

6.6 RITUXIMAB, solution for IV infusion, 100 mg in 10 mL, 500 mg in 50 mL, Mabthera[®], Roche Products Pty Ltd.

1 Purpose of Application

- 1.1 Minor submission regarding the review of the effectiveness and cost-effectiveness of rituximab for maintenance therapy of follicular lymphoma in patients who have achieved a partial or complete response to induction treatment in first-line and relapsed treatment settings.

2 Background

- 2.1 The current PBS-listings for rituximab in non-Hodgkin's lymphoma (NHL) were intended for induction therapy only. There is currently no specific PBS listing for rituximab maintenance therapy in NHL - this is an indication for which the sponsor has not previously sought PBS subsidy. Despite this, there is strong evidence that use of rituximab maintenance therapy is widespread in Australian clinical practice.
- 2.2 At its November 2012 meeting, the PBAC considered a DUSC utilisation report of rituximab, and noted:
"that prior to the listing of rituximab for chronic lymphocytic leukaemia [in December 2011], that PBS expenditure for rituximab was approximately \$110 million per year for NHL. According to the DUSC analysis, up to \$23 million per annum may be for use beyond the very specific indications that rituximab has been assessed for cost-effectiveness by the PBAC. The Committee considered that the majority of additional use is likely to be for maintenance treatment of follicular lymphoma as this is a TGA registered indication." (PBAC Minutes, November 2012)
- 2.3 In light of this, and noting that it had not previously considered the cost-effectiveness of rituximab maintenance therapy in NHL, in November 2012 the PBAC requested a review of the efficacy and cost-effectiveness of rituximab for maintenance therapy in lymphoma. As a submission was not received from the sponsor, the review was commissioned by the Department.
- 2.4 The review considered the efficacy and cost-effectiveness of rituximab maintenance therapy in NHL compared with observation, using a cost-utility analysis.
- 2.5 This review report was considered by the PBAC at its March 2014 meeting. In its consideration of the review, the March 2014 PBAC meeting was satisfied that rituximab maintenance provides, for some patients, a significant improvement in efficacy over observation. However, the PBAC concluded that rituximab maintenance therapy in follicular lymphoma (FL) was not cost-effective in this indication at the current price (highly favourable, plausible estimate of ICER in the range of \$70,000-\$80,000/QALY), and that a price reduction would be required to produce an ICER in an acceptable cost effective range.
- 2.6 The minor submission:
- Proposed a rebate to the price of rituximab in maintenance therapy;
 - Proposed a maximum of 8 rituximab infusions per maintenance course;
 - Re-iterated a number of changes to the economic model and discussed the modelled gain in overall survival (OS) and other matters relating to the economic evaluation; and

- Provided restriction wording for rituximab maintenance in FL and to clarify the intent of the existing restriction.

3 Requested listing

- 3.1 The restriction for rituximab maintenance in FL that was proposed in the restriction is outlined below.

Proposed restriction for rituximab maintenance in the public and private hospital settings

Name, Restriction, Manner of administration and form	Max. Amount	No. of Rpts	Proprietary Name and Manufacturer	
Rituximab Injection 100 mg/10 mL injection, 2 x 10 mL vials 500 mg/50 mL injection, 1 x 50 mL vial	800 mg	7	Mabthera®	Roche
Authority Required (streamlined) Maintenance treatment for a maximum of 8 cycles following a partial or complete response to first line induction treatment for CD20 positive, Stage III or IV, follicular, B-cell non-Hodgkin's lymphoma				
Rituximab Injection 100 mg/10 mL injection, 2 x 10 mL vials 500 mg/50 mL injection, 1 x 50 mL vial	800 mg	7	Mabthera®	Roche
Authority Required (streamlined) Maintenance treatment for a maximum of 8 cycles following a partial or complete response to induction treatment for CD20 positive, Stage III or IV, relapsed or refractory follicular B-cell non-Hodgkin's lymphoma				

- 3.2 The extensive use of rituximab outside the intended restriction appears to be occurring under the current Streamlined Authority Required item codes intended for induction therapy. In March 2014, the PBAC recommended that the intent of the current restrictions for rituximab in NHL be clarified for prescribers, and that Medicare Australia administer approval for rituximab in line with the restrictions.
- 3.3 Therefore, the minor submission also proposed revised wording for the existing listings for NHL to clarify that these restrictions are intended for induction treatment only.

