PUBLIC SUMMARY DOCUMENT

Product: TOCILIZUMAB, solution for IV infusion, 80 mg in 4 mL, 200 mg in 10 mL and 400 mg in 20 mL, Actemra®

Sponsor: Roche Products Pty Ltd

Date of PBAC Consideration: March 2010

1. Purpose of Application:

The submission sought a Section 100 (Highly Specialised Drugs Program) listing for first line use in the treatment of severe active rheumatoid arthritis.

Highly Specialised Drugs are medicines for the treatment of chronic conditions, which, because of their clinical use or other special features, are restricted to supply to public and private hospitals having access to appropriate specialist facilities.

2. Background:

In July 2009, the PBAC recommended that tocilizumab solution for infusion 80 mg in 4 mL, 200 mg in 10 mL and 400 mg in 20 mL be listed as a Section 100 item, for the treatment of severe, active rheumatoid arthritis in combination with methotrexate in patients who have failed to demonstrate a response to at least one TNF-alfa antagonist treatment on a cost-minimisation basis compared to abatacept.

The PBAC was concerned with respect to comparative safety, in particular long-term safety. Tocilizumab was associated with a higher incidence of infection than abatacept, more than doubling of incidence of malignancy in the long-term data compared to trial data, sustained elevations in total cholesterol requiring additional treatment, and 15 deaths reported in a post-marketing surveillance study of Japanese patients. Therefore, given the toxicity concerns of the increased risks of infection and raised lipid profile the PBAC considered that a second-line listing on a cost-minimisation basis with abatacept appropriate. The sponsor did not proceed with listing.

At the same meeting, the PBAC noted that listing was also requested for the treatment of severe active rheumatoid arthritis with tocilizumab in combination with a non-biological disease modifying anti-rheumatic drug (DMARD). The PBAC considered there was uncertainty associated with the costings for the use of DMARDs in combination with tocilizumab. The PBAC decided not to recommend listing in combination with other DMARDs on the basis of uncertain equivalent efficacy of tocilizumab in combination with non-methotrexate DMARDs and the uncertain costs of non-methotrexate DMARDs in the cost minimisation equation.

In November 2009, the PBAC recommended that tocilizumab be listed as monotherapy for the treatment of severe active rheumatoid arthritis in patients who have failed to demonstrate a response to a TNF-alfa antagonist treatment on a cost-minimisation basis compared to etanercept. With respect to the adverse event profile of tocilizumab, the PBAC remained concerned. At the time, the follow-up in trials was considered too short to adequately assess the long-term toxicity risks. Therefore, the PBAC considered that at that time the place of tocilizumab, both as combination therapy with methotrexate, and as monotherapy, was second line to TNF-alfa antagonists.

3. Registration Status:

Tocilizumab was TGA registered on 21 May 2009 for the treatment of moderate to severe active rheumatoid arthritis in adult patients:

- in combination with methotrexate or other non-biological DMARD in case of either an inadequate response or intolerance to previous therapy with one or more DMARDs; or
- as monotherapy in case of intolerance to methotrexate or where continued treatment with methotrexate is inappropriate.

4. Listing Requested and PBAC's View:

The sponsor requested the same restrictions that apply to the currently listed bDMARDs. The PBAC agreed that this approach was appropriate.

5. Clinical place for the Proposed Therapy:

Rheumatoid arthritis is an inflammatory disorder, typically featuring a combination of peripheral symmetrical inflammatory arthritis and a number of well-described extra-articular symptoms. Tocilizumab would provide another treatment option for adult patients with severe active rheumatoid arthritis.

6. Comparator:

The submission nominated abatacept, infliximab, etanercept and adalimumab as the main comparators. The previous submission nominated abatacept and infliximab as the appropriate comparators and this was agreed by the PBAC.

7. Clinical Trials

For the comparison of efficacy no changes were made to the trial data presented in the July 2009 submission. The basis of the re-submission was an indirect comparison of safety outcomes of four tocilizumab trials (versus three trials in the July 2009 submission), four abatacept studies (versus two trials in the July 2009 submission), three infliximab studies (versus two trials in the July 2009 submission), one randomised controlled trial of abatacept and infliximab plus methotrexate (MTX) therapy (which was identified in the July 2009 submission), four etanercept trials and five adalimumab trials.

