

5.19 RITUXIMAB

Solution for I.V. infusion 100 mg in 10 mL, 2 vials

Solution for I.V. infusion 500 mg in 50 mL, 1 vial

Riximyo[®], Sandoz Pty Ltd

1 Purpose of Application

- 1.1 The minor submission sought listing for a new biosimilar brand of rituximab (Riximyo[®]) for all indications for which the rituximab IV infusion reference brand (MabThera[®]) is currently PBS listed, on the Section 100 Efficient Funding of Chemotherapy (EFC) and Highly Specialised Drug (HSD) programs.

2 Requested listing

- 2.1 The submission requested listing for the 100 mg per 10 mL and 500 mg per 50 mL injection vial forms of Riximyo[®] for the following indications for which the reference brand MabThera[®] is currently PBS listed:
- Non-Hodgkin's lymphoma (NHL) – S100 EFC
 - Chronic lymphocytic leukaemia (CLL) – S100 EFC
 - Rheumatoid arthritis (RA) – S100 HSD
 - Granulomatosis with polyangiitis (Wegener's granulomatosis) (GPA) – S100 HSD
 - Microscopic polyangiitis (MPA) – S100 HSD
- 2.2 The submission did not request listing for a subcutaneous formulation of rituximab.
- 2.3 The submission requested Riximyo be 'a' flagged with MabThera.
- 2.4 The submission requested that Authority required (STREAMLINED) be applied to the treatment phases specified in the table below for RA, GPA and MPA indications. All other restrictions for these indications are to remain the same as MabThera.

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Table 1. Indications and the corresponding treatment phase whereby a lower level of authority is requested

Indication	Schedule	Restriction	Treatment phase
Severe active rheumatoid arthritis	S100 HSD Public	Authority required (STREAMLINED)	Continuing treatment
Severe active rheumatoid arthritis	S100 HSD Private	Authority required (STREAMLINED)	Continuing treatment
Severe active granulomatosis with polyangiitis (Wegeners granulomatosis)	S100 HSD Public	Authority required (STREAMLINED)	Re-induction of remission
Severe active microscopic polyangiitis			
Severe active granulomatosis with polyangiitis (Wegeners granulomatosis)	S100 HSD Private	Authority required (STREAMLINED)	Re-induction of remission
Severe active microscopic polyangiitis			

Source: Minor submission, pg.7

- 2.5 The submission proposed not to split the continuing phase, as the time to retreatment in RA, GPA and MPA is variable; the first continuing treatment or first re-induction of remission could take 6 to 12 months for RA patients and up to 18 months for GPA and MPA patients after initial treatment.
- 2.6 The submission suggested that since the RA, GPA and MPA indications constitute approximately 10% of the total rituximab market and that all the oncology indications for rituximab are already streamlined, the impact of leakage from reducing the level of authority for the continuing treatment and re-induction of remission treatment phases for the RA, GPA and MPA indications would be minimal.
- 2.7 The submission did not provide proposed revised restrictions to support the request for a lower level of authority for RA, GPA & MPA.

3 Background

- 3.1 The Riximyo brand of rituximab was TGA registered on 30 November 2017 for both the 100 mg/10 mL and 500 mg/50 mL forms.
- 3.2 The PBAC has not previously considered an application for this brand of rituximab.

Brand equivalence and substitution at the pharmacist level ('a' flagging)

- 3.3 The Schedule of Pharmaceutical Benefits provide the following definition of brand equivalence:

Extract from the Explanatory Notes to the PBS Schedule¹

BRAND EQUIVALENCE

'a' located immediately before brand names of a particular strength of an item indicates that the sponsors of these brands have submitted evidence that they have been demonstrated to be bioequivalent or therapeutically equivalent, or that justification for not needing bioequivalence or therapeutic equivalence data has been provided to and accepted by the Therapeutic Goods Administration. It would thus be expected that these brands may be interchanged without differences in clinical effect.