Proposed restriction for rituximab induction in the public and private hospital settings

Name, Restriction, Manner of administration and form	Max. Amount	No. of Rpts	Proprietary Name and Manufacturer	
Rituximab Injection 100 mg/10 mL injection, 2 x 10 mL vials 500 mg/50 mL injection, 1 x 50 mL vial	800 mg	7	Mabthera®	Roche
Authority Required (streamlined) Induction treatment of previously untreated, CD20 positive, diffuse large B-cell non-Hodgkin's lymphoma, in combination with chemotherapy Induction treatment of symptomatic patients with previously untreated, CD20 positive, Stage III or IV, follicular, B-cell non-Hodgkin's lymphoma, in combination with chemotherapy				

Rituximab Injection 100 mg/10 mL injection, 2 x 10 mL vials 500 mg/50 mL injection, 1 x 50 mL vial	800 mg	3	Mabthera®	Roche
Authority Required (streamlined) Induction treatment of relapsed or refractory low-grade B-cell non-Hodgkin's lymphoma Induction treatment of relapsed or refractory follicular B-cell non-Hodgkin's lymphoma				

- 3.4 The minor submission proposed a maximum amount of 800mg of rituximab with 7 repeats for maintenance therapy in the 'first-line' (previously untreated) setting. This would align with the approved Product Information. However, the PBAC noted that this would provide fewer doses than the maximum number administered in the PRIMA trial. This trial formed the basis for the PBAC's March 2014 consideration of the comparative efficacy and cost-effectiveness of rituximab maintenance in the first-line setting.
- 3.5 In NHL, rituximab is TGA indicated for the treatment of patients with:
- CD20 positive, previously untreated, Stage III/IV follicular, B-cell non-Hodgkin's lymphoma,
 - CD20 positive, relapsed or refractory low grade or follicular, B-cell non-Hodgkin's lymphoma,
 - CD20 positive, diffuse large B-cell non-Hodgkin's lymphoma, in combination with chemotherapy.
- 3.6 The review report considered the comparative efficacy of rituximab maintenance (compared to observation) in patients who have responded to induction treatment in each of the three above-mentioned conditions. The March 2014 PBAC meeting accepted that rituximab maintenance therapy in FL provides superior comparative effectiveness over observation in both the previously untreated and relapsed/refractory settings. However, for the latter condition, diffuse large B-cell NHL, the March 2014 PBAC concluded that rituximab maintenance is associated with harms, while no benefits accrued in Australian practice where rituximab induction therapy is standard.

4 Clinical place for the proposed therapy

- 4.1 The proposed place of therapy is unchanged from the March 2014 consideration: maintenance therapy following a partial or complete response to induction treatment for CD20 positive, Stage III or IV, follicular B-cell NHL. Listing is requested following a patient's first induction ('previously untreated patients') and following subsequent inductions ('relapsed or refractory patients').

5 Comparator

- 5.1 Observation had previously been accepted by the PBAC as the appropriate comparator and this had remained unchanged in the minor submission.

6 Consideration of the evidence

Sponsor hearing

- 6.1 As a minor submission, there was no hearing for this item.

