for 12 weeks of adalimumab but not for ongoing maintenance, the Delegates' Overview suggested that maintenance therapy may be appropriate for responders at week 12. Subsequently, the ACPM advised that use beyond 12 weeks should be contingent on evidence of benefit.
- 3.3 Hidradenitis Suppurativa Clinical Response (HiSCR) is defined as a $\geq 50\%$ reduction in inflammatory lesion count (abscesses + inflammatory nodules), and no increase in abscesses or draining fistulas when compared with baseline. The ESC noted that it was developed during the PIONEER I and II trials for evaluation of response and has since been accepted by the TGA as an appropriate index of measuring response to adalimumab.
- 3.4 The PBAC has previously considered adalimumab for this indication in March 2016 and July 2016.

Table 1: Summary of the previous resubmission and current resubmission

	July 2016 minor resubmission	Current resubmission
Requested PBS listing	Moderate-to-severe hidradenitis suppurativa PBAC Comment: "The PBAC considered that the continuing restriction should be Authority Required (in-writing) as per the requested initial restriction (as opposed to the requested STREAMLINED authority). (paragraph 7.3, adalimumab PSD, July 2016 PBAC meeting). The PBAC requested "revised restriction criteria which include the removal of retreatment for non-responders as proposed in the pre-PBAC response, as well as wording clarifying the re treatment of responders who re-initiate treatment after a treatment break" (paragraph 7.10, adalimumab PSD, July 2016 PBAC meeting).	Removed retreatment for non-responders. 1 st continuation- written Authority; subsequent continuation - Streamlined.
Requested price	Initial treatment 6 pack (induction pack): \$4,792.37 (\$██████ effective price) 2 x 2 pack: \$3,243.87 (\$██████ effective price) Continuing treatment 2 x 2 pack: \$3,243.87 (\$██████ effective price) Note: Prices proposed in pre-PBAC response	Same
Main comparator	Best supportive care (placebo) PBAC Comment: "The PBAC considered that BSC was the appropriate comparator" (paragraph 7.5, adalimumab PSD, March 2016 PBAC meeting).	Same
Clinical evidence	No new clinical data were presented in the minor resubmission. The March 2016 submission included three head-to-head trials comparing adalimumab to placebo: M10 467 (n=102), PIONEER I (n=307) and PIONEER II (n=326). PBAC Comment: "The PBAC noted that no new clinical trial data were presented in the minor re submission but that outcomes from the OLE study were provided in the pre-PBAC response. The pre-PBAC response stated that the OLE results demonstrated "the efficacy of adalimumab in terms of achievement of HiSCR for up to 2 years of treatment". The PBAC noted that this was new evidence in the pre-PBAC response and that this had not been formally evaluated." (paragraph 7.6, adalimumab PSD, July 2016 PBAC meeting).	Final results of an open label extension (OLE) study M12-555 available or HiSCR responders at Week 12 from both PIONEER trials (n=45).

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	July 2016 minor resubmission	Current resubmission
Key effectiveness data	<p>Trial results remain unchanged from the major submission considered in March 2016. Across the three studies, patients treated with adalimumab were twice as likely to respond to therapy compared with placebo treated patients (██████████) at Week 12.</p> <p>PBAC Comment: “It was noted in the March 2016 adalimumab PSD that the claim of superior comparative effectiveness was adequately supported by the data for the first 12 weeks of treatment but not for the maintenance of efficacy beyond 12 weeks of therapy. The PBAC considered results from Period B of the PIONEER trials (weeks 12 to 36) were highly uncertain because of the exploratory nature of the analysis and small patient numbers.” (paragraph 6.8, adalimumab PSD, July 2016 PBAC meeting).</p>	<p>Additional analyses: HiSCR (to Week 108); percentage change in the number of abscesses and inflammatory nodules; percentage change in the number of draining fistulae; and DLQI score (mean score, change from baseline, proportion with DLQI score of 0 or 1) (to Week 72).</p>
Key safety data	<p>The trial results remain unchanged from the previous major submission considered in March 2016.</p> <p>PBAC Comment: “In the March 2016 adalimumab PSD, the PBAC noted that there were similar numbers of patients reported in both the adalimumab and BSC arms of the three trials experiencing any adverse events (AEs), treatment-emergent infections and AEs leading to discontinuations.” (paragraph 6.9, adalimumab PSD, July 2016 PBAC meeting).</p>	Same
Clinical claim	<p>The resubmission did not explicitly state a clinical claim. The clinical claim in the March 2016 submission was superior efficacy and inferior safety of adalimumab compared with BSC.</p> <p>PBAC Comment: “...The PBAC noted that the requested listing restricted continuing treatment to those patients who responded to adalimumab. While the PBAC considered that the claim of superior comparative effectiveness may be reasonable beyond 12 weeks, the PBAC did not accept the extrapolation of the treatment benefit beyond treatment discontinuation modelled in the resubmission. The PBAC considered that the claim of inferior comparative safety was reasonable.”(paragraph 6.12, adalimumab PSD, July 2016 PBAC meeting).</p>	Same
Economic evaluation	<p>Cost-utility model with cost/QALY \$45,000 - \$75,000 (corrected to \$45,000 - \$75,000)</p> <p>PBAC Comment: “If the time horizon and convergence of benefit period were reduced to 10 years, for example, the minor resubmission base case ICER increased to \$75,000 - \$105,000. Given the method used to converge the benefit to 10 years in the pre-PBAC model, it was not possible to calculate a similar figure for a 5 year period (however this would increase the ICER to beyond \$75,000 - \$105,000 per QALY).” (paragraph 6.25, adalimumab PSD, July 2016 PBAC meeting).</p>	Cost-utility model with cost/QALY \$45,000 - \$75,000.
Number of patients	<p>Treated patients per year: Less than 10,000 in Year 1 increasing to less than 10,000 in Year 5.</p> <p>PBAC Comment: “The estimates in Table 3 [Estimated use and financial implications using revised price offer] incorporate the adapted prevalence, diagnosis rate and uptake rate. Consistent with DUSC advice, uptake was increased (from ██████████% to ██████████%).”(paragraph 6.29, adalimumab PSD, July 2016 PBAC meeting).</p>	Less than 10,000 in Year 1 increasing to less than 10,000 in Year 5.
Estimated cost to PBS	<p>Less than \$10 million in Year 1 increasing to \$10 - \$20 million in Year 5 for a total of \$30 - \$60 million over the first 5 years of listing.</p> <p>PBAC Comment: “The PBAC agreed with DUSC that the diagnosis rate was likely to be underestimated in the original submission, so potentially further underestimated in the minor resubmission. Applying the diagnosis rate from the original submission ██████████ results in substantially higher financial implications...” (paragraph 6.30, adalimumab PSD, July 2016 PBAC meeting).</p>	\$10 - \$20 million in Year 1 increasing to \$20 - \$30 million in Year 5 for a total of \$60 - \$100 million over the first 5 years of listing.

	July 2016 minor resubmission	Current resubmission
PBAC decision	Rejected. “The PBAC did not recommend adalimumab for PBS listing for moderate to severe hidradenitis suppurativa (HS) on the basis of high and uncertain cost effectiveness.” (paragraph 7.1, adalimumab PSD, July 2016 PBAC meeting).	-

Source: Compiled during the evaluation

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

4 Clinical place for the proposed therapy

- 4.1 HS is an chronic inflammatory skin disease of the hair follicle associated with inflammatory cytokines including TNF- α and interleukins. HS is associated with painful nodules causing morbidity and poor quality of life (QoL).
- 4.2 Adalimumab is proposed for the treatment of patients with moderate-to-severe disease with an abscesses and inflammatory nodule count greater or equal to 3, and prior treatment with 2 courses of at least 3 months duration of antibiotics.

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

5 Comparator

- 5.1 As in the March and July 2016 submissions, the current resubmission nominated best supportive care (placebo) as the comparator. The PBAC has previously accepted best supportive care (placebo) as the appropriate comparator.

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

6 Consideration of the evidence

Sponsor hearing

- 6.1 The sponsor requested a hearing for this item. At the hearing, a clinician discussed the natural history of the disease, reflected on patient experience to emphasize adalimumab’s efficacy in an area of unmet clinical need, and addressed other matters in response to the Committee’s questions. The PBAC considered that the hearing was informative as it provided a clinical perspective on treating this uncommon disease.

Consumer comments

- 6.2 The PBAC noted and welcomed the input from individuals (4), and health care professionals (8) via the Consumer Comments facility on the PBS website. The comments described a high clinical need for more treatment options for this condition and a range of benefits of treatment with adalimumab including reduction in lesion inflammation and count, and the associated improvement in quality of life.