- 3.4 Many medicines are available on the PBS in different brands. The Schedule of Pharmaceutical Benefits indicates where different brands are considered equivalent for the purposes of substitution at the point of dispensing by using 'a' flags.
- 3.5 The ability for prescribers and pharmacists to substitute generic or biosimilar brands for originator brands is an important part of encouraging use of generics and biosimilars in the marketplace and adds to the sustainability of the PBS.
- 3.6 For any individual prescription, a prescriber may choose to not permit brand substitution by indicating 'substitution not permitted' on the prescription. Likewise, when substitution is permitted, a patient may nominate which 'a' flagged brand they wish to receive from the pharmacist, except when State or Territory Law prohibits substitution (e.g. for Schedule 8 drugs of dependence). The substitution process allows for patient and prescriber choice and is not automatic.
- 3.7 The National Health Act 1953 ("The Act") makes it an offence for a pharmacist to supply a pharmaceutical benefit other than the benefit directed to be supplied in a prescription except when, amongst other criteria, the Schedule issued by the Department of Health states that the specified benefit and the substitute benefit are equivalent.
- 3.8 At the March 2018 meeting, the PBAC advised that the following revised considerations will be used to make a recommendation on brand equivalence ('a' flagged) of biosimilars with the reference brand;
- The Therapeutic Goods Administration has determined that the product is a biosimilar of the reference medicine as evidenced by ARTG registration documentation;
 - Availability of supportive data relating to the effects of switching between the reference product and the biosimilar product/s; and
 - Practical considerations relating to substitution by the pharmacist at the point of dispensing. This includes strength of formulation, number of units

¹ Symbols used in the Schedule - <http://www.pbs.gov.au/info/healthpro/explanatory-notes/section2/section-2-symbols>

per pack and maximum quantities between the brands, which may make substitution at the pharmacy level difficult from a practical perspective.

- 3.9 The PBAC considered that where a biosimilar product could not be recommended to be brand equivalent ('a' flagged) at the time of PBS listing, data should be collected to support this consideration at a later point.
- 3.10 If the PBAC provides advice on brand equivalence ('a' flagging), the decision to apply brand equivalence to listings in the Schedule is made by the Minister for Health (or Delegate).

Biosimilar uptake measures

- 3.11 The biosimilar uptake measures were agreed as part of the strategic agreements that the Government reached with Medicines Australia, the Generic and Biosimilar Medicines Association and the Pharmacy Guild of Australia as part of the 2017 Budget process.
- 3.12 The PBAC will advise whether implementation of the uptake drivers is likely to raise any clinical or other concerns about appropriate use on the PBS. The PBAC may, on a case-by-case basis, provide advice relating to:
- encouraging the prescribing of a biosimilar brand for treatment naïve patients; and
 - applying a lower level of authority to biosimilar brand(s) than exists for the reference brand of biological medicines.
- 3.13 After PBAC advice is received, a decision will be made about applying the drivers for the relevant medicine. The policy provides for lower authority requirements only for biosimilar brands, but there will be no increase in authority requirements to prescribe reference brands.
- 3.14 The PBAC has previously stated it had no concerns about encouraging prescribing of a biosimilar brand rather than the reference biological agent brand for treatment naïve patients, including through notes in the Schedule and prescribing software changes. (Etanercept (Brenzys) Public Summary Document, August 2017 PBAC Meeting).

For more detail on PBAC's view, see section 6 PBAC outcome.

4 Comparator

- 4.1 The minor submission nominated the reference brand of rituximab (MabThera) as the comparator.

5 Consideration of the evidence

Sponsor hearing

5.1 There was no hearing for this item as it was a minor submission.

Consumer comments

5.2 The PBAC noted and welcomed the input from organisations (2) via the Consumer Comments facility on the PBS website. Lymphoma Australia provided comments seeking reassurance that the introduction of a biosimilar rituximab will not change outcomes for patients with this type of cancer, patients will be informed of the brand they are being prescribed as well as tracking of brands used and side effects a patient may encounter from use of a particular brand.