Consumer comments

- 6.2 The PBAC noted and welcomed the input from individuals (3) and organisations (1) via the Consumer Comments facility on the PBS website. The comments described a range of benefits with rituximab maintenance therapy in FL including that it may help prevent recurrence of the condition and prolong survival, and that consumers cannot afford rituximab unless it is subsidised.
- 6.3 The PBAC noted the advice received from Lymphoma Australia that outlined that the use of rituximab maintenance leads to extended remission periods, eliminated or delayed need for more toxic chemotherapy options, improved quality of life, and longer survival times. The PBAC noted that this advice was supportive of the evidence provided in the submission, but did not resolve the PBAC’s concern about the cost-effectiveness of rituximab maintenance in FL.

Benefits/harms

- 6.4 Information regarding the benefits and harms of rituximab maintenance therapy in patients with FL is reproduced below, unchanged, from the March 2014 PBAC Minutes. The first table relates to patients with previously untreated FL (first-line maintenance) and the second table relates to patients with relapsed/refractory FL (later-line maintenance).

Benefit/harms summary, ‘previously untreated’ (first-line) follicular lymphoma (Salles *et al*/2011 and 2013)

Outcome	N participants	Relative effect (95% CI)	Obs event rate per 100 patients for treatment duration	MR rate per 100 patients for treatment duration	Increment
Benefits					
Progression Free Survival (PFS)					
36 months	1,018	HR: 0.55 (0.44, 0.68)	43.1.	26.7	-16.3
48 months		HR: [REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
73 months		HR: 0.59 (0.48, 0.69)	56.5	39.0	-17.5
Overall survival (OS)					
36 months	1,018	HR: 0.87 (0.51, 1.47)	5.8	5.1	-0.7
48 months		HR: [REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
73 months		HR: 1.02 (0.71, 1.47)	11.3	11.7	0.4
Harms at 36 months follow-up ¹					
All AEs	1,009 ^a	RR: 1.51 (1.31, 1.73)	37	56	18.9
Disc due to AE		RR: 2.41 (1.06, 5.45)	2	4	2.2
Neutropenia		RR: 3.65 (1.37, 9.76)	1	4	2.6
Infections *		RR: 4.46 (1.70, 11.7)	1	4	3.4

* Grade 3/4 ^a Nine patients were withdrawn from the trial before treatment
 AE = adverse event; Obs = observation; MR = rituximab maintenance treatment; disc = discontinuation; RR = relative risk; HR = hazard ratio; CI = confidence interval; **Bold** = statistically significant.

Benefit/harms summary, relapsed or refractory (later-line) follicular lymphoma

Outcome	N participants	Relative effect (95% CI)	Obs event rate per 100 patients for treatment duration	MR rate per 100 patients for treatment duration	Increment
Benefits					
<i>Van Oers et al 2006/2010</i>					
Median follow-up 33.3 months					
PFS					
All	334	HR: 0.40; P < 0.001			
CHOP ind	145	HR: 0.30; P < 0.001			
R-CHOP ind	189	HR: 0.54; P = 0.004			
OS					
All	334	HR: 0.52; P = 0.011	77.1	85.1	7.8
CHOP ind	145	NR			
R-CHOP ind	189	NR			
Median follow-up 6 year					
PFS					
All	334	HR 0.55, p<0.001			
CHOP ind	145	HR 0.37, p<0.001			
R-CHOP ind	189	HR 0.69, p<0.043			
OS					
All	334	HR: 0.70 (0.48, 1.03)	64.7	74.3	9.6
CHOP ind	145	HR: 0.59 (NS)			
R-CHOP ind	189	HR 0.80 (NS)			
<i>Hainsworth et al 2005, median follow up 41 months</i>					
PFS, median (mnths)	90	31.3 vs 7.4, P = .007			
OS, 3yr		NS	68	72	4
Harms					
<i>Van Oers et al 2010</i>					
Disc due to AE	334	NE	0	4	4.2
Neutropenia		RR: 1.90 (0.91, 3.96)	6	11	5.4
Infections *		RR: 4.00 (1.36, 11.7)	2	10	7.2
<i>Hainsworth et al 2005</i>					
Neutropenia *	90	NE	0	2	2.3
Infusion related toxicity		NE	0	5	4.5

* Grade 3/4. ind = induction; AE = adverse event; (R)-CHOP = (rituximab +) cyclophosphamide, doxorubicin, vincristine, and prednisone; OS = overall survival; PFS = progression free survival; Obs = observation; MR = rituximab maintenance treatment; disc = discontinuation; RR = relative risk; HR = hazard ratio; NE = not estimable; CI = confidence interval; **Bold** = statistically significant.