Clinical trials

- 6.3 The resubmission was based on three head-to-head trials comparing adalimumab with placebo, M10-467 (n=102), PIONEER I (n=307) and PIONEER II (n=326). The resubmission presented the final results from the open label extension (OLE) study M12-555 (n=497).
- 6.4 Details of the trials presented in the resubmission are provided in the table below.

Table 2: Trials and associated reports presented in the resubmission

Trial ID	Protocol title/ Publication title	Publication citation
Direct randomised trials		
M10-467	<p>Trial report M10-467. A phase 2, multicentre study of the safety and efficacy of adalimumab in subjects with moderate to severe chronic hidradenitis suppurativa.</p> <p>Kimball et al. Adalimumab for the treatment of moderate to severe hidradenitis suppurativa: a parallel randomised trial.</p> <p>Kimball et al. Efficacy and safety of adalimumab in treatment of moderate to severe hidradenitis suppurativa: results from the placebo-controlled portion of a phase II, randomised, double-blind study.</p> <p>Gottlieb et al. Efficacy and safety of adalimumab treatment in women with moderate to severe hidradenitis suppurativa: Analysis from the placebo-controlled portion of a phase II, randomised, double-blind study.</p> <p>Kimball et al. Adalimumab reduces pain in patients with hidradenitis suppurativa: Results from a placebo-controlled phase II trial.</p> <p>Kimball et al. Efficacy and safety of adalimumab for moderate to severe hidradenitis suppurativa: Results from the open-label phase of a 52-week phase II, randomised, study</p> <p>Mrowietz et al. Adalimumab improves health-related quality of life and work productivity in patients with hidradenitis suppurativa: Results from a placebo-controlled phase II trial.</p> <p>Zouboulis et al. High-sensitivity C-reactive protein response to adalimumab in hidradenitis suppurativa patients.</p> <p>Zouboulis et al. Impact of weight and body mass index on high-sensitivity C-reactive protein response to adalimumab in hidradenitis suppurativa patients.</p> <p>Gottlieb et al. Efficacy and safety of adalimumab treatment in women with moderate to severe hidradenitis suppurativa: Analysis from the placebo-controlled portion of a phase II, randomised, double-blind study.</p> <p>Scheinfeld et al. Adalimumab treatment is associated with pain reduction in patients with hidradenitis suppurativa, regardless of the presence of depression: Results from a phase II, randomised, placebo-controlled trial.</p> <p>Scheinfeld et al. Reduction in pain scores and improvement in depressive symptoms in patients with hidradenitis suppurativa treated with adalimumab in a phase 2, randomized, placebo-controlled trial.</p>	<p>22 April 2009</p> <p><i>Ann Intern Med</i> 2012;157(2):846-55</p> <p><i>J Am Acad Dermatol</i> 2011; 64(2 Suppl 1):AB155.</p> <p><i>Int J Gynecol Obstet</i> 2012;119: S360.</p> <p><i>J Am Acad Dermatol</i> 2012; 66(4 Suppl 1):AB42.</p> <p><i>J Am Acad Dermatol</i> 2012; 66(4 Suppl 1):AB50.</p> <p><i>J Am Acad Dermatol</i> 2012; 66(4 Suppl 1):AB42.</p> <p><i>J Invest Dermatol</i> 2012;132: S67.</p> <p><i>J Am Acad Dermatol</i> 2012;66(4 Suppl 1):AB53.</p> <p><i>J Am Acad Dermatol</i> 2013;68(4 Suppl 1):AB49.</p> <p><i>J Am Acad Dermatol</i> 2014;70(5):AB35.</p> <p><i>Dermatology online Journal</i> 2016, 22(3).</p>
PIONEER I (M11-313)	<p>Trial report M11-313. A phase 3 multicenter study of the safety and efficacy of adalimumab in subjects with moderate to severe hidradenitis suppurativa – PIONEER I.</p> <p>Trial report M12-555. A phase 3 open-label study of the safety and efficacy of adalimumab in subjects with moderate to severe hidradenitis suppurativa – PIONEER (open-label extension).</p>	<p>29 November 2011</p> <p>12 April 2012</p>

	<p>Armstrong et al. HUMIRA Improves Health-Related Quality of Life (HRQoL) in patients with moderate to severe Hidradenitis Suppurativa (HS): Results from the first 12 weeks of PIONEER I.</p> <p>Jemec et al. Adalimumab improves treatment satisfaction with medication (TS-M) in patients with moderate to severe Hidradenitis Suppurativa (HS) in a 12-week randomised controlled trial (PIONEER I).</p> <p>Kimball et al. Safety and efficacy of adalimumab in patients with moderate to severe hidradenitis suppurativa: Results from first 12 Weeks of PIONEER I, a Phase 3, Randomised, placebo - controlled trial.</p> <p>Herra et al. Safety and efficacy of Adalimumab in patients with moderate to severe hidradenitis suppurativa: results from first 12 weeks of PIONEER I, a phase 3, randomised, placebo - controlled trial.</p> <p>Kimball et al. Safety and efficacy of adalimumab in patients with moderate to severe hidradenitis suppurativa: Results from first 12 weeks of PIONEER I, a phase 3, randomised, placebo - controlled trial.</p>	<p><i>J Invest Dermatol</i> 2014;134:S34.</p> <p><i>J Invest Dermatol</i> 2014;134:S31.</p> <p><i>J Invest Dermatol</i> 2015;134:S36.</p> <p><i>Aust J Dermatol</i> 2015 56:34-35.</p> <p><i>J Am Acad Dermatol</i> 2015 72(5):AB60.</p>
PIONEER II (M11-810)	<p>Trial report M11-810. A phase 3 multicenter study of the safety and efficacy of adalimumab in subjects with moderate to severe hidradenitis suppurativa – PIONEER II.</p> <p>Trial report M12-555. A phase 3 open-label study of the safety and efficacy of adalimumab in subjects with moderate to severe hidradenitis suppurativa – PIONEER (open-label extension).</p> <p>Jemec et al. Efficacy and safety of adalimumab in patients with moderate to severe hidradenitis suppurativa: Results from PIONEER II, a phase 3, randomised, placebo - controlled trial</p> <p>Herra et al. Efficacy and safety of Adalimumab in patients with moderate to severe hidradenitis suppurativa: results from PIONEER II, a phase 3 randomised placebo - controlled trial.</p> <p>Jemec et al. Adalimumab improves treatment satisfaction with medication (TS-M) in patients with moderate to severe hidradenitis suppurativa (HS) in a 12-week randomised controlled trial (PIONEER II).</p> <p>Kimball et al. Progression of hidradenitis suppurativa: Outcomes of placebo-treated patients in a phase 3, randomized, placebo-controlled trial (PIONEER II).</p> <p>Armstrong et al. Adalimumab improves health-related quality of life (HRQoL) in patients with moderate to severe hidradenitis suppurativa (HS): Results from the first 12 weeks of PIONEER II.</p> <p>Kimball et al. Adalimumab is associated with reduced skin pain in patients with moderate to severe hidradenitis suppurativa (HS): Results from the first 12 weeks of PIONEER II.</p> <p>Zouboulis et al. Adalimumab treatment is associated with a trend toward reduced need for acute surgical interventions in patients with moderate to severe hidradenitis suppurativa.</p>	<p>28 December 2011</p> <p>12 April 2012</p> <p><i>J Am Acad Dermatol</i> 2014 72(5):AB45.</p> <p><i>Aust J Dermatol</i> 2015;56:34-35.</p> <p><i>J Am Acad Dermatol</i> 2015;72(5):AB39.</p> <p><i>J Am Acad Dermatol</i> 2016, 74(5):AB68.</p> <p><i>J Am Acad Dermatol</i> 2015, 72(5):AB38.</p> <p><i>J Am Acad dermatol</i> 2015, 72 (5):AB39.</p> <p><i>J Invest Dermatol</i> 2015, 135:S10</p>

Source: Table B.2.1, p.38-39 of the re submission

6.5 The key features of the direct randomised trials are summarised in Table 3.

Table 3: Key features of the included evidence, adalimumab vs. placebo

Trial	N	Design/ duration	Risk of bias	Patient population	Outcomes	Use in modelled evaluation
M10-467	102	R, DB, 16 weeks	Low	Hurley Stage I,II,III	HS-PGA score at week 16	Not used
PIONEER I	307	R, DB, 36 weeks	Low	Hurley Stage II and III	HiSCR at Week 12	Used
PIONEER II	326	R, DB, 36 weeks	Low	Hurley Stage II and III	HiSCR at Week 12	Used
M12-555	497	OL	High	Hurley Stage II and III	HiSCR after week 12 and DLQI over time	Used

DB=double blind; HS-PGA; hidradenitis suppurativa physician global assessment; HiSCR=hidradenitis suppurativa clinical response; MC=multi-centre; OL=open label; OS=overall survival; PFS=progression-free survival; R=randomised
Source: compiled during the evaluation

6.6 The resubmission relied on the data from PIONEER I and PIONEER II and the final results from the OLE study M12-555. The OLE data presented were not from an ITT analysis and are non-comparative. The OLE study included a total of 497 patients from the PIONEER trials who received adalimumab every week or every other week or placebo in the prior studies. Of these, [REDACTED] patients had received adalimumab every week for each period. The resubmission presented analyses based on only [REDACTED] patients in the OLE who received adalimumab every week and were HiSCR responders at week 12. The study results are thus subject to bias and should be interpreted with caution.