All of the trials presented in the re-submission had been published at the time of submission, as follows:

Trial ID / First author	Protocol title / Publication title	Publication citation
Tocilizumab+MTX		
OPTION		
Smolen JS et al (2008)	Effect of interleukin-6 receptor inhibition with tocilizumab in patients with RA (OPTION study): a double-blind, placebo-controlled, randomised trial.	Smolen JS et al, Lancet 2008; 371(9617):987-997
LITHE		
Kremer JM et al (2008)	Tocilizumab inhibits structural joint damage in rheumatoid arthritis patients with an inadequate response to methotrexate: The LITHE study.	Kremer JM et al, American College of Rheumatology 2008 abstract/presentation number L11
TOWARD		
Genovese J et al (2008)	Interleukin-6 receptor inhibition with tocilizumab reduces disease activity in rheumatoid arthritis	Genovese J et al, Arthritis and

Trial ID / First author	Protocol title / Publication title	Publication citation
	with inadequate response to disease-modifying antirheumatic drugs.	Rheumatism 2008; 58 (10): 2968-2980
RADIATE		
Emery P et al (2008)	IL-6 receptor inhibition with tocilizumab improves treatment outcomes in patients with rheumatoid arthritis refractory to anti-tumor necrosis factor biologicals: results from a 24-week multicentre randomised placebo-controlled trial.	Emery P et al, Annals of the Rheumatic Diseases 2008; 67: 1516-1523
Abatacept + MTX		
AIM		
Kremer JM et al (2008)	Results of a two-year follow up study of patients with rheumatoid arthritis who received a combination of abatacept and methotrexate.	Kremer JM et al, Arthritis & Rheumatism 2008; 58(4): 953-963
ATTAIN		
Genovese MC et al 2005)	Abatacept for rheumatoid arthritis refractory to tumor necrosis factor α inhibition.	Genovese MC et al , New England Journal of Medicine 2005; 353 (11): 1114-1123
Genovese MC et al 2008)	Efficacy and safety of the selective co-stimulation modulator abatacept following 2 years of treatment in patients with rheumatoid arthritis and an inadequate response to anti-tumour necrosis factor therapy.	Genovese MC et al , Annals of the Rheumatic Diseases 2008; 67: 547-554
Wells G et al (2008)	Responsiveness of patient reported outcomes including fatigue, sleep quality, activity limitation, and quality of life following treatment with abatacept for rheumatoid arthritis.	Wells G et al, Annals of the Rheumatic Diseases 2008; 67(2): 260-265
Hassett AL et al (2008)	The multi-faceted assessment of independence in patients with rheumatoid arthritis: preliminary validation from the ATTAIN study.	Hassett AL et al, Current Medical Research and Opinion 2008; 24(5): 1443-1453.
Westhovens R et al (2006)	Improved health-related quality of life for rheumatoid arthritis patients treated with abatacept who have inadequate response to anti-TNF therapy in a double-blind, placebo-controlled, multicentre randomized clinical trial.	Westhovens R et al,, Rheumatology 2006; 45 10): 1238-1246
ASSURE		
Weinblatt M et al (2006)	Safety of the selective co stimulation modulator abatacept in rheumatoid arthritis patients receiving background biologic and nonbiologic disease-modifying antirheumatic drugs: A one-year randomized, placebo-controlled study.	Weinblatt M et al, Arthritis and rheumatism 2006; 54 (9): 2807-16
ATTEST		
Schiff M et al (2008)	Efficacy and safety of abatacept or infliximab vs placebo in ATTEST: a phase III, multi-centre, randomised, double-blind, placebo-controlled study in patients with rheumatoid arthritis and an inadequate response to methotrexate.	Schiff M et al, Annals of the rheumatic diseases 2008; 67(8): 1096-103
Infliximab +MTX		
ATTRACT		
Maini R et al (1999)	Infliximab (chimeric anti-tumour necrosis factor alpha monoclonal antibody) versus placebo in	Maini R et al, Lancet 1999; 354 (9194):