6.5 Based on the PRIMA trial (Salles et al, 2013), for every 100 patients with FL treated with rituximab maintenance therapy following their first induction treatment compared to observation:

- An additional 18 patients would be progression free after 73 months.
- An additional 3 patients would have neutropenia.
- An additional 3 patients would have grade 3 or 4 infections.

Clinical trials, clinical claim and modelled Overall Survival

6.6 The PBAC recalled that in March 2014 it had concluded that rituximab maintenance, compared to observation, resulted in superior efficacy with regard to PFS in patients with FL. However, it had further “noted that rituximab maintenance did not statistically significantly improve overall survival in patients who were previously untreated, or those who were relapsed/refractory at the longer follow-up (6 years).” Despite this, the model resulted in an increase in life years gained in the rituximab arm compared

to the observation arm because the model structure transformed some of the PFS gains into increased OS.

- 6.7 The minor submission presented a systematic review and meta-analysis of rituximab maintenance in FL (*Vidal et al 2011*) to demonstrate that a modelled gain in OS was appropriate in the absence of statistically significant improvement in OS in the pivotal clinical trials. The meta-analysis found a gain in OS across all lines of maintenance with a hazard ratio of 0.76 (95% CI: 0.62, 0.92). OS was not statistically significantly increased in the first-line setting only (HR 0.86, 95% CI: 0.60, 1.25) but was in the relapsed/refractory setting (HR 0.72, 95% CI: 0.57, 0.91).
- 6.8 This meta-analysis had been discussed in the Review Report. Many of the trials presented in *Vidal et al 2011* were excluded from the review report, for reasons such as: patients received maintenance therapy for less than one year; and patients had not received rituximab as induction treatment - rituximab is part of standard induction therapy in Australia. Therefore the PBAC considered that the trials included in the review report were more applicable to estimating OS in the Australian setting than the *Vidal et al* meta-analysis.

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

Economic analysis

- 6.9 The minor submission presented a cost-utility analysis that resulted in an ICER of \$15,000/QALY - \$45,000/QALY. This lower ICER, compared to the base case accepted by the PBAC in March 2014, arose because the minor submission proposed the following changes to the economic model:

- a ■% rebate to the price of rituximab for maintenance treatment in FL "to account for some of the uncertainty regarding the extent of an overall survival benefit associated with maintenance treatment" (Page 2 of minor submission).
- a progressive 10% reduction in the likelihood and the response rate of induction therapy from the second relapse. The decrease in the efficacy of re-inductions was based on analyses of the *Van Oers et al 2010* trial and observational data. The decrease in the rate of re-inductions was based on expert opinion. The PBAC accepted the introduction of a progressive decrease in both the efficacy and rate of re-inductions of 10% as proposed by the sponsor.
- the introduction of a 2% monthly probability of failing salvage treatment and transitioning to palliative care, based on expert advice. The PBAC remained of the view that the review model had already sufficiently accounted for this issue. The PBAC did not accept the probability of failing salvage treatment and transitioning to palliative care as proposed in the minor submission.
- a maximum of 8 rituximab infusions per maintenance course. (i.e. dosing every 3 months) in both the first- and later-line settings. This would align with the current Product Information, which states: "Patients who have responded to induction treatment may receive maintenance therapy with MABTHERA given at 375 mg/m² body surface area once every 3 months until disease progression or for a maximum period of two years." (p 47 of Product Information)

However, rituximab was administered up to a maximum of 12 infusions (once every 2 months) in the PRIMA trial, which was the basis for the PBAC's March

2014 consideration of the comparative effectiveness of rituximab maintenance in the first-line setting. The pre-PBAC response (pg 1) stated that, when evaluating the PRIMA trial data, the ACPM decided that ‘no efficacy and safety data were submitted to establish that the increase in dose results in improved outcomes for patients’ (ACPM Resolution 9530, April 2011).