- The PSCR (p1) argued that OLE studies are routinely non-comparative, and claimed that the efficacy and discontinuation rates due to lack of efficacy in the patients in the OLE study mirrored the proposed use of adalimumab in clinical practice.
- The PSCR acknowledged the uncertainty of long-term benefits with adalimumab, and stated that the proposed continuation rule restricting further treatment to patients who have a demonstrated HiSCR response at 12 weeks would ensure that adalimumab is administered to the population in which it is most cost-effective.
- The ESC agreed with the PSCR's arguments but noted comparative data are not available and that the absence of data on the natural history of the disease made the response rates for adalimumab hard to interpret.
- The ESC considered that response rates for placebo over time would have been helpful in interpreting the results of adalimumab's effectiveness.
- The Pre-PBAC response (p1) acknowledged that the OLE study was non-comparative, but claimed that the data from this study informed the magnitude of efficacy that patients were likely to experience from adalimumab treatment.

6.7 Results from Period B of the PIONEER trials (Week 12 to Week 36) should be interpreted with caution due to the exploratory nature of the analyses and small patient numbers (n=99 for both trials).

Comparative effectiveness

6.8 New data were presented from the OLE M12-555 study (up to Week 108). The additional analyses were for HiSCR (to Week 108), percentage change in the number of abscesses and inflammatory nodules; percentage change in the number of draining fistulae; and dermatology life quality index (DLQI) score (mean score, change from baseline, proportion with DLQI score of 0 or 1) (to Week 72).

Table 4: Proportion of subjects achieving a HiSCR at Week 12 across the direct randomised trials (NRI)

Trial ID	Adalimumab 40mg ew n/N (%)	Placebo n/N (%)	Risk difference [95% CI]	Relative risk [95% CI]
M10-467				
PIONEER I				
PIONEER II				
Pooled result from random effects model				
Chi-square (Q) for heterogeneity: P =				
I ² statistic with 95% uncertainty interval =				
Test for overall effect: P =				
Pooled result from random effects model excluding study M10-467				
Chi-square (Q) for heterogeneity: P =				
I ² statistic with 95% uncertainty interval =				
Test for overall effect: P =				

Abbreviations: CI, confidence interval; ew, every week; HiSCR, Hidradenitis Suppurativa Clinical Response, NRI; non-responder imputation

Source: Table B.6.1, p.55 of the resubmission

The redacted table above shows that adalimumab is better than placebo in achieving HiSCR.

Table 5: HiSCR results over time of the ■ patients who received adalimumab 40 mg every week and were HiSCR responders at Week 12 (OC)

Weeks from baseline	Total evaluation (HiSCR responders at Week 12 remaining in trial)	HiSCR responders N	HiSCR responders %
2			
4			
8			
12			
16			
20			
24			
36			
48			
60			
72			
84			
96			
108			

Note: ■ EW-EW-EW patients included in the global dataset (dataset M12-555) were HiSCR responders at week 12

Abbreviations: HiSCR, Hidradenitis Suppurativa Clinical Response; OC, observed cases

Source: Excel spreadsheet EW-EW-EW evolution_OLE Analysis, Attachment 7 of the re submission and compiled during the evaluation

The redacted table above shows that HiSCR was maintained amongst adalimumab responders.

Table 6: Mean DLQI score and change from baseline in DLQI score of the [redacted] patients achieving HiSCR at week 12 and received adalimumab 40 mg every week (OC)

Week from baseline	DLQI score				Change from baseline			
	N	Mean	SD	95% CI	N	mean	SD	95% CI
0	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
4	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
12	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
24	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
36	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
48	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
72	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

Note: [redacted] patients included in the global dataset (dataset M12-555) are HiSCR responders at week 12.

Italics indicate compiled during evaluation. There is a discrepancy between the number of mean DLQI score and change in baseline in Attachment 7 of the re submission (final OLE data).

Abbreviations: DLQI, Dermatology Life Quality Index; HiSCR, Hidradenitis Suppurativa Clinical Response; OC, observed cases; SD, standard deviation

Source: Table B.6.4, p.60 of the resubmission and Excel spreadsheet EW-EW-EW evolution_OLE Analysis, Attachment 7 of the re submission

The redacted table above shows that DLQI consistently improves over time.

6.9 The ESC noted the estimated proportion of responders for adalimumab did not decline from week 48 to week 108; however, the number of patients in the analysis declined substantially (Tables 5 and 6). The ESC further noted that the resubmission did not provide the reasons for declining patient numbers over time, e.g. whether this was due to patients discontinuing, due to loss of response (LOR) or adverse events, or reflected the available follow-up. The ESC considered that the key uncertainty with the clinical data is the proportion of continuing patients (beyond 12 weeks) who maintain a response to treatment. The pre-PBAC response (p2) noted that discontinuations from the OLE study were due to variety of reasons, including adverse events, lack of efficacy, withdrawal of consent and lack of follow-up.

6.10 The ESC noted the response rate in the placebo arm of the PIONEER trials was approximately [redacted] however, the ESC also noted this did not necessarily inform the natural course of the disease, as the placebo effect within a trial environment is known to be higher than in clinical practice.

Comparative harms

6.11 The comparative harms were unchanged from the previous submission. In March 2016, the PBAC noted that there were similar numbers of patients experiencing any adverse events (AEs), treatment-emergent infections and AEs leading to discontinuations reported in both the adalimumab and placebo arms of the three trials (paragraph 6.9, adalimumab Public Summary Document (PSD), July 2016 PBAC meeting).

Benefits/harms

6.12 A summary of the comparative benefits and harms for adalimumab compared with placebo is presented in the table below.

Table 7: Summary of comparative benefits and harms for adalimumab and placebo

Trial	ADA	PBO	RD (95% CI)	RR (95% CI)		
Benefits						
HiSCR response at Week 12						
M10-467 ^a						
PIONEER I	64/153 (41.8)	40/154 (26.0)				
PIONEER II	96/163 (59.0)	45/163 (27.6)				
Pooled result from random effects model RR [redacted] and RD [redacted]						
Pooled result from random effects model excluding M10-467 [redacted] and RD [redacted]						
Harms						
	ADA	PBO	RD (95% CI)	Event rate/100 patients*		RR (95% CI)
				ADA	PBO	
Any adverse event						
M10-467						
PIONEER I						
PIONEER II					66.9	
AE leading to discontinuation						
M10-467						
PIONEER I						
PIONEER II						

*Maximum duration of exposure: M10-467 = 16 weeks; PIONEER I = 12 weeks; PIONEER II = 12 weeks

^a.MiTT: Modified intention to treat analysis

Abbreviations: ADA = adalimumab; PBO = placebo; RD = risk difference; RR = risk ratio

Source: Compiled during the evaluation; Table B.6.14, p. 130 of the submission; RD (95% CI) and RR(95% CI) were calculated during the evaluation for each trial using RevMan.

- 6.13 On the basis of direct randomised evidence presented by the submission, for every 100 patients treated with adalimumab in comparison to placebo, approximately 29 additional patients would have achieved HiSCR over a maximum duration of exposure of 12 weeks.
- 6.14 The ESC noted that a comparative statement for the benefits and harms beyond 12 weeks based on the OLE study was not possible given data were presented for adalimumab only.