5.3 The PBAC noted the queries received from Lymphoma Australia and considered that the Australian Government Biosimilar Awareness Initiative be requested to support the PBS listing of the first monoclonal biosimilar in the oncology setting via the development of a fact sheet aimed at consumers and health care professionals.

Clinical trials

5.4 The minor submission outlined the studies required by the TGA in determining comparability between the biosimilar and reference brands of rituximab. There were four key clinical studies, of which the submission presented two pivotal studies that demonstrated clinical comparability between Riximyo and the MabThera; GP13-201 in rheumatoid arthritis, and GP13-301 in advanced stage follicular lymphoma.

Table 2: Trials and associated reports presented in the re-submission

Trial ID/First Author	Protocol title/ Publication title	Publication citation
Direct randomised trial(s)		
GP13-201 Study Part I	A Randomized, Double-blind, Controlled Study to Evaluate PK, PD, Safety and Efficacy of GP2013 and Rituximab in Patients With Rheumatoid Arthritis Refractory or Intolerant to Standard DMARDs and up to Three Anti-TNF Therapies	Ann Rheum Dis. 2017 Sep;76(9):1598-1602. doi: 10.1136/annrheumdis-2017-211281. Epub 2017 Jun 21.
GP13-301	A Randomized, Controlled, Double-Blind Phase III Trial to Compare the Efficacy, Safety and Pharmacokinetics of GP2013 vs. MabThera® in Patients With Previously Untreated, Advanced Stage Follicular Lymphoma	Lancet Haematol. 2017 Aug;4(8):e350-e361. doi: 10.1016/S2352-3026(17)30106-0. Epub 2017 Jul 14.

Source: Minor submission, pg.2-3

5.5 The minor submission did not present the results of the study in a summarised form; however summaries of clinical efficacy and clinical safety were provided as attachments to the submission.

Comparative effectiveness

The PBAC noted that in October 2017, the ACM advised that therapeutic equivalence was demonstrated in the GP13-301 study, based on the primary endpoint of comparative objective response rates (ORR) [ACM Minutes]. The secondary endpoint of Progression Free Survival (PFS) did not show close similarity across arms [pg.4], which may suggest potential inferiority for rituximab compared to the reference product, however the ACM noted the outcomes were “entirely too immature to contribute to comparison of therapeutic efficacy” in the treatment of a typically indolent lymphoma.

- 5.6 Efficacy was also assessed in GP13-201 Parts I and II in RA patients. ACM considered the studies showed non-inferiority of the biosimilar against the reference brand to 52 weeks [ACM Minutes, pg.4].

Comparative harms

- 5.7 The TGA Delegate and ACM considered the comparative safety of the Riximyo brand of rituximab against the originator brand as part of its application for Australian Registration.
- 5.8 Safety was assessed across all four studies. The ACM noted that the clinical evaluator concluded that there were no clinically meaningful differences in safety between Riximyo and Mabthera. [ACM Minutes]
- 5.9 Immunogenicity was assessed across studies. Neutralising antibodies were infrequent across studies (16.5% vs. 15.1% in the Riximyo and MabThera groups, respectively), and the majority of these were transient (i.e. Anti-drug antibodies were not detected in subsequent samples). Five patients in the Riximyo group and one in the MabThera group developed neutralising Anti-drug antibodies (ADAs), however neutralising antibodies were not associated with decreased efficacy or increased toxicity.
- 5.10 The ACM concluded that there were no clinically meaningful differences in safety between Riximyo and MabThera.
- 5.11 The PBAC noted the switching study (GP13-302), in 107 RA patients, tested safety and immunogenicity up to 24 weeks after either switching from the reference brand to Riximyo, or continuing on the reference brand. At 12 weeks, no major safety issues were identified, however there was one report of serum sickness in a patient switched to Riximyo.[TGA Delegate Overview, pg.20]

Clinical claim

- 5.12 The submission described Riximyo as a biosimilar rituximab, and equivalent in terms of comparative efficacy and comparative safety against the reference brand, MabThera.