However, the PBAC noted that that the submission did not provide any evidence relating the 3-monthly dosing regimen to clinical effectiveness in the first-line setting. Therefore the PBAC was not persuaded by the evidence presented by the sponsor and considered the dosing in the PRIMA trial was more relevant. Therefore, the PBAC reiterated its March 2014 conclusion that the economic model should be informed by the dosing schedule used in the trials.

6.10 The PBAC therefore considered a respecified base case for the modelled economic evaluation based on:

- the 10% reduced rate and efficacy of re-induction as proposed in the submission, but no transition from salvage to palliative care.
- a maximum of 12 infusions in the first-line setting (per the PRIMA trial).

PBAC revised base case for rituximab maintenance in the first-line setting only, or in both first and later-lines, with the price of rituximab as proposed in the minor submission (█% rebate)

	Change in Cost	Change in QALY	ICER
Rituximab maintenance in the first-line setting <u>only</u> (i.e. no maintenance for patients who have relapsed)	\$ █	█	\$ █
Rituximab maintenance in the first-line setting and in relapsed/refractory patients (use across the treatment algorithm).	\$ █	█	\$ █

ICER = incremental cost effectiveness ratio; QALY = quality adjusted life year

6.11 The PBAC noted that the aforementioned base case resulted in an ICER of \$45,000/QALY - \$75,000/QALY if rituximab maintenance is used only in the first-line setting, and an ICER of \$45,000/QALY - \$75,000/QALY for use in both the first and later-line settings. The PBAC considered that these were the most plausible estimates of the cost-effectiveness of rituximab in this indication, if it was accepted that the clinical trial results would translate fully into Australian practice.

6.12 The PBAC concluded that even with the proposed price reduction the ICER/QALY was unacceptably high, particularly given the uncertainty around the extent of survival benefit from the trial data. The PBAC considered that an additional price reduction would be required to reduce the financial risk to the Commonwealth. Given the large and ongoing annual expenditure on rituximab for a clinical indication which is not PBS listed (likely to have been around \$20 million per year), the PBAC recommended that this practice should not continue.

6.13 The PBAC noted the price reduction offered for rituximab for maintenance therapy was lower than the price reduction proposed by the sponsor to the PBAC in January 2011 for the treatment of CLL in combination with chemotherapy.

6.14 The PBAC considered these matters in the context of a medicine that has been widely used outside the intended restrictions under the streamlined authority settings, and the consequent large financial outlay that has already been spent on a medicine that is cost-ineffective at the existing price. In the absence of a further price reduction, the PBAC considered that these risks must be addressed through the use

of written Authorities for all of rituximab's PBS listings in NHL and clarification of the intent of these listings.

Drug cost/patient/course

- 6.15 The cost per course of rituximab maintenance, at the price requested by the sponsor, is \$ [REDACTED] in first-line maintenance and \$ [REDACTED] in later-line maintenance. This is based on a maximum of 12 infusions in first-line maintenance and 8 infusions in later-line maintenance over 2 years, using rituximab drug costs only.

Estimated PBS usage & financial implications

- 6.16 In March 2014, the PBAC considered that the extent of rituximab maintenance therapy currently being used under the PBS was difficult to determine, but that the co-administration analysis included in the March 2014 DUSC advice estimated that, as currently listed, expenditure on rituximab maintenance therapy would be \$104 million over the next 5 years (the total expenditure for rituximab induction and maintenance for FL was estimated to be \$226.9 million over 5 years).