Clinical claim

- 6.15 The resubmission described adalimumab as superior to placebo in patients with moderate to severe HS, in terms of efficacy, and is marginally worse than placebo, in terms of safety. With respect to the original submission “The PBAC considered that the claim of superior comparative effectiveness was adequately supported by the data for the first 12 weeks of treatment. However, the PBAC noted that there was limited comparative data and no clear evidence of a clinically meaningful maintenance of efficacy beyond 12 weeks of therapy” (6.16, adalimumab PSD, March 2016 PBAC meeting). With respect to the OLE data presented in the pre-PBAC response to the July 2016 resubmission which had not been formally evaluated “...the PBAC considered that the claim of superior comparative effectiveness may be reasonable beyond 12 weeks, the PBAC did not accept the

extrapolation of the treatment benefit beyond treatment discontinuation modelled in the resubmission (paragraph 6.12, adalimumab PSD, July 2016 PBAC meeting). The PBAC previously considered that the submission's claim of inferior safety was reasonable (paragraph 7.9, adalimumab PSD, March 2016 PBAC meeting).

6.16 In order to support the ongoing use of adalimumab in responders, the resubmission stated that:

- In patients treated with adalimumab every week continuously throughout the study, this response was maintained by approximately [REDACTED] of patients demonstrating a clinically meaningful maintenance of treatment effect (p61). The data presented in the OLE study out to week 108 are not comparative. At Week 12, the number of HiSCR responders who received adalimumab every week throughout the PIONEER trial and OLE was [REDACTED]. By week 108, the proportion of the week 12 responders who continued to demonstrate a response was [REDACTED] based on observed cases.
- Data demonstrated that a decrease in lesion count was not only maintained with continued treatment with adalimumab but, in the case of draining fistulae, continued to decrease over time. However, these results are subject to the biases inherent in the OLE data arising from a non-comparative, small study sample.
- Results from the OLE study showed that patients had a significantly larger improvement from baseline in the DLQI score with a decrease greater than the minimum clinically important difference of 4 after 12 weeks which was maintained in patients treated with adalimumab every week continuously out to 72 weeks. The ESC noted that this was based on the OLE study and considered that this data should be considered in the context of it being non-comparative and of a small sample size ([REDACTED]).
- Additionally, the number of patients whose disease had no impact on their quality of life, as represented by a DLQI score of 0 or 1, continued to increase over time with continued adalimumab treatment.

6.17 The ESC agreed that HS was a condition with unmet clinical need, and considered that the clinical claim presented in the resubmission was reasonable, but noted that the claim for maintaining response beyond week 36 should be considered in the context of the small sample size and non-comparative data.

6.18 The PBAC considered that the claim of superior comparative effectiveness was adequately supported by the data for the first 12 weeks of treatment. While the PBAC considered that the claim of superior comparative effectiveness was likely to be reasonable beyond week 12, the magnitude of the incremental benefit, as measured by the proportion of continuing patients who maintain a response to treatment, remained the key uncertainty.

6.19 The PBAC reaffirmed that the claim of inferior comparative safety was reasonable.

Economic analysis

6.20 The resubmission presented a modelled cost utility analysis. The key changes from the model included in the March 2016 submission and July 2016 minor resubmission were:

- Response and no response health states disaggregated between Hurley Stage II and Hurley Stage III disease. The following parameters were Hurley Stage specific:
 - transition probabilities for first 12 weeks of treatment;
 - utility increment from baseline; and
 - health state disease cost for responders.
- Removal of the assumption of treatment benefit for adalimumab after treatment has stopped.
- Transition to non-response states (i.e. LOR) from Week 12-36 based on data from the PIONEER trials and from Week 36-108 based on OLE data. From Week 109 onwards patients did not transition out of the response states (based on assumption). In the previous model the rate of transition to the non-response state was assumed to be constant from week 36 (based on data from the PIONEER trials).
- For patients receiving adalimumab who achieve long-term (48 weeks) response, the model included an annual utility improvement of [REDACTED] for adalimumab responders (based on the OLE data).

Table 8: Summary of model structures and rationale

Component	March 2016 submission	Current resubmission
Time horizon	20 years in the model base case; 36 week trial data.	20 years in the model base case; 36 week trial data and data from OLE extension 108 week.
Outcomes	QALYs	Unchanged
Methods used to generate results	Cohort expected value analysis.	Unchanged
Health states	High response, Response, Partial Response, No Response and Dead.	1. Initiation Period (Hurley II) 2. Initiation Period (Hurley III) 3. Response (Hurley II) 4. Response (Hurley III) 5. No Response (Hurley II) 6. No Response (Hurley III) 7. Dead
Cycle length	Based on selected key time-points in PIONEER I and PIONEER II: First cycle (Week 0 to Week 2): 2 weeks Second cycle (Week 2 to Week 4): 2 weeks Third cycle onwards (Week 4 onwards): 4 weeks Half-cycle correction applied.	Cycle length is 12 weeks. Half-cycle correction applied.
Transition probabilities	Results from PIONEER I and PIONEER II trial for weeks 0-36 Constant probabilities from week 36 onwards based on week 13-36 results from the PIONEER I and II trials	Weeks 0-12: Results from the PIONEER I and PIONEER II trial stratified by Hurley Stage Weeks 12-36: Adalimumab - Time to loss of response from adalimumab (PIONEER I and PIONEER II). Placebo - Probability of movement to response health state based on 4-week transition matrices for placebo (PIONEER II) as used in the March 2016 submission. Weeks 36 to 108: Loss of response from OLE, same rate applied to adalimumab and placebo. Week 108 onwards: Loss of response assumed to be 0% applied to adalimumab and placebo.
Utility values	Based on PIONEER II trial, EQ-5D.	Based on PIONEER II trial, EQ-5D. Long-term responder utility improvement based on OLE data, DLQI.
Discount rate	5% for costs and outcomes	Unchanged
Software package	Excel 2010	TreeAge Pro 2009

Source: compiled during the evaluation

Table 9: Key drivers of the model

Description	Method/Value	Impact
Time horizon	20 years; assumed from 36 week trial duration (comparative data) and to Week 108 (OLE study).	High (comparing Steps 5 and 6 of the stepped analysis), favours adalimumab
Transition probabilities beyond Week 12	Modelled as loss of response: Adalimumab arm - trial-based survival curves for Period B of the PIONEER studies. Placebo arm - probabilities of moving between the two response-related health states based on 4-week transition matrices from Period B of PIONEER II.	High (as assumes independence between each four-week period), favours adalimumab
Progression of disease	Progression from Hurley II to Hurley III (██████████ for non-responders).	High, favours adalimumab
Utility increment for responders	Hurley II = ██████████; Hurley III = ██████████.	High, favours adalimumab
Utility increment for non-responders	Hurley II ██████████; Hurley III ██████████.	High, favours adalimumab
Health state costs for medical resource use	No Response = \$ ██████████; Responder = \$ ██████████. (Hurley II) / \$ ██████████. (Hurley III)) In the model, due to being in worse health states, the health state costs for treating HS (excluding adalimumab) are higher for the BSC arm compared with the adalimumab arm	High, favours adalimumab

Source: compiled during the evaluation

6.21 Table 10 presents the stepped economic evaluation for the current resubmission. The model structure and parameters used in the current resubmission differ from the minor resubmission. The incremental cost per QALY gained in the current resubmission was \$45,000 - \$75,000 (compared with \$45,000 - \$75,000 in the July 2016 minor resubmission and \$15,000 - \$45,000 in the July 2016 pre-PBAC response). The evaluation noted a discrepancy in the transition probabilities used in the model for patients receiving placebo from week 12 to 36. The PSCR (p4) stated that there was a transcription error and correcting this increased the ICER to \$45,000 - \$75,000 per QALY gained. The impact is relatively small and the ICERs in this PSD have not been corrected.