	rheumatoid arthritis patients receiving concomitant methotrexate: A randomised phase III trial.	1932-1939
Breedveld FC et al (2004)	Infliximab in active early rheumatoid arthritis.	Breedveld FC et al, Annals of the Rheumatic Diseases 2004; 63(2): 149-155
ASPIRE		
St. Clair EW et al (2004)	Combination of infliximab and methotrexate therapy for early rheumatoid arthritis.	St. Clair EW et al, Arthritis and Rheumatism 2004; 50 (11): 3432-3443
START		
Westhovens R et al (2006)	The safety of infliximab, combined with background treatments, among patients with rheumatoid arthritis and various co morbidities: a large, randomized, placebo-controlled trial.	Westhovens R et al, Arthritis and rheumatism 2006; 54(4): 1075-86
Etanercept +MTX		
Weinblatt ME et al (1999) Bankhurst AD (1999)	A trial of etanercept, a recombinant tumor necrosis factor receptor: Fc fusion protein, in patients with rheumatoid arthritis receiving methotrexate. Etanercept and methotrexate combination therapy.	Weinblatt ME et al, New England Journal of Medicine 1999; 340(4): 253-259. Bankhurst AD, Clinical and Experimental Rheumatology 1999; 17 6, Suppl. 18): 69-72
Combe B et al (2006)	Etanercept and sulfasalazine, alone and combined, in patients with active rheumatoid arthritis despite receiving sulfasalazine: a double-blind comparison.	Combe B et al, Annals of Rheumatic Diseases 2006; 65(10): 1357-1362

TEMPO		
Klareskog L et al (2004)	Therapeutic effect of the combination of etanercept and methotrexate compared with each treatment alone in patients with rheumatoid arthritis: double-blind randomised controlled trial.	Klareskog L et al, Lancet 2004; 363(9410): 675-681
van der Heijde D et al (2006a)	Patient reported outcomes in a trial of combination therapy with etanercept and methotrexate for rheumatoid arthritis: the TEMPO trial.	van der Heijde D et al, Annals of Rheumatic Diseases 2006a; 65(3): 328-334
van der Heijde D et al (2007)	Disease remission and sustained halting of radiographic progression with combination etanercept and methotrexate in patients with rheumatoid arthritis.	van der Heijde D et al, Arthritis and Rheumatism 2007; 56(12): 3928-3939
COMET Study		
Emery P et al (2008)	Comparison of methotrexate monotherapy with a combination of methotrexate and etanercept in active, early, moderate to severe rheumatoid arthritis (COMET): a randomised, double-blind, parallel treatment trial.	Emery P et al, Lancet 2008; 372 (9636): 375-382
Adalimumab +MTX		
Bejarano V et al (2008)	Effect of the early use of the anti-tumor necrosis	Bejarano V et al, Arthritis and

	factor adalimumab on the prevention of job loss in patients with early rheumatoid arthritis.	Rheumatism 2008; 59(10): 1467-1474
ARMADA		
Weinblatt ME et al (2003)	Adalimumab, a fully human anti-tumor necrosis factor alpha monoclonal antibody, for the treatment of rheumatoid arthritis in patients taking concomitant methotrexate: the ARMADA trial.	Weinblatt ME et al, Arthritis and Rheumatism 2003; 48(1): 35-45
STAR Study		
Furst DE et al (2003)	Adalimumab, a fully human anti tumor necrosis factor-alpha monoclonal antibody, and concomitant standard antirheumatic therapy for the treatment of rheumatoid arthritis: results of STAR (Safety Trial of Adalimumab in Rheumatoid Arthritis).	Furst DE et al, Journal of Rheumatology 2003; 30(12): 2563-2571
DE019 Study		
Keystone EC et al (2004)	Radiographic, clinical and functional outcomes of treatment with adalimumab (a human anti-tumor necrosis factor monoclonal antibody) in patients with active rheumatoid arthritis receiving concomitant methotrexate therapy: a randomized, placebo-controlled, 52-week trial.	Keystone EC et al, Arthritis and Rheumatism 2004; 50(5): 1400-1411
PREMIER		
Breedveld FC et al (2006)	The PREMIER Study: A multicenter, randomized, double-blind clinical trial of combination therapy with adalimumab plus methotrexate versus methotrexate alone or adalimumab alone in patients with early, aggressive rheumatoid arthritis who had not had previous methotrexate therapy.	Breedveld FC et al, Arthritis and Rheumatism 2006; 54(1): 26-37

8. Results of trials

The key results are summarised in the table below, and are the same as those submitted in the July 2009 submission, however, with new toxicity data comparing tocilizumab and the currently listed first-line bDMARDs abatacept, infliximab, etanercept and adalimumab.