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

- 6.17 The PBAC considered, among other matters, that its assessment that the cost-effectiveness of rituximab in NHL would be acceptable if either of the measures below were implemented to contain risks associated with the cost of the drug to the PBS:
- In the absence of a specific listing for rituximab maintenance therapy in FL, all of rituximab's intended listings that relate to the treatment of NHL should be amended to written authority listings; OR
 - listing in both the first- and later-line maintenance settings at a cost-effective price. In this case listing of all of rituximab's indications that relate to the treatment of NHL could be appropriately managed through an Authority Required (Streamlined) listing.

These arrangements were considered to be appropriate to reduce the risk of high total cost given the evidence of extensive use of rituximab outside the current restriction and because the extent of rituximab maintenance therapy currently being used under the PBS was difficult to determine.

7 PBAC Outcome

- 7.1 The PBAC reiterated its previous recommendation to extend the current listing for rituximab to include maintenance therapy following a partial or complete response to induction treatment for CD20 positive, Stage III or IV, follicular B-cell NHL, in the first- and later-line (relapsed/refractory) settings. This was on the basis that it should be made available only under special arrangements under Section 100.

- 7.2 The PBAC recalled the background to the minor submission:

- Rituximab is not specifically listed on the PBS for maintenance treatment in follicular lymphoma. This is an indication for which the sponsor has not previously sought subsidy and for which the PBAC has not previously assessed the cost-effectiveness of rituximab. Despite this, use of rituximab maintenance under the PBS appears to be widespread, and is associated with significant costs, which are likely to be in the order of \$100 million over 5 years.

- Therefore in November 2012 the PBAC requested ‘a review of the efficacy and cost-effectiveness of rituximab for maintenance therapy in lymphoma’. This review report was considered by the PBAC at its March 2014 meeting. While the March 2014 PBAC meeting was satisfied that rituximab maintenance therapy in FL provides superior comparative efficacy over observation, it concluded that rituximab was not cost-effective in this indication at the current price (highly favourable plausible estimate of ICER in the range of \$70,000-\$80,000/QALY).
- 7.3 The PBAC’s views on rituximab’s comparative benefits and harms remained unchanged from those formed in March 2014.
- 7.4 The PBAC remained of the view that a modelled gain in OS may not be appropriate given that the relevant clinical trial evidence did not show a consistent statistically significant improvement in OS and given the lack of evidence that PFS is a reliable surrogate for OS. The PBAC acknowledged that the sponsor had offered a ■■■% rebate to account for some uncertainty regarding the extent of an OS gain.
- 7.5 The PBAC did not accept the sponsor’s proposal to limit the number of rituximab infusions to 8 per maintenance course (3-monthly dosing) in the first-line setting. The PBAC had not seen any evidence relating 3-monthly dosing to clinical effectiveness in this setting. Therefore the PBAC considered that the dosing protocol used in the relevant clinical trial (PRIMA) should be the basis for the maximum number of doses in first-line maintenance in both the economic model and the PBS-listing. Listing was recommended with a maximum amount of 800mg and 11 repeats in first-line maintenance, and 7 repeats in later-line maintenance.
- 7.6 The PBAC accepted one of the submission’s proposed changes to the economic model: to introduce a progressive 10% decrease in the rate and efficacy of subsequent re-inductions. However, the PBAC did not accept the introduction of a probability of failing salvage treatment and transitioning to palliative care, re-iterating it’s view from Mach 2014 that the review model had already sufficiently accounted for this issue. The PBAC specified a base case that it considered to be the most plausible analysis for decision-making.
- 7.7 In view of the extensive use of rituximab outside the intended restrictions, the PBAC noted the consequent large financial outlay that has already been spent on a medicine that is cost ineffective at the existing price. This use appears to be occurring under the current Authority Required (streamlined) restrictions intended for induction treatment in NHL.
- 7.8 Therefore, should rituximab remain unlisted for maintenance therapy then Authority applications for rituximab in NHL should be in writing to prevent leakage into maintenance therapy. The PBAC considered that this change to restriction level, if required, should be accompanied by a letter from the PBAC to affected prescribers outlining the reasons for this change. The PBAC considered that this amendment should occur as soon as practicable.
- 7.9 The PBAC advised that rituximab is not suitable for prescribing by nurse practitioners.
- 7.10 The PBAC recommended that the Safety Net 20 Day Rule should not apply.
- 7.11 The PBAC noted that this submission is not eligible for an Independent Review.

