

14.2 RITUXIMAB injection for infusion, 100mg/10mL, 2 x 10 mL vials, Mabthera®, Roche Products Pty Ltd.

1 Purpose of Application

- 1.1 To seek a PBAC recommendation to add the 100 mg/10 mL injection presentation of rituximab to the July 2015 recommendation to list the 500 mg/50 mL injection for severe active granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA). The 100mg vial was omitted from the sponsor's submission.

2 Background

- 2.1 At the March 2015 meeting, the PBAC considered a submission requesting listing for rituximab 500 mg/50 mL for the treatment of patients with GPA and MPA.
- 2.2 The PBAC deferred its consideration of rituximab for the treatment of cyclophosphamide contraindicated or resistant severe active GPA and MPA because it could not determine whether rituximab was cost-effective at the price proposed. Given that no further data is likely to become available to inform this consideration, the PBAC deferred the submission to enable the Department to negotiate an appropriate price.
- 2.3 Subsequent to the March 2015 meeting, the sponsor provided the PBAC with additional information including a revised price offer (██████% rebate on the ex-manufacturer price of the 500 mg vial, as per the listing for ██████████) and revised financial estimates.
- 2.4 At the July 2015 meeting, the PBAC recommended listing rituximab 500 mg/50 mL injection, on the basis that it should be available only under special arrangements under the Section 100 Highly Specialised Drugs Program, for remission induction in patients with severe, active GPA and MPA.

3 Consideration of the evidence

- 3.1 Subsequent to this decision, the Department identified that the sponsor had assumed a proportion of use as weight based dosing in its financial estimates. The average dose for this is 800mg per treatment and the sponsor had used a combination of 500mg and 100mg vials to achieve this in their model. The sponsor applied the ████████% rebate to both the 500 mg and 100 mg vials in its financial estimates.
- 3.2 If only the 500 mg vial were listed for this indication, there may be issues of wastage for a small number of patients who are dosed on the basis of weight.

4 PBAC Outcome

- 4.1 The PBAC recommended listing rituximab 100 mg/10 mL injection on the basis that it should be available only under special arrangements under the Section 100 Highly Specialised Drugs Program, for remission induction in patients with severe, active GPA and MPA.
- 4.2 The PBAC requested that the Department include this listing in the Risk Share Arrangement for the 500 mg/50 mL injection.
- 4.3 The PBAC advised that rituximab is not suitable for prescribing by nurse practitioners.
- 4.4 The PBAC recommended that the Safety Net 20 Day Rule should not apply.

Outcome:

Recommended

5 Recommended listing

- 5.1 Amend recommended listing.

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Name and Manufacturer	
RITUXIMAB			Mabthera®	RO
500 mg/50 mL injection, 1 x 50 mL vial	1	0		
100 mg/10 mL injection, 2 x 10mL vial	1	0		
Category / Program	Section 100 – Highly Specialised Drugs Program			
Prescriber type:	<input checked="" type="checkbox"/> Medical Practitioners			

PBS Indication:	Severe active granulomatosis with polyangiitis
Treatment phase:	Induction of remission
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
Clinical criteria:	<ul style="list-style-type: none"> • The treatment must be for the induction of remission, <p>AND</p> <ul style="list-style-type: none"> • Patient must not have previously received this drug for this condition, OR • Patient must have received this drug for this condition prior to 1 January 2016 <p>AND</p> <ul style="list-style-type: none"> • The treatment must in combination with glucocorticoids, <p>AND</p> <ul style="list-style-type: none"> • Patient must be at risk of end-organ damage or mortality, <p>AND</p> <ul style="list-style-type: none"> • Patient must be contraindicated, refractory or unable to tolerate

	cyclophosphamide.
Prescriber Instructions	Diagnosis should be made according to the Chapel Hill Consensus Conference Nomenclature of the Vasculitides with anti-neutrophil cytoplasmic antibody (ANCA) positive serology. This drug is not PBS-subsidised for maintenance of remission.
Administrative Advice	<p>Risk of end-organ damage or mortality includes a minimum of one of the following:</p> <ul style="list-style-type: none"> • Glomerulonephritis with risk of progression • Risk to sight including scleritis/episcleritis, sudden visual loss, uveitis, retinal changes (vasculitis/thrombosis/exudates/haemorrhage) • Bronchial/subglottic obstruction • Pulmonary haemorrhage • Parenchymal lung disease • Sensory neural hearing loss • Recurrent sinonasal disease requiring recurrent surgical interventions • Meningitis, organic confusion, seizures, stroke, cord lesion, cranial nerve palsy, sensory peripheral neuropathy, motor mononeuritis multiplex <p>Patients could be considered contraindicated, refractory or unable to tolerate cyclophosphamide for one of the following reasons:</p> <ul style="list-style-type: none"> • Cyclophosphamide is contraindicated as per the TGA approved Product Information; • Cyclophosphamide is not recommended due to the need to preserve gonad function; • Patient experiences severe toxicity to cyclophosphamide that warrants cessation of treatment; • Patient has life- or organ-threatening deterioration at any time during treatment with cyclophosphamide, where the deterioration is thought to be due to severe uncontrolled active vasculitis; • Commencing a further treatment cycle with cyclophosphamide would exceed the maximum cumulative dose of cyclophosphamide of 25g; or • Patient's condition with this indication is persistent despite at least 3 months therapy with cyclophosphamide. <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:</p> <p>Department of Human Services Prior Written Approval of Complex Drugs Reply Paid 9826 HOBART TAS 7001</p> <p>At the time of authority application, medical practitioners must request the appropriate number of vials to provide sufficient drug for four weeks of treatment.</p>