- 5.13 The PBAC noted the ACM had declared the Riximyo brand of rituximab to be a biosimilar of the reference brand, MabThera, and considered the claim of non-inferior comparative efficacy in FL and in RA, safety and immunogenicity was therefore adequately supported.

Financial implications

- 5.14 As it would be the first biosimilar brand of rituximab to be listed on the PBS it would trigger a 16% statutory price reduction to the reference brand MabThera and Riximyo would be listed at this lower price. As a result of the 16% SPR, the minor submission estimated a net save to the PBS of \$10 - \$20 million in Year 5 of listing with a total net save to the PBS of \$60 - \$100 million over the first 5 years of listing.
- 5.15 The submission also assumed a decline in script numbers for rituximab of 5% per year. PBS script data indicates a decline of approximately 5% in 2016 and 2017, however this was preceded by growth of approximately 5% in the two years prior, and so it is unclear whether this trend will continue.

For more detail on PBAC's view, see section 6 PBAC outcome.

6 PBAC Outcome

- 6.1 The PBAC recommended the listing of rituximab (Riximyo) for the same indications as the IV infusion reference brand of rituximab, under the S100 Efficient Funding of Chemotherapy and Highly Specialised Drug programs. In making this recommendation, the PBAC noted the TGA Advisory Committee for Medicines (ACM) has declared Riximyo to be a biosimilar of the reference brand, MabThera.
- 6.2 The PBAC advised, under Section 101 (4AACD) of the National Health Act, that rituximab (Riximyo) and rituximab (MabThera IV) should be considered equivalent for the purposes of substitution (i.e., 'a' flagged in the Schedule) at the pharmacy level.
- 6.3 The PBAC noted that although brand substitution at the pharmacy level has been recommended, the uptake of this biosimilar brand of rituximab will largely be driven by which brand of rituximab hospitals choose to keep in stock via tendering and formulary arrangements.
- 6.4 The PBAC advised that there are no clinical or other concerns about appropriate use of medicines, if the policy decision were made to apply the biosimilar uptake measures agreed as part of the strategic agreement with Medicines Australia to rituximab, provided the recommendations below are followed.
- The PBAC deemed it reasonable to lower the authority level of the GPA/MPA and RA indications from a written authority to Authority Required (STREAMLINED) at the re-induction phase for GPA/MPA and at the subsequent continuing phase for RA.
 - The PBAC advised the continuing phase for treatment of RA should be split into

first continuing and subsequent continuing phases, with the first continuing restriction remaining as a written authority and the lower authority level uptake driver applied to the subsequent continuing restriction, changing it to an Authority Required (STREAMLINED) restriction. This would align with the etanercept RA indication.

- The PBAC were comfortable that lowering the level of authority to streamlined at the re-induction phase for the GPA/MPA indications would be clinically appropriate and would be unlikely to lead to leakage outside of the restriction. The recommended maximum quantities for the streamlined listing were based on a dosing regimen of 375 mg/m² once a week for 4 weeks via intravenous infusion and a body surface area of 2.02m² (assuming an average patient weight of 85.9kg and height at 175.6cm).
- The PBAC advised against lowering the benefit level of the oncology indications from a Streamlined Authority to a Restricted Benefit, as it expected that this would have minimal effect on prescribing behaviours and may inadvertently lead to an increase in prescribing beyond the current restrictions.
- A note encouraging prescribing of the biosimilar brand to treatment naïve patients, would be appropriate for all indications