Outcome:

Recommended

8 Recommended listing

8.1 Amend existing and recommended listings as follows:

New listing: maintenance therapy for previously untreated follicular lymphoma:

Name, Restriction, Manner of administration and form	Max. Amt	No. of Rpts
RITUXIMAB		
Injection	800 mg	11
Available brands: Mabthera (rituximab 100 mg/10 mL injection, 2 x 10 mL vials) Mabthera (rituximab 500 mg/50 mL injection, 1 x 50 mL vial)		

Category/Program	Chemotherapy items for Public/Private Hospital Use
Episodicity:	
Severity:	Stage III or IV
Condition:	CD20 positive follicular B-cell Non-Hodgkin's lymphoma]
Indication:	Stage III or IV CD20 positive follicular B-cell Non-Hodgkin's lymphoma
Treatment Phase:	Maintenance therapy
Restriction level:	To be determined: Authority required (STREAMLINED)
Treatment criteria:	Patient must not receive more than 12 doses or 2 years duration of treatment, whichever comes first, under this restriction.
Clinical criteria:	Patient must have demonstrated a partial or complete response to the induction phase of treatment for previously untreated follicular B-cell Non-Hodgkin's lymphoma, received immediately prior to this current Authority application. AND The treatment must be for maintenance therapy
Administrative Advice	<u>NOTE:</u> A patient may only qualify for PBS-subsidised treatment under this restriction once in a lifetime. <u>NOTE:</u> No increase in the maximum number of repeats may be authorised. <u>NOTE:</u> Special pricing arrangements apply

New listing: maintenance therapy for relapsed/refractory follicular disease:

Name, Restriction, Manner of administration and form	Max. Amt	No. of Rpts
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RITUXIMAB

Injection	800 mg	7
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Available brands:

Mabthera

(rituximab 100 mg/10 mL injection, 2 x 10 mL vials)

Mabthera

(rituximab 500 mg/50 mL injection, 1 x 50 mL vial)

Category/Program	Chemotherapy items for Public/Private Hospital Use
Episodicity:	Relapsed or refractory
Severity:	Stage III or IV
Condition:	CD20 positive follicular B-cell Non-Hodgkin's lymphoma
Indication:	Relapsed or refractory Stage III or IV CD20 positive follicular B-cell Non-Hodgkin's lymphoma
Treatment Phase:	Maintenance therapy
Restriction level:	Authority required (STREAMLINED)
Treatment criteria:	Patient must not receive more than 8 cycles or 2 years duration of treatment, whichever comes first, under this restriction.
Clinical criteria:	The treatment must be for maintenance therapy AND Patient must have demonstrated a partial or complete response to re-induction treatment received immediately prior to this current Authority application
Administrative Advice	<u>NOTE:</u> No increase in the maximum number of repeats may be authorised. <u>NOTE:</u> Special pricing arrangements apply

Clarification of existing listings for rituximab induction

Induction for previously untreated diffuse large B-cell disease:

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Name, Restriction, Manner of administration and form	Max. Amt	No. of Rpts
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RITUXIMAB

Injection	800 mg	7
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Available brands:

Mabthera

(rituximab 100 mg/10 mL injection, 2 x 10 mL vials)