PBS Indication:	Severe active granulomatosis with polyangiitis
Treatment phase:	Re-induction of remission
Restriction Level /	<input type="checkbox"/> Restricted benefit

Method:	<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
Clinical criteria:	<ul style="list-style-type: none"> • The treatment must be for the re-induction of remission, <p>AND</p> <ul style="list-style-type: none"> • Patient must have previously received and responded to this drug for this condition, <p>AND</p> <ul style="list-style-type: none"> • The treatment must in combination with glucocorticoids, <p>AND</p> <ul style="list-style-type: none"> • Patient must be at risk of end-organ damage or mortality, <p>AND</p> <ul style="list-style-type: none"> • Patient must be contraindicated, refractory or unable to tolerate cyclophosphamide.
Prescriber Instructions	<p>Diagnosis should be made according to the Chapel Hill Consensus Conference Nomenclature of the Vasculitides with anti-neutrophil cytoplasmic antibody (ANCA) positive serology.</p> <p>This drug is not PBS-subsidised for maintenance of remission.</p>
Administrative Advice	<p>Risk of end-organ damage or mortality includes a minimum of one of the following:</p> <ul style="list-style-type: none"> • Glomerulonephritis with risk of progression • Risk to sight including scleritis/episcleritis, sudden visual loss, uveitis, retinal changes (vasculitis/thrombosis/exudates/haemorrhage) • Bronchial/subglottic obstruction • Pulmonary haemorrhage • Parenchymal lung disease • Sensory neural hearing loss • Recurrent sinonasal disease requiring recurrent surgical interventions • Meningitis, organic confusion, seizures, stroke, cord lesion, cranial nerve palsy, sensory peripheral neuropathy, motor mononeuritis multiplex <p>Patients could be considered contraindicated, refractory or unable to tolerate cyclophosphamide for one of the following reasons:</p> <ul style="list-style-type: none"> • Cyclophosphamide is contraindicated as per the TGA approved Product Information; • Cyclophosphamide is not recommended due to the need to preserve gonad function; • Patient experiences severe toxicity to cyclophosphamide that warrants cessation of treatment; • Patient has life- or organ-threatening deterioration at any time during treatment with cyclophosphamide, where the deterioration is thought to be due to severe uncontrolled active vasculitis; • Commencing a further treatment cycle with cyclophosphamide would exceed the maximum cumulative dose of cyclophosphamide of 25g; or • Patient's condition with this indication is persistent despite at least 3 months therapy with cyclophosphamide. <p>Any queries concerning the arrangements to prescribe may be directed to the Department of</p>

	<p>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 HOBART TAS 7001</p> <p>At the time of authority application, medical practitioners must request the appropriate number of vials to provide sufficient drug for four weeks of treatment.</p>
--	--

PBS Indication:	Severe active microscopic polyangiitis
Treatment phase:	Induction of remission
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
Clinical criteria:	<ul style="list-style-type: none"> • The treatment must be for the induction of remission, <p>AND</p> <ul style="list-style-type: none"> • Patient must not have previously received this drug for this condition, OR • Patient must have received this drug for this condition prior to 1 January 2016, <p>AND</p> <ul style="list-style-type: none"> • The treatment must in combination with glucocorticoids, <p>AND</p> <ul style="list-style-type: none"> • Patient must be at risk of end-organ damage or mortality, <p>AND</p> <ul style="list-style-type: none"> • Patient must be contraindicated, refractory or unable to tolerate cyclophosphamide.
Prescriber Instructions	<p>Diagnosis should be made according to the Chapel Hill Consensus Conference Nomenclature of the Vasculitides with anti-neutrophil cytoplasmic antibody (ANCA) positive serology.</p> <p>This drug is not PBS-subsidised for maintenance therapy.</p>
Administrative Advice	<p>Risk of end-organ damage or mortality includes a minimum of one of the following:</p> <ul style="list-style-type: none"> • Glomerulonephritis with risk of progression • Risk to sight including scleritis/episcleritis, sudden visual loss, uveitis, retinal changes (vasculitis/thrombosis/exudates/haemorrhage) • Bronchial/subglottic obstruction • Pulmonary haemorrhage • Parenchymal lung disease • Sensory neural hearing loss • Recurrent sinonasal disease requiring recurrent surgical interventions • Meningitis, organic confusion, seizures, stroke, cord lesion, cranial nerve palsy,