Table 10: Results of the stepped economic evaluation in the current resubmission

Step and component	Adalimumab	Placebo	Increment
Step 1: ITT Pooled Pioneer, drug/initiation costs only			
Costs	\$ [REDACTED]	\$0	\$ [REDACTED]
HiSCR responder	[REDACTED]	[REDACTED]	[REDACTED]
Incremental cost/ additional HiSCR responder at 12 weeks			\$ [REDACTED]
Step 2: Apply continuation rule, extend to 36 weeks			
Costs	\$ [REDACTED]	\$0	\$ [REDACTED]
HiSCR responder	[REDACTED]	[REDACTED]	[REDACTED]
Incremental cost/ additional HiSCR responder at 36 weeks			\$ [REDACTED]
Step 3: Apply discontinuation rate, allow all-cause mortality			
Costs	\$ [REDACTED]	\$0	\$ [REDACTED]
HiSCR responder	[REDACTED]	[REDACTED]	[REDACTED]
Incremental cost/ additional HiSCR responder at 36 weeks			\$ [REDACTED]
Step 4: Transform to QALYs			
Costs	\$ [REDACTED]	\$0	\$ [REDACTED]
QALYs	[REDACTED]	[REDACTED]	[REDACTED]
Incremental cost/ additional QALYs at 36 weeks			\$ [REDACTED]
Step 5: Apply health state costs			
Costs	\$ [REDACTED]	\$5,459	\$ [REDACTED]
QALYs	[REDACTED]	[REDACTED]	[REDACTED]
Incremental cost/ additional QALYs at 36 weeks			\$ [REDACTED]
Step 6: Extrapolate to 20 years			
Costs	\$ [REDACTED]	\$109,657	\$ [REDACTED]
QALYs	[REDACTED]	[REDACTED]	[REDACTED]
Incremental cost/ additional QALYs at 20 years			\$ [REDACTED]
Step 7: Apply utility improvement in long term responders			
Costs	\$ [REDACTED]	\$109,657	\$ [REDACTED]
QALYs	[REDACTED]	[REDACTED]	[REDACTED]
Incremental cost/ additional QALYs at 20 years			\$ [REDACTED]
Step 8: Allow H2 to H3 progression			
Costs	\$ [REDACTED]	\$109,657	\$ [REDACTED]
QALYs	[REDACTED]	[REDACTED]	[REDACTED]
Incremental cost/ additional QALYs at 20 years			\$ [REDACTED]

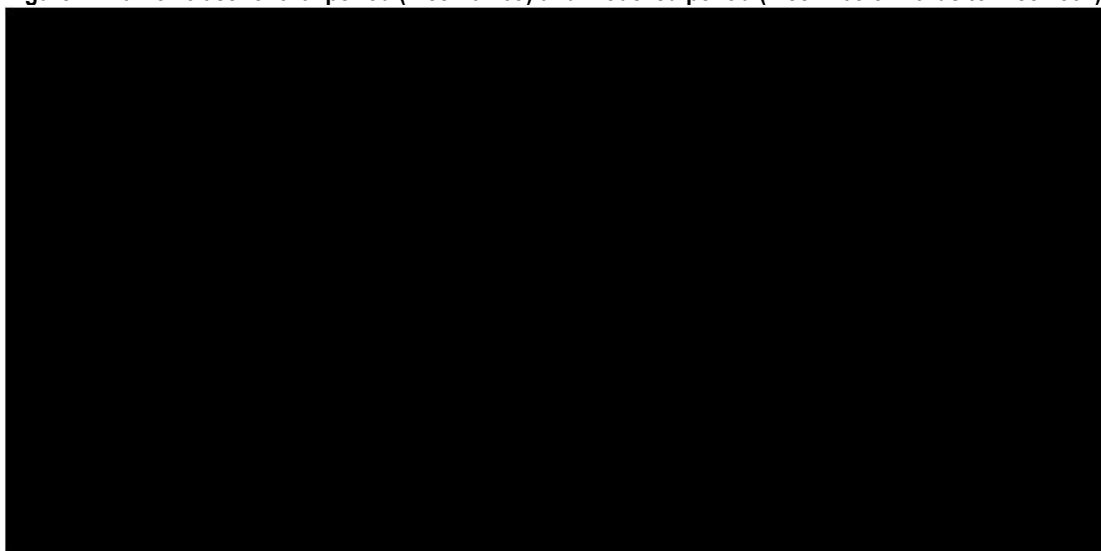
Source: Table D.5.1, p. 102 of the resubmission and Table D.5.4, p. 103 of the resubmission

6.22 Markov traces prepared during the evaluation are presented in Figure 1.

- From week 36 to week 108 there is a very low LOR [REDACTED] for both treatment groups. Post-week 108, there is no LOR for patients treated with adalimumab or placebo in either Hurley II or III states. Thus patients on adalimumab treatment and in the response health state by week 108 [REDACTED] will continue to remain in the response health state for the duration of the modelled time horizon (at week 1040, [REDACTED] remain in that state; [REDACTED] move into the death health state). Correspondingly, for patients on placebo at week 108, [REDACTED] are in the response health state at week 108 and [REDACTED] remain at week 1040. The low LOR beyond week 36 means that the difference in the proportion of responders for adalimumab and placebo at week 36 is a key driver for the model. The difference at week 36 is greater than at week 12, and this is because [REDACTED] of adalimumab responders at week 12 lose their response by week 36 compared with [REDACTED] of placebo patients. The ESC noted that the LOR for placebo was calculated using a different method to that for adalimumab and the estimate used in the model was inconsistent with the available trial data (see below). The ESC considered that this favoured adalimumab.

- Post-week 12, there is an assumption of no additional response among placebo patients; this is not plausible as some patients are likely to experience resolution of their condition without active treatment. This assumption favoured adalimumab as it overestimated the incremental benefit of treatment compared with placebo. The PSCR (p2) stated that there was no clinical evidence of untreated patients achieving HiSCR in clinical practice. The ESC acknowledged that more severe HS is generally ongoing and progressive, but given the cyclical nature of the condition with fluctuations in periods of active disease (as evidenced by the OLE data presented in the resubmission), it was unreasonable to assume that there was no response in the placebo group beyond week 12. The pre-PBAC response (p3) claimed that the decline in QoL and utility values due to ongoing progression of disease is likely to outweigh any temporary/cyclical improvements in QoL that may occur in the placebo group, especially given the relatively faster rate of LOR in the placebo arm.

Figure 1: Markov trace for trial period (Week 0-108) and modelled period (Week 108 onwards to Week 504)



Source: Extracted during the evaluation from the economic model 'Adalimumab HS PBAC model July 2016', TreeAge

Note: 1. These traces have been truncated at 10 years (Week 516). The model time horizon is 20 years (Week 1040).

2. The health states "initiation period – H2", "initiation period – H3" and "Dead" are not included in these traces.

6.23 The results of the sensitivity analyses indicate that the model is most sensitive to the following:

- Progression from Hurley Stage II to Hurley Stage III: The inclusion of progression in the model may not have been appropriate given there are no data on progression. Moreover, the data from the PIONEER trials do not address the question of the efficacy of adalimumab on disease progression on the basis of Hurley stage. The exclusion of progression was tested in the sensitivity analyses; this had a significant impact on the ICER increasing it to \$75,000 - \$105,000 per QALY gained (from \$45,000 - \$75,000 in the base case). The PSCR (p2) stated that there is emerging evidence in the literature that HS is a progressive disease and that treatment with adalimumab could inhibit disease progression.
- The difference in LOR between adalimumab and placebo between Weeks 12 and 36 (see paragraph 6.24).

- The assumption of no utility gain for non-responders: Including a 0.05 utility increment to all non-responders (regardless of Hurley Stage), increased the ICER to \$75,000 - \$105,000 per QALY gained.
- The inclusion of higher costs for disease management for the no response compared with response health states: Excluding the disease management costs increased the ICER to \$75,000 - \$105,000 per QALY gained.

6.24 In addition, the evaluation considered it may not have been appropriate to apply [REDACTED] in long-term responders to adalimumab (post 1 year) given that [REDACTED]. Further, the OLE data used to inform the estimates were based on a small number of patients (n=25). Excluding the utility benefit for long-term responders increased the ICER to \$75,000 - \$105,000 per QALY gained and, based on this result, was not a key driver of the model results. The PSCR (p4) acknowledged that the majority of QoL benefits in the model accrued in the first year of treatment, but argued that there was a strong clinical rationale for assuming additional long-term improvement in QoL with continued adalimumab treatment. The ESC considered the long-term additional gain in quality of life was inconsistent with the majority of the improvement being in the first [REDACTED] weeks of treatment.

6.25 The ESC considered the revised economic model presented in the current resubmission remained optimistic. In particular, (i) the LOR from week 12 to 36 for placebo was overestimated, and (ii) the choice of utility estimate applied to adalimumab responders was optimistic given that it was based on the week 12 utility value, which may not be maintained.