Results of the indirect comparisons of tocilizumab and abatacept and tocilizumab and infliximab for American College of Rheumatology (ACR) response and Disease Activity Score including 28 joints (DAS28) response at 6 months

Outcome	Tocilizumab versus abatacept RR (95% CI)	Tocilizumab versus infliximab RR (95% CI)
ACR response		
ACR20	1.35 (1.14, 1.61)	1.16 (0.79, 1.69)
ACR50	1.62 (1.19, 2.20)	1.33 (0.75, 2.35)
ACR70	2.31 (1.13, 4.71)	2.48 (1.38, 4.45)
DAS28 response		
DAS remission (DAS28 <2.6)	3.34 (1.70, 6.54)	4.76 (2.19, 10.36)
Low disease activity (DAS28 ≤3.2)	3.54 (2.29, 5.49)	3.60 (1.84, 7.06)

Abbreviation: RR=relative risk

The results of the indirect comparisons showed that tocilizumab has a statistically significant advantage over abatacept for all ACR outcomes and DAS remission and low disease activity. Tocilizumab also demonstrated a statistically significant advantage compared to infliximab in

proportion of patients achieving ACR70 response as well as DAS remission and low disease activity.

The re-submission presented new toxicity data comparing tocilizumab and the currently listed first-line bDMARDs abatacept, infliximab, etanercept and adalimumab. Safety was assessed by the re-submission at six months (by relative risks versus placebo and indirect comparisons), one year (indirect comparisons) and two years (summary of numerical comparisons). Statistically significant results of the pooled comparisons of each drug compared to placebo for all adverse events at six months are summarised below.

Adverse event	**Pooled tocilizumab trials RR(95%CI)**	**Pooled abatacept trials RR(95%CI)**	**Pooled infliximab trials RR(95%CI)**	**Pooled etanercept trials RR(95%CI)**	**Pooled adalimumab trials RR(95%CI)**
Infection	**1.17 (1.05,1.30)**	1.02 (0.82,1.28)	1.13 (0.86,1.49)	0.92 (0.63,1.35)	1.06 (0.91,1.23)
Headache	**1.50 (1.03,2.17)**	1.25 (0.55,2.84)	**1.85 (1.24,2.77)**	1.47 (0.73,2.97)	1.02 (0.63,1.68)
Rash	**2.57 (1.50,4.41)**	NR	**2.18 (1.07,4.41)**	1.98 (0.44,8.98)	**1.67 (1.00,2.78)**
Increased ALT levels	**4.09 (1.69,9.87)**	NR	1.30 (0.58, 2.93)	NR	NR
Hypercholesterol-aemia defined as an adverse event	**25.15 (1.51,418.21)**	NR	NR	NR	NR
Infusion/injection site reactions	**1.55 (1.01,2.36)**	0.88 (0.28,2.82)	1.82 (0.95,3.47)	**6.82 (2.20,21.1)**	**1.76 (1.21,2.54)**
Musculoskeletal and connective tissue disorders	0.76 (0.63,0.93)	NR	NR	0.43 (0.10,1.81)	**3.40 (1.27,9.10)**

Note: Statistically significant differences between the treatment groups are **bolded**
Abbreviations: ALT=alanine aminotransferase; RR=relative risk

The infection rates for tocilizumab and adalimumab at one year were statistically significantly higher than MTX. Issues with increased liver enzymes (ALT levels) and hypercholesterolemia were not recorded for other first-line bDMARDs in the trials identified by the re-submission. The table below presents statistically significant adverse events at one year versus placebo.

Adverse event	**Pooled tocilizumab trials RR (95% CI)**	**Pooled abatacept trials RR (95% CI)**	**Pooled infliximab trials RR (95% CI)**	**Pooled etanercept trials RR (95% CI)**	**Pooled adalimumab trials RR (95% CI)**
Infection	**1.30 (1.11, 1.53)**	1.03 (0.94, 1.13)	Not calculable	1.03 (0.91, 1.18)	**1.25 (1.04, 1.50)**
Headache	2.21 (0.97, 5.02)	**1.40 (1.13, 1.73)**	1.09 (0.70, 1.68)	1.05 (0.67, 1.64)	**1.93 (1.10, 3.38)**
Increased ALT levels	**3.44 (1.40, 8.43)**	Not reported	Not reported	Not reported	Not reported
Musculoskeletal and connective tissue disorders	1.30 (0.91, 1.84)	1.19 (0.73, 1.94)	Not reported	1.18 (0.67, 2.08)	**0.56 (0.36, 0.86)**
Hypertension	1.88 (0.95, 3.73)	**4.05 (1.23, 13.29)**	Not reported	Not reported	Not reported
Infusion/injection site reactions	1.41 (0.76, 2.63)	Not reported	3.13 (0.14, 69.13)	**5.68 (1.99, 16.15)**	1.09 (0.78, 1.52)

Hypercholesterol-aemia based on ATPIIIa Guideline thresholds	**3.21 (2.20, 4.67)**	Not reported	Not reported	Not reported	Not reported
Hyperlipidaemia based on ATPIIIa Guideline thresholds	**4.61 (2.69, 7.90)**	Not reported	Not reported	Not reported	Not reported

Note: Statistically significant differences between the treatment groups are **bolded**
Abbreviations: ALT=alanine aminotransferase; RR=relative risk

The following table presents an indirect comparison of adverse events at six months of special interest of tocilizumab versus all four comparators.