	<p>sensory peripheral neuropathy, motor mononeuritis multiplex</p> <p>Patients could be considered contraindicated, refractory or unable to tolerate cyclophosphamide for one of the following reasons:</p> <ul style="list-style-type: none"> • Cyclophosphamide is contraindicated as per the TGA approved Product Information; • Cyclophosphamide is not recommended due to the need to preserve gonad function; • Patient experiences severe toxicity to cyclophosphamide that warrants cessation of treatment; • Patient has life- or organ-threatening deterioration at any time during treatment with cyclophosphamide, where the deterioration is thought to be due to severe uncontrolled active vasculitis; • Commencing a further treatment cycle with cyclophosphamide would exceed the maximum cumulative dose of cyclophosphamide of 25g; or • Patient’s condition with this indication is persistent despite at least 3 months therapy with cyclophosphamide. <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:</p> <p>Department of Human Services Prior Written Approval of Complex Drugs Reply Paid 9826 HOBART TAS 7001</p> <p>At the time of authority application, medical practitioners must request the appropriate number of vials to provide sufficient drug for four weeks of treatment.</p>
--	---

PBS Indication:	Severe active granulomatosis with polyangiitis
Treatment phase:	Re-induction of remission
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
Clinical criteria:	<ul style="list-style-type: none"> • The treatment must be for the re-induction of remission, <p>AND</p> <ul style="list-style-type: none"> • Patient must have previously received and responded to this drug for this condition, <p>AND</p> <ul style="list-style-type: none"> • The treatment must in combination with glucocorticoids, <p>AND</p> <ul style="list-style-type: none"> • Patient must be at risk of end-organ damage or mortality, <p>AND</p> <ul style="list-style-type: none"> • Patient must be contraindicated, refractory or unable to tolerate

	cyclophosphamide.
Prescriber Instructions	<p>Diagnosis should be made according to the Chapel Hill Consensus Conference Nomenclature of the Vasculitides with anti-neutrophil cytoplasmic antibody (ANCA) positive serology.</p> <p>This drug is not PBS-subsidised for maintenance therapy.</p>
Administrative Advice	<p>Risk of end-organ damage or mortality includes a minimum of one of the following:</p> <ul style="list-style-type: none"> • Glomerulonephritis with risk of progression • Risk to sight including scleritis/episcleritis, sudden visual loss, uveitis, retinal changes (vasculitis/thrombosis/exudates/haemorrhage) • Bronchial/subglottic obstruction • Pulmonary haemorrhage • Parenchymal lung disease • Sensory neural hearing loss • Recurrent sinonasal disease requiring recurrent surgical interventions • Meningitis, organic confusion, seizures, stroke, cord lesion, cranial nerve palsy, sensory peripheral neuropathy, motor mononeuritis multiplex <p>Patients could be considered contraindicated, refractory or unable to tolerate cyclophosphamide for one of the following reasons:</p> <ul style="list-style-type: none"> • Cyclophosphamide is contraindicated as per the TGA approved Product Information; • Cyclophosphamide is not recommended due to the need to preserve gonad function; • Patient experiences severe toxicity to cyclophosphamide that warrants cessation of treatment; • Patient has life- or organ-threatening deterioration at any time during treatment with cyclophosphamide, where the deterioration is thought to be due to severe uncontrolled active vasculitis; • Commencing a further treatment cycle with cyclophosphamide would exceed the maximum cumulative dose of cyclophosphamide of 25g; or • Patient's condition with this indication is persistent despite at least 3 months therapy with cyclophosphamide. <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:</p> <p>Department of Human Services Prior Written Approval of Complex Drugs Reply Paid 9826 HOBART TAS 7001</p> <p>At the time of authority application, medical practitioners must request the appropriate number of vials to provide sufficient drug for four weeks of treatment.</p>

6 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.

7 Sponsor's Comment

Roche agrees with the PBAC's decision to add the rituximab 100 mg/10 mL injection to the PBS listing for patients with severe, active GPA/MPA.