- 6.5 The PBAC recommended the addition of the following note to all MabThera PBS items: “Prescribing of the biosimilar brand, Riximyo, is encouraged for treatment naïve patients. Encouraging biosimilar prescribing for treatment naïve patients is Government policy. A viable biosimilar market is expected to result in reduced costs for biological medicines, allowing the Government to reinvest in new treatments. Further information can be found on the Biosimilar Awareness Initiative webpage (www.health.gov.au/biosimilars).”
- 6.6 The PBAC advised that rituximab is not suitable for prescribing by nurse practitioners.
- 6.7 The PBAC recommended that the Early Supply Rule should not apply.
- 6.8 The PBAC noted the restriction is complex as substantial remodelling of these restrictions is required.
- 6.9 The PBAC noted that this submission is not eligible for an Independent Review as it received a positive recommendation.

Outcome:

Recommended

7 Recommended listing

- 7.1 Add new items with brand equivalence (‘a’ flag) for all the same indications as intravenous MabThera. This includes indications for:
- Rheumatoid arthritis (RA) – S100 HSD

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- Granulomatosis with polyangiitis (Wegener’s granulomatosis) – S100 HSD
- Microscopic polyangiitis – S100 HSD
- Non-Hodgkin’s lymphoma (NHL) – S100 EFC
- Chronic lymphocytic leukaemia (CLL) – S100 EFC

7.2 Restrictions were revised as follows to apply the biosimilar uptake measures for initial (Initial 1 and Initial 2) and continuing (First continuing and Subsequent continuing) treatment restrictions for RA, and re-induction of GPA and MPA. Changes are indicated in italics, strikethrough and bold text.

An additional administrative advice encouraging biosimilar prescribing for treatment naïve patients was added to all indications.

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Manufacturer	Name and
RITUXIMAB 500 MG/50 ML I.V. INFUSION, 1 VIAL	1	0	Riximyo	Sandoz Pty Ltd

Category / Program	Section 100 – Highly Specialised Drugs Program (Public and Private Hospital)
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:	Severe active rheumatoid arthritis
Treatment phase:	Initial treatment - Initial 1 (patient recommencing treatment after a break of more than 24 months)
Restriction Level / Method:	<input checked="" type="checkbox"/> Authority Required - In Writing
Treatment criteria:	Must be treated by a rheumatologist; OR Must be treated by a clinical immunologist with expertise in the management of rheumatoid arthritis.
Clinical criteria:	Patient must have severe active rheumatoid arthritis, AND Patient must have failed to respond to at least 1 PBS-subsidised tumour necrosis factor (TNF) alfa antagonist, AND Patient must have received no PBS-subsidised treatment with a biological disease modifying anti-rheumatic drug (bDMARD) for this condition in the previous 24 months, AND Patient must not have failed previous PBS-subsidised treatment with rituximab for this condition, and have not already failed, or ceased to respond to, PBS-subsidised bDMARD treatment for this condition 5 times, AND <ul style="list-style-type: none"> • Patient must have failed, in the 24 months immediately prior to the date of the application, to achieve an adequate response to a trial of at least 6 months of intensive treatment with disease modifying anti-rheumatic drugs (DMARDs) which must include at least 3 months continuous treatment with each of at least 2 DMARDs, one of which must be methotrexate at a dose of at least 20 mg weekly and one of which must be: (i) hydroxychloroquine at a dose of at least 200 mg daily; or (ii) leflunomide at a dose of at least 10 mg daily; or (iii) sulfasalazine at a dose of at least 2 g daily; OR • Patient must have failed, in the 24 months immediately prior to the date of the