- The PSCR (p2) argued that the rates of LOR between weeks 12 and 36 were calculated using trial-justifiable data from the PIONEER clinical studies and contended that this was consistent with expectations in clinical practice. The ESC considered the placebo data were used incorrectly in the model.
- For adalimumab LOR was calculated based on the number of 12 week responders who lost their response by week 24. In PIONEER I, [REDACTED] lost their response. In PIONEER II, [REDACTED] lost their response. The estimate used in the model [REDACTED] was the average from PIONEER I and II. The variability across the trials highlights this estimate is uncertain.
- The submission acknowledged that there was a substantial placebo response rate up to week 12 and that week 12-36 data were not reported according to whether patients were responders or non-responders in the placebo study arm. Therefore a survival curve with a starting population of responders at week 12 was not available. In the absence of these data, the submission calculated LOR for the placebo arm, based on the probability of maintaining a response at weeks 16, 20, 24, 28, 32 and 36 in PIONEER II. The probability at each time point was multiplied together (probability of maintaining a response [REDACTED]). The ESC considered the approach of multiplying the probabilities was incorrect as the probabilities at each time point are not independent events. The approach also did not consider that some non-responders become responders e.g. from week 12 to week 16, [REDACTED] of non-responders became responders. The data provided allows a calculation of placebo response which is likely to be more comparable with the adalimumab approach. Using the data only from week 36, the LOR is estimated to be [REDACTED] responding patients at week 12 [REDACTED] maintained a response and therefore the LOR = [REDACTED]

██████████. The ESC considered the estimate of ██████████ to be a lower bound as it includes some patients who moved between response and non-response in the weeks between 16 and 36. However, the ESC acknowledged that with the data presented in the submission it was not possible to estimate the LOR for the placebo arm more accurately. Assuming a LOR for the placebo arm of ██████████ increased the ICER to \$105,000 - \$200,000 per QALY gained (from \$45,000 - \$75,000 in the base case). The Pre-PBAC response (p2) contended that the LOR rates applied in the model were informed by trial data, and were therefore more likely to reflect clinical practice than the rate suggested by the ESC which was based on assumptions.

6.26 The ESC considered the utility increment for responders ██████████ to be relatively large. It was noted that the increments were based on 12 week data from PIONEER II, and that there was an inconsistent trend ██████████ (e.g. for Hurley III the increment was ██████████ relative to baseline). Regardless, the ESC considered the utility gains were very unlikely to be preserved to twenty years. Decreasing the utility increments for responders by 0.05 increased the ICER to \$75,000 - \$105,000 per QALY gained (from \$45,000 - \$75,000 in the base case). The pre-PBAC response (p2) stated that the utility increments for response are based on utility data collected in clinical trials.

6.27 The ESC considered the modelled time horizon (20 years) to be too long, especially given it was essentially assumed that response at week 36 is maintained for the remainder of the model duration. The ESC further considered the maintenance of treatment effect did not reflect the fluctuating nature of disease severity. The PSCR (p.1-2) stated that the revised model was not sensitive to extrapolation beyond 12 weeks, largely because of the incorporation of a continuation rule requiring patients to demonstrate a HiSCR response at week 12. The ESC noted that reducing the time horizon to 10 years increased the ICER to \$75,000 - \$105,000 per QALY gained (from \$45,000 - \$75,000 in the base case).

Drug cost/patient/year: \$██████████

6.28 For the first 12 months of treatment: an initial prescription (4 weeks of treatment) with an effective DPMQ of \$██████████ (6 x 40 mg injections per script), 3 prescriptions (Week 5 to 16, 12 weeks of treatment), and 9 prescriptions (remaining 36 weeks) for the continuing treatment with an effective DPMQ of \$██████████ (2 x 2 x 40 mg injections per script).

Estimated PBS usage & financial implications

- 6.29 This resubmission was not considered by DUSC. The major changes from previous submissions include:
- A change in the diagnosis rate from ██████████ over the five years in the minor submission to ██████████;
 - A reduced DPMQ for adalimumab;
 - Increased patient co-payments;
 - Removal of retreatment;
 - Updated Australian adult population estimates;
 - A constant discontinuation rate from adalimumab; and

- Inclusion of an updated number of compassionate use program patients.

Table 11: Estimated use and financial implications

	Year 1	Year 2	Year 3	Year 4	Year 5
Estimated extent of use					
Number eligible					
Uptake rate	%	%	%	%	%
Number treated					
Number treated– March 2016					
Number treated– July 2016					
6x40 mg pack					
2 x (2x40 mg pack)					
Estimated net cost to PBS/MBS					
Net cost to PBS	\$	\$	\$	\$	\$
Net cost to MBS	NA	NA	NA	NA	NA
Estimated total net cost					
Net cost PBS/MBS	\$	\$	\$	\$	\$
Net cost PBS/MBS – March 2016	\$	\$	\$	\$	\$
Net cost PBS/MBS – July 2016	\$	\$	\$	\$	\$

^a 1 x 6-pack for initial script (4 weeks supply)
Source: Compiled during the evaluation

- 6.30 At year 5, the estimated number of patients was less than 10,000 and the net cost to the PBS would be \$20 - \$30 million. The financial estimates in Year 5 are most sensitive to assumptions about the prevalence of HS, the proportion of Hurley II and III patients and the uptake rate for adalimumab.
- 6.31 The ESC considered that there was potential for usage beyond the requested listing:
- The continuation criteria might not be adhered to in clinical practice and patients with less severe disease (Hurley Stage I) may be treated. This was based on evidence presented in the resubmission which indicated that the DLQI scores were similar between Hurley Stage I and Hurley Stage II in an Australian cohort of patients; therefore the ESC considered that Hurley Stage I patients might be considered sufficiently affected as to require treatment.
 - The PSCR (p4-5) contended that DLQI was not part of the eligibility criteria proposed in the requested listing. Further, the PSCR claimed that the written Authority process was rigorous, and would be sufficient to ensure that adalimumab was prescribed to the most cost-effective population.
 - The ESC disagreed, noting that the potential of adalimumab usage in Hurley Stage I patients remained a concern.

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

7 PBAC Outcome

- 7.1 The PBAC deferred making a recommendation on whether adalimumab should be listed for the treatment of moderate-to-severe Hidradenitis Suppurativa (HS) pending further discussion with the sponsor regarding an acceptable price and risk-sharing arrangements.

- 7.2 The PBAC reaffirmed that there is a high clinical need for an effective treatment for moderate-to-severe HS, and that the chronic nature of the inflammatory skin disease causes significant morbidity and poor quality of life. The PBAC considered that the consumer comments received in relation to the resubmission, both from people living with the condition and on behalf of patients, were informative in providing a clinical perspective on this uncommon disease.
- 7.3 The PBAC recalled that in March 2016 and July 2016, it rejected submissions for adalimumab for moderate to severe HS on the basis of uncertain cost effectiveness. In March 2016, the PBAC considered that a major resubmission should include a revised model of ongoing therapy with adalimumab and more conservative assumptions regarding the maintenance of treatment benefit. In its consideration of the July 2016 minor resubmission, the PBAC noted that it requested the same restriction and presented the same model as the March 2016 pre-PBAC response with a reduced price offer. The PBAC further noted that the pre-PBAC response for the July 2016 minor resubmission removed the treatment of non-responders in the requested restriction and presented a revised price offer (paragraphs 7.1-7.2 adalimumab PSD, July 2016 PBAC meeting). In rejecting the July 2016 minor resubmission, the PBAC advised that a future major resubmission should include the changes to the restriction and additional OLE data presented in the pre-PBAC response for evaluation and a revised economic model with more conservative assumptions regarding the incremental benefit of adalimumab following treatment cessation and other issues raised by the ESC (paragraph 7.10, adalimumab PSD, July 2016 PBAC meeting).
- 7.4 The PBAC noted that the current resubmission included a stopping rule at 12 weeks for all non-HiSCR responders. The PBAC considered that the proposed restriction criteria were reasonable, and noted that the continuation rule was consistent with the ACPM's advice that adalimumab use beyond 12 weeks should be contingent on evidence of benefit. The PBAC reiterated that the continuing restriction should be Authority Required (in-writing) as per the initial restriction (as opposed to the requested STREAMLINED authority) (paragraph 7.3, adalimumab PSD, July 2016 PBAC meeting). The PBAC considered that there was a risk of leakage outside the proposed restriction to a patient sub-population with lower disease severity, i.e. those with Hurley Stage I disease.
- 7.5 The PBAC recalled that it previously accepted best supportive care as the appropriate comparator (paragraphs 7.5, adalimumab PSDs, March and July 2016 PBAC meetings).
- 7.6 The PBAC recalled that based on the evidence presented in the March 2016 submission, it had previously considered that the claim of superior comparative effectiveness was adequately supported by the data for the first 12 weeks of adalimumab treatment; however, there was no clear evidence of a clinically meaningful maintenance of efficacy beyond 12 weeks of therapy (paragraph 7.8, adalimumab PSD, March 2016 PBAC meeting). In July 2016, the PBAC further considered that while the claim of superior comparative effectiveness may be reasonable beyond 12 weeks, the PBAC did not accept the extrapolation of the treatment benefit beyond treatment discontinuation modelled in the minor resubmission (paragraph 7.7, adalimumab PSD, July 2016 PBAC meeting).