Mabthera

(rituximab 500 mg/50 mL injection, 1 x 50 mL vial)

Category/Program	Chemotherapy items for Public/Private Hospital Use
Episodicity:	Previously untreated
Severity:	
Condition:	CD20 positive diffuse large B-cell Non-Hodgkin's lymphoma
Indication:	Previously untreated CD20 positive diffuse large B-cell Non-Hodgkin's lymphoma [
Treatment Phase:	Induction treatment
Restriction level:	To be determined: Authority required (STREAMLINED) OR Authority required - written
Treatment criteria:	Patient must not receive more than 8 doses under this restriction.
Clinical criteria:	The treatment must be in combination with chemotherapy AND The condition must be previously untreated AND The treatment must be for induction treatment purposes only
Administrative Advice	<u>NOTE:</u> A patient may only qualify for PBS-subsidised treatment under this restriction once in a lifetime. <u>NOTE:</u> No increase in the maximum number of repeats may be authorised.

Induction for previously untreated follicular disease:

Name, Restriction, Manner of administration and form	Max. Amt	No. of Rpts
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RITUXIMAB

Injection	800 mg	7
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Available brands:

Mabthera

(rituximab 100 mg/10 mL injection, 2 x 10 mL vials)

Mabthera

(rituximab 500 mg/50 mL injection, 1 x 50 mL vial)

Category/Program	Chemotherapy items for Public/Private Hospital Use
Episodicity:	Previously untreated
Severity:	Stage III or IV
Condition:	CD20 positive follicular B-cell Non-Hodgkin's lymphoma
Indication:	Previously untreated Stage III or IV CD20 positive follicular B-cell Non-Hodgkin's lymphoma
Treatment Phase:	Induction treatment
Restriction level:	To be determined: Authority required (STREAMLINED) OR Authority required - written
Treatment criteria:	Patient must not receive more than 8 doses under this restriction.
Clinical criteria:	The treatment must be in combination with chemotherapy AND The condition must be previously untreated AND The condition must be symptomatic AND The treatment must be for induction treatment purposes only
Administrative Advice	<u>NOTE:</u> A patient may only qualify for PBS-subsidised treatment under this restriction once in a lifetime. <u>NOTE:</u> No increase in the maximum number of repeats may be authorised.

Induction and re-induction for relapsed/refractory low grade disease:

Name, Restriction, Manner of administration and form	Max. Amt	No. of Rpts
RITUXIMAB		
Injection	800 mg	3
Available brands: Mabthera (rituximab 100 mg/10 mL injection, 2 x 10 mL vials) Mabthera (rituximab 500 mg/50 mL injection, 1 x 50 mL vial)		

Injection	800 mg	3
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Available brands:
Mabthera
(rituximab 100 mg/10 mL injection, 2 x 10 mL vials)
Mabthera
(rituximab 500 mg/50 mL injection, 1 x 50 mL vial)

Category/Program	Chemotherapy items for Public/Private Hospital Use
Episodicity:	Relapsed or refractory
Condition:	Low-grade B-cell Non-Hodgkin's lymphoma
Indication:	Relapsed or refractory low-grade B-cell Non-Hodgkin's lymphoma
Treatment Phase:	Re-induction treatment
Restriction level:	To be determined: Authority required (STREAMLINED) OR Authority required - written
Treatment criteria:	Patient must not receive more than 4 doses under this restriction.
Clinical criteria:	The treatment must be for re-induction treatment purposes only AND The condition must have relapsed or be refractory to treatment
Administrative Advice	<u>NOTE:</u> No increase in the maximum number of repeats may be authorised.

9 Context for Decision

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

10 Sponsor's Comment

The sponsor acknowledges the positive recommendation by the PBAC, however maintains that rituximab use in the maintenance setting is cost-effective at the proposed price. Subsequent to the PBAC meeting, the sponsor offered a further price reduction in light of the additional financial cost to the Government should PBS listing occur.