Ratio of relative risks (95% CI) for adverse events of special interest with 8 mg/kg tocilizumab and other bDMARDs at six months and 12 months

Adverse events	Time	8 mg/kg tocilizumab versus abatacept	8 mg/kg tocilizumab versus infliximab	8 mg/kg tocilizumab versus etanercept	8 mg/kg tocilizumab versus adalimumab
All infections and infestations	6 mths 12 mths	1.15 (0.90, 1.47) **1.26 (1.05, 1.52)**	1.04 (0.77, 1.39) Not calculable	1.27 (0.86, 1.89) **1.26 (1.02, 1.55)**	1.11 (0.92, 1.33) 1.04 (0.81, 1.33)
Upper respiratory tract infection	6 mths 12 mths	1.24 (0.68, 2.25) 1.42 (0.76, 2.65)	0.95 (0.42, 2.14) 1.42 (0.82, 2.44)	1.33 (0.63, 2.77) Not calculable	0.94 (0.61, 1.45) 1.18 (0.62, 2.25)
Serious infections	6 mths 12 mths	1.99 (0.58,6.77) 1.22 (0.38,3.90)	1.74 (0.57, 5.31) 2.05 (0.18,23.62)	Not calculable 2.40 (0.73, 7.82)	2.29 (0.58, 9.12) 0.53 (0.06, 4.99)
Neoplasms	6 mths 12 mths	2.26 (0.12,43.46) 3.28 (0.61,17.57)	0.34 (0.02, 4.58) Not calculable	Not calculable 1.50 (0.17, 13.08)	0.55 (0.05, 6.72) 0.34 (0.01, 9.41)
Infusion/injection site reactions	6 mths 12 mths	1.76 (0.51, 6.03) Not calculable	0.85 (0.39, 1.85) 0.45 (0.02,10.59)	**0.23 (0.07, 0.76)** **0.25 (0.07, 0.84)**	0.88 (0.50, 1.55) 1.30 (0.64, 2.64)

Notes: Statistically significant results are shown in **bold**

At both six (6) and 12 month time points, tocilizumab was associated with a higher risk of infection, compared to other first line bDMARDs. This was a statistically significant increased risk as compared to abatacept and etanercept at 12 months. In addition, it was associated with twice the rate of serious infections as compared to infliximab and etanercept. These differences did not reach statistical significance, however these events were rare and hence it was not generally possible to prove statistically significant differences in rare adverse events as studies were powered to detect differences in efficacy between a drug and a comparator and not for differences in adverse events. Tocilizumab had a lower risk of infusion/injection site reactions, compared to infliximab and etanercept.

The two year data presented in the re-submission was not comparable as relative risks could not be calculated.

Extended assessment of safety was presented by the re-submission and the rates and types of adverse events were similar to that presented in the July 2009 submission.

The PBAC noted that the re-submission's analysis of safety data at one year showed that there was a statistically significant increase in infections (but not for serious infections) for both tocilizumab and adalimumab, a significantly higher incidence of headache with abatacept and adalimumab, a significant increase in hypertension with abatacept and a significant increase in injection/infusion site reactions with etanercept, and no significant

difference in the incidence of malignancy for any of the bDMARDs compared with placebo. The PBAC also accepted that adverse events that are significantly higher for tocilizumab, but not any of the other bDMARDs, compared to placebo are events for which there are no reported data for the other bDMARDs: i.e. ALT elevations, hyperlipidaemia and hypercholesterolaemia. The PBAC noted that the Product Information for both infliximab and tocilizumab similarly report the observation of mild or moderate elevations of hepatic transaminases.

Whilst the safety results showed a higher rate of hypercholesterolaemia with tocilizumab treatment compared to placebo, the PBAC agreed that the 95 % confidence intervals around these comparisons were wide. Further, the PBAC acknowledged the evidence suggesting an association between hyperlipidaemia and hypercholesterolaemia and treatment with other bDMARDs has also been reported, including in a systematic review by Choy and Sattar (2009)[1].