- 7.7 The current resubmission included the final results from the OLE study M12-555 (██████) for HiSCR responders at week 12. The PBAC noted that ██████ of patients (██████) achieving HiSCR at week 12 and remaining on treatment up to week 108 maintain their response. The PBAC further noted the estimated proportion of responders for adalimumab did not decline from week 48 to week 108; however, the number of patients in the analysis declined substantially. The PBAC considered that while the claim of superior comparative effectiveness was likely to be reasonable beyond week 12, the magnitude of the incremental benefit, as measured by the proportion of continuing patients who maintain a response to treatment remained the key uncertainty.
- 7.8 The PBAC reaffirmed that the claim of inferior comparative safety over best supportive care was reasonable (paragraph 6.12, adalimumab PSD, July 2016 PBAC meeting).
- 7.9 The PBAC considered that the ICER for adalimumab for HS was underestimated due to the following issues, as identified by the ESC:
- The model was sensitive to different rates of loss of response from weeks 12 to 36 (██████ for adalimumab and ██████ for placebo), and loss of response in the placebo arm was likely overestimated (see paragraph 6.24).
 - The utility gains for responders were relatively large and were unlikely to be preserved for the model duration (see paragraph 6.25).
 - The annual utility gain for achieving long-term response was not reasonable, given that the majority of the improvement was ██████████ of treatment (see paragraph 6.23).
 - The assumption of no response in the placebo arm beyond week 12 was optimistic as some patients are likely to experience resolution of their condition without active treatment (see paragraph 6.22).
 - The assumptions underlying progression from Hurley Stages II to III were uncertain and not supported by clinical evidence (see paragraph 6.23).
 - The time horizon of 20 years was optimistic, as it assumed that response at 36 weeks was maintained for the remainder of the model duration (see paragraph 6.26).
- Notwithstanding these issues, the PBAC considered that the ICER at the requested price, of \$45,000 - \$75,000 per QALY gained, was unacceptably high.
- 7.10 The PBAC noted the sponsor's willingness to negotiate an appropriate price and risk sharing arrangement with the Department in order to address the Committee's ongoing uncertainties regarding the long-term clinical and cost effectiveness of adalimumab.
- 7.11 The PBAC acknowledged that there was a clinical need for PBS-subsidised access to adalimumab for moderate-to-severe HS, and advised that for adalimumab to be acceptably cost-effective for this condition, the following should form the basis of future negotiations with the Department:
- a significant price reduction to account for the uncertainty about the proportion of continuing patients beyond 12 weeks who maintain a response to adalimumab; and
 - a risk sharing arrangement based on agreed subsidisation caps in order to mitigate the risk of high total cost to government.

Outcome:

Deferred

ADDENDUM

Subsequent to the November 2016 meeting, the sponsor provided the PBAC with the following information:

- a revised price offer (see Table 12)
- a revised ICER of \$45,000 - \$75,000 per QALY gained;
- revised financial estimates; and
- a proposed risk sharing arrangement with yearly subsidisation caps ranging from \$ [REDACTED] in year 1 to \$ [REDACTED] in year 6 with a rebate of [REDACTED] % of the effective price for any expenditure above the caps in any year.

Table 12: Requested effective DPMQ by submission

ADALIMUMAB, 40 MG/ 0.8 ML INJECTION	Maximum quantity (packs)	Maximum quantity (units)	Effective DPMQ			
			Mar-16 submission	Jul-16 submission	Nov-16 submission	Current price offer
6 X 0.8 ML SYRINGES	1	6	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]
2 X 0.8 ML SYRINGES	2	4	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]

CHANGES TO PRESENT (OR RECOMMENDED) PBS AVAILABILITY

When the PBAC makes a recommendation under section 101(3) of the *National Health Act 1953* (“the Act”) in relation to a drug/medicinal preparation which it considers should be made available as a pharmaceutical benefit under Part VII of the Act, it is also required to consider whether the drug/medicinal preparation should be made available only in certain circumstances (see section 101(3C) of the Act). Where the PBAC considers that the drug/medicinal preparation should be made available only in certain circumstances, it specifies the circumstances in its recommendation under section 101(3).

At its meeting held on **16 December 2016**, the PBAC in making its recommendation under section 101(3) of the Act, decided to recommend a change to the circumstances under which adalimumab is made available as a pharmaceutical benefit under Part VII of the Act.

A note of the PBAC’s decision follows.

The PBAC recommended the listing of adalimumab on the General Schedule for the treatment of patients with moderate-to-severe HS under certain conditions (see recommended listing) on a cost-effectiveness basis. The PBAC recommended that the Department negotiate a Risk Share Arrangement comprising of yearly subsidisation caps

[REDACTED]

The PBAC noted that this is the first treatment for moderate-to-severe HS recommended for listing on the PBS. The PBAC was satisfied that adalimumab provides, for some patients, a significant improvement in effectiveness compared with best supportive care.

The PBAC noted that the revised price resulted in an ICER of \$ [REDACTED] per QALY gained. Key sensitivity analyses from the submission and ESC Advice compared with ICERs based on the post-November 2016 PBAC meeting price offer are summarised in Table 13 below. The PBAC noted that at the reduced requested price, the ICER remained within \$45,000 - \$75,000 per QALY gained for the majority of scenarios tested.

The PBAC considered that the cost effectiveness of adalimumab for HS was acceptable following the reduction in the requested price and in conjunction with the requested continuation rule and risk sharing measures to provide additional certainty.

Table 13: Key sensitivity analyses based on proposed price

Parameter (base-case value)	Description	ICER (\$/QALY gained)	
		Nov-2016	Current price offer*
Base-case		\$ [REDACTED]	\$ [REDACTED]
Discontinuation rates (weeks 12 to 36); Difference between ADA and BSC (ADA rates kept constant)	Decreased by 50%	\$ [REDACTED]	\$ [REDACTED]
	Increased by 50%	\$ [REDACTED]	\$ [REDACTED]
Progression from Hurley II to Hurley III ([REDACTED] for non-responders)	Off – progression not allowed	\$ [REDACTED]	\$ [REDACTED]
	Halved	\$ [REDACTED]	\$ [REDACTED]
	Doubled	\$ [REDACTED]	\$ [REDACTED]
Utility Improvement from baseline in responders (Hurley II [REDACTED]; Hurley III [REDACTED])	Decreased by 0.05	\$ [REDACTED]	\$ [REDACTED]
	Increased by 0.05	\$ [REDACTED]	\$ [REDACTED]
Utility Improvement from baseline in non-responders (Hurley II [REDACTED]; Hurley III [REDACTED])	Decreased by 0.05	\$ [REDACTED]	\$ [REDACTED]
	Increased by 0.05	\$ [REDACTED]	\$ [REDACTED]
Long term utility improvement ([REDACTED] after at least 48 weeks with response)	Off – no long term utility improvement	\$ [REDACTED]	\$ [REDACTED]
	After 96 weeks	\$ [REDACTED]	\$ [REDACTED]
Model horizon (20 years)	10 years	\$ [REDACTED]	\$ [REDACTED]
	Lifetime (63 years)	\$ [REDACTED]	\$ [REDACTED]
Loss of response from week 12 to 36 for placebo arm [REDACTED]	[REDACTED] (considered to be the lower bound by ESC)	\$ [REDACTED]	\$ [REDACTED]

*\$ [REDACTED] per 2 pack

The PBAC recommended that the Early Supply Rule should apply to adalimumab for the treatment of moderate of severe HS.

The PBAC advised that adalimumab is not suitable for prescribing by nurse practitioners.

The PBAC recommended that adalimumab should not be treated as interchangeable on an individual patient basis with any other currently PBS listed drugs.

The PBAC noted that this submission is not eligible for an Independent Review because the PBAC has made a positive recommendation.

Recommended listing

Name, Restriction, Manner of administration and form	Max. Qty (packs)	No. of Rpts	Proprietary Name and Manufacturer	
ADALIMUMAB			Humira®	Abbvie
40 MG/0.8 ML INJECTION, 6 X 0.8 ML SYRINGES	1	0		
40 MG/0.8 ML INJECTION, 2 X 0.8 ML SYRINGES	2	2		
40 MG/0.8 ML INJECTION, 6 X 0.8 ML CARTRIDGES	1	0		
40 MG/0.8 ML INJECTION, 2 X 0.8 ML CARTRIDGES	2	2		

Category / Program	GENERAL – 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
Severity:	Moderate to severe
Condition:	hidradenitis suppurativa
PBS Indication:	Moderate to severe hidradenitis suppurativa
Treatment phase:	Initial 1: (new patient) or recommencement of treatment
Restriction Level / Method:	<input type="checkbox"/> Restricted benefit <input checked="" type="checkbox"/> Authority Required - In Writing <input type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required - Emergency <input type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined
Treatment criteria:	Must be treated by a dermatologist
Clinical criteria:	Patient must have failed to achieve an adequate response to 2 courses of different antibiotics each for 3 months prior to initiation of PBS subsidised treatment with this drug for this condition; OR Patient must have a documented intolerance to antibiotics of a severity necessitating permanent treatment withdrawal with 2 different courses of antibiotics each for 3 months prior to initiation of PBS-subsidised treatment with this drug for this condition; OR Patient must have a medical contraindication to treatment with 2 different courses of antibiotics each for 3 months prior to initiation of PBS-subsidised treatment with this drug for this condition; AND Patient must have, at the time of application, a Hurley stage II or III grading with an abscesses and inflammatory nodule (AN) count greater than or equal to 3; AND Patient must not have previously received PBS-subsidised treatment with this drug for this condition; OR Patient must have demonstrated response to previous PBS-subsidised treatment with this drug for this condition.

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<p>Prescriber Instructions</p>	<p>A maximum of 16 weeks treatment will be authorised under this criterion.</p> <p>Assessment of disease severity must be no more than 1 month old at the time of application</p> <p>A response to treatment is defined as: Achieving Hidradenitis Suppurativa Clinical Response (HiSCR) of a 50% reduction in AN count compared to baseline with no increase in abscesses or draining fistulae.</p> <p>An assessment of the patient's response to this initial course of treatment must be made following a minimum of 12 weeks of treatment.</p> <p>At the time of authority application the prescriber must request: For the first 4 weeks of treatment: A prescription for up to 6 injections and no repeats to provide for up to 4 weeks treatment according to the dosage specified in the approved Product Information for this drug for this condition. For weeks 5 to 16: A separate prescription for up to 4 injections with 2 repeats to provide for up to 12 weeks treatment at the dosage specified in the Product Information for this drug for this condition.</p> <p>The authority application must be made in writing and must include:</p> <ul style="list-style-type: none"> (a) two completed authority prescription forms; and (b) a completed hidradenitis suppurativa PBS authority application supporting Information form which must include: <ul style="list-style-type: none"> (i) the Hurley stage grading; and (ii) the AN count; and (iii) the two different courses of antibiotics; or (iv) confirmation of intolerance to two different courses of antibiotics necessitating permanent treatment withdrawal; or (v) confirmation of medical contraindication to two different courses of antibiotics; and (vi) a signed patient acknowledgement.
<p>Administrative advice</p>	<p>No increase in the maximum number of repeats may be authorised.</p> <p>No increase in the maximum quantity or number of units may be authorised.</p> <p>Special Pricing Arrangements apply.</p> <p>Any queries concerning the arrangements to prescribe may be directed to the Department of Human Services on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday).</p> <p>Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Department of Human Services website at www.humanservices.gov.au</p> <p>Applications for authority to prescribe should be forwarded to: Department of Human Services Prior Written Approval of Complex Drugs Reply Paid 9826 GPO Box 9826 HOBART TAS 7001</p>

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Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Name and Manufacturer	
ADALIMUMAB			Humira®	Abbvie
40 MG/0.8 ML INJECTION, 2 X 0.8 ML SYRINGES	2	5		
40 MG/0.8 ML INJECTION, 2 X 0.8 ML CARTRIDGES	2	5		

Category / Program	GENERAL – 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
Episodicity:	-
Severity:	Moderate to severe
Condition:	hidradenitis suppurativa
PBS Indication:	Moderate to severe hidradenitis suppurativa
Treatment phase:	Continuing treatment
Restriction Level / Method:	<input type="checkbox"/> Restricted benefit <input checked="" type="checkbox"/> Authority Required - In Writing <input type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required - Emergency <input type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined
Treatment criteria:	Must be treated by a dermatologist
Clinical criteria:	Patient must have previously received PBS-subsidised treatment with this drug for this condition; AND Patient must demonstrate response to treatment with this drug for this condition.

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Prescriber Instructions	<p>A response to treatment is defined as: Achieving HiSCR (50% reduction in AN count as compared to baseline with no increase in abscesses or draining fistulae)</p> <p>For the first application for continuing treatment a HiSCR assessment must be made following a minimum of 12 weeks of treatment. For subsequent continuing treatment a HiSCR assessment must be made every 24 weeks.</p> <p>The assessment of the patient's response to a continuing course of treatment must be made within the 4 weeks prior to completion of that course and posted to the Department of Human Services no less than 2 weeks prior to the date the next dose is scheduled, in order to ensure continuity of treatment.</p> <p>Where an assessment is not submitted to the Department of Human Services within these timeframes, patients will be deemed to have failed to respond, or to have failed to sustain a response, to treatment with this drug.</p> <p>A maximum of 24 weeks treatment will be authorised under this criterion per continuing treatment</p> <p>The authority application must be made in writing and must include: (a) a completed authority prescription form; and (b) a completed hidradenitis suppurativa PBS authority application supporting Information form which must include the HiSCR result.</p>
Administrative advice	<p>No increase in the maximum number of repeats may be authorised.</p> <p>No increase in the maximum quantity or number of units may be authorised.</p> <p>Special Pricing Arrangements apply.</p> <p>Any queries concerning the arrangements to prescribe may be directed to the Department of Human Services on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday).</p> <p>Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Department of Human Services website at www.humanservices.gov.au</p> <p>Applications for authority to prescribe should be forwarded to: Department of Human Services Prior Written Approval of Complex Drugs Reply Paid 9826 GPO Box 9826 HOBART TAS 7001</p>

Category / Program	GENERAL – 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
Episodicity:	-
Severity:	Moderate to severe
Condition:	hidradenitis suppurativa

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PBS Indication:	Moderate to severe hidradenitis suppurativa
Treatment phase:	Initial 2: grandfathered patient
Restriction Level / Method:	<input type="checkbox"/> Restricted benefit <input checked="" type="checkbox"/> Authority Required - In Writing <input type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required - Emergency <input type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined
Treatment criteria:	Must be treated by a dermatologist
Clinical criteria:	<p>Patient must have been receiving treatment with this drug for this condition prior to [listing date], AND Patient must have had a Hurley stage II or III with an abscesses and inflammatory nodule (AN) count greater than or equal to 3 prior to starting treatment with this drug AND Patient must have demonstrated a response to treatment by achieving HiSCR after 12 weeks of treatment. AND Patient must have failed to achieve an adequate response to 2 courses of different antibiotics each for 3 months prior to initiation of treatment with this drug for this condition; OR Patient must have a documented intolerance to antibiotics of a severity necessitating permanent treatment withdrawal with 2 different courses of antibiotics each for 3 months prior to initiation of treatment with this drug for this condition; OR Patient must have a medical contraindication to treatment with 2 different courses of antibiotics each for 3 months prior to initiation of treatment with this drug for this condition</p>
Prescriber Instructions	<p>The assessment of the patient's response to a continuing course of treatment must be made within the 4 weeks prior to completion of that course and posted to the Department of Human Services no less than 2 weeks prior to the date the next dose is scheduled, in order to ensure continuity of treatment.</p> <p>Where an assessment is not submitted to the Department of Human Services within these timeframes, patients will be deemed to have failed to respond, or to have failed to sustain a response, to treatment with this drug.</p> <p>A maximum of 24 weeks treatment will be authorised under this criterion.</p> <p>The authority application must be made in writing and must include:</p> <ol style="list-style-type: none"> (a) a completed authority prescription form; and (b) a completed hidradenitis suppurativa PBS authority application supporting Information form which must include: <ol style="list-style-type: none"> (i) the Hurley stage grading prior to starting treatment with this drug; and (ii) the AN count prior to starting treatment with this drug; and (iii) the two different courses of antibiotics; or (iv) confirmation of intolerance to two different courses of antibiotics necessitating permanent treatment withdrawal; or (v) confirmation of medical contraindication to two different courses of antibiotics; and (vi) a signed patient acknowledgement.

Administrative advice	<p>No increase in the maximum number of repeats may be authorised.</p> <p>No increase in the maximum quantity or number of units may be authorised.</p> <p>Special Pricing Arrangements apply.</p> <p>Any queries concerning the arrangements to prescribe may be directed to the Department of Human Services on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday).</p> <p>Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Department of Human Services website at www.humanservices.gov.au</p> <p>Applications for authority to prescribe should be forwarded to: Department of Human Services Prior Written Approval of Complex Drugs Reply Paid 9826 GPO Box 9826 HOBART TAS 7001</p>
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8 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.

9 Sponsor's Comment

AbbVie welcomes the PBAC's recognition that hidradenitis suppurativa has a high unmet clinical need and is pleased that patients will soon be able to access HUMIRA to effectively treat their condition.