9. Clinical Claim

The re-submission claimed tocilizumab was no worse than abatacept and infliximab in terms of efficacy and no worse in terms of safety than all first-line bDMARDs abatacept, infliximab, etanercept and adalimumab in patients with severe, active rheumatoid arthritis over a six-month, one-year and two-year treatment period.

10. Economic Analysis

The submission presented a cost minimisation analysis using abatacept as the comparator. The equi-effective doses were calculated to be tocilizumab 8mg/kg administered on days 1 and 29 and then every 28 days, and abatacept 10mg/kg administered on days 1, 15, 29 and then every 28 days. This was unchanged from the July 2009 submission.

Given the evidence in the literature suggesting that other bDMARDs may have a similar effect on hyperlipidaemia and hypercholesterolaemia as tocilizumab, the PBAC noted that the inclusion of statin costs for a proportion of tocilizumab patients was appropriate, and possibly conservative. Additionally, the PBAC noted the sponsor's advice that standard blood chemistry tests are conducted for all patients with rheumatoid arthritis who are receiving bDMARDs, so there would be no additional costs associated with monitoring ALT levels specific to tocilizumab treatment.

11. Estimated PBS Usage and Financial Implications:

The submission estimated the financial cost per year to the PBS to be less than $10 million per year for Year 1 to Year 5, and estimated the likely patient number to be less than 10,000 per year.

12. Recommendation and Reasons:

The PBAC recommended amending the recommended restriction for the section 100 (Highly Specialised Drugs Program) listing of tocilizumab as a pharmaceutical benefit to allow first line use for the treatment of severe active rheumatoid arthritis whether used as monotherapy or in combination with methotrexate.

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[1] Choy E, Sattar N, *Review Interpreting lipid levels in the context of high-grade inflammatory states with a focus on rheumatoid arthritis: a challenge to conventional cardiovascular risk actions*, Ann Rheum Dis., 2009;68:460-469

The PBAC noted that the re-submission's analysis of safety data at one year show that there was a statistically significant increase in infections (but not for serious infections) for both tocilizumab and adalimumab, a significantly higher incidence of headache with abatacept and adalimumab, a significant increase in hypertension with abatacept and a significant increase in injection/infusion site reactions with etanercept, and no significant difference in the incidence of malignancy for any of the bDMARDs compared with placebo. The PBAC also accepted that adverse events that are significantly higher for tocilizumab, but not any of the other bDMARDs, compared to placebo are events for which there are no reported data for the other bDMARDs: i.e. ALT elevations, hyperlipidaemia and hypercholesterolaemia. The PBAC noted that that the Product Information documents for both infliximab and tocilizumab similarly report the observation of mild or moderate elevations of hepatic transaminases.

Whilst the safety results showed a higher rate of hypercholesterolaemia with tocilizumab treatment compared to placebo, the PBAC agreed that the 95 % confidence intervals around these comparisons were wide. Further, the PBAC acknowledged the evidence suggesting an association between hyperlipidaemia and hypercholesterolaemia and treatment with other bDMARDs has also been reported, including in a systematic review by Choy and Sattar (2009).

Given the evidence in the literature suggesting that other bDMARDs may have a similar effect on hyperlipidaemia and hypercholesterolaemia as tocilizumab, the PBAC noted that the inclusion of statin costs for a proportion of tocilizumab patients was appropriate, and possibly conservative. Additionally, the PBAC noted the sponsor's advice that standard blood chemistry tests are conducted for all patients with rheumatoid arthritis who are receiving bDMARDs, so there would be no additional costs associated with monitoring ALT levels specific to tocilizumab treatment.

The PBAC recommended that the restriction changes for bDMARDs for the treatment of rheumatoid arthritis recommended at the December 2009 PBAC Special Meeting would also apply to tocilizumab's listing. These include revised eligibility criteria and a maximum of five bDMARDs in a lifetime.

Recommendation:
TOCILIZUMAB, solution for I.V. infusion, 80 mg in 4 mL, 200 mg in 10 mL and 400 mg in 20 mL

Restriction:	Section 100 listing (Highly Specialised Drug) Public and Private hospital authority required Complex restriction to be finalised and will be available at www.pbs.gov.au from the date of listing.
Pack size:	1

13. 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.

14. Sponsor's Comment

The sponsor has no further comment.