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	<p>application, to achieve an adequate response to a trial of at least 6 months of intensive treatment with DMARDs which, if methotrexate is contraindicated according to the Therapeutic Goods Administration (TGA)-approved Product Information or cannot be tolerated at a 20 mg weekly dose, must include at least 3 months continuous treatment with each of at least 2 of the following DMARDs: (i) hydroxychloroquine at a dose of at least 200 mg daily; and/or (ii) leflunomide at a dose of at least 10 mg daily; and/or (iii) sulfasalazine at a dose of at least 2 g daily; OR</p> <ul style="list-style-type: none"> • Patient must have failed, in the 24 months immediately prior to the date of the application, to achieve an adequate response to a trial of at least 6 months of intensive treatment with DMARDs which, if 3 or more of methotrexate, hydroxychloroquine, leflunomide and sulfasalazine are contraindicated according to the relevant TGA-approved Product Information or cannot be tolerated at the doses specified above, must include at least 3 months continuous treatment with each of at least 2 DMARDs, with one or more of the following DMARDs being used in place of the DMARDs which are contraindicated or not tolerated: (i) azathioprine at a dose of at least 1 mg/kg per day; and/or (ii) cyclosporin at a dose of at least 2 mg/kg/day; and/or (iii) sodium aurothiomalate at a dose of 50 mg weekly, <p>AND Patient must not receive more than 2 infusions of rituximab under this restriction, AND The treatment must be given concomitantly with methotrexate at a dose of at least 7.5 mg weekly.</p>
Population criteria:	Patient must be aged 18 years or older.
Prescriber Instructions	<p>For the purposes of this restriction 'TNF' alfa antagonist means adalimumab, certolizumab pegol, etanercept, golimumab and infliximab.</p> <p>For the purposes of this restriction bDMARD means abatacept, adalimumab, certolizumab pegol, etanercept, golimumab, infliximab, rituximab, tocilizumab or tofacitinib.</p> <p>If methotrexate is contraindicated according to the TGA-approved product information or cannot be tolerated at a 20 mg weekly dose, the application must include details of the contraindication or intolerance including severity to methotrexate. The maximum tolerated dose of methotrexate must be documented in the application, if applicable.</p> <p>The application must include details of the DMARDs trialled, their doses and duration of treatment, and all relevant contraindications and/or intolerances including severity.</p> <p>The requirement to trial at least 2 DMARDs for periods of at least 3 months each can be met using single agents sequentially or by using one or more combinations of DMARDs.</p> <p>If the requirement to trial 6 months of intensive DMARD therapy with at least 2 DMARDs cannot be met because of contraindications and/or intolerances of a severity necessitating permanent treatment withdrawal to all of the DMARDs specified above, details of the contraindication or intolerance including severity and dose for each DMARD must be provided in the authority application.</p> <p>The authority application must be made in writing and must include: (1) completed authority prescription form(s); and (2) a completed Rheumatoid Arthritis PBS Authority Application - Supporting Information Form; and (3) a signed patient acknowledgement.</p> <p>Assessment of a patient's response to an initial course of treatment must be made at least 12 weeks after the first infusion so that there is adequate time for a response to be demonstrated. This assessment, which will be used to determine eligibility for continuing</p>

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	<p>treatment, must be submitted to the Department of Human Services within 4 weeks of the date it was conducted. Where a response assessment is not undertaken and submitted to the Department of Human Services within these timeframes, the patient will be deemed to have failed to respond to treatment with rituximab.</p> <p>A patient whose most recent course of PBS-subsidised therapy was with rituximab and whose response to this treatment is sustained for more than 12 months, may apply for a further course of rituximab under the <i>First Continuing</i> treatment restriction.</p> <p>If a patient who fails to demonstrate a response to treatment with rituximab under this restriction they will not be eligible to receive further PBS-subsidised treatment with this drug for this condition.</p> <p>A patient who fails to demonstrate a response to rituximab treatment and who qualifies to trial an alternate bDMARD according to the interchangeability arrangements for bDMARDs for the treatment of severe rheumatoid arthritis, may do so without having to have a 22 week treatment-free period.</p> <p>The following criteria indicate failure to achieve an adequate response and must be demonstrated in all patients at the time of the initial application: an elevated erythrocyte sedimentation rate (ESR) greater than 25 mm per hour or a C-reactive protein (CRP) level greater than 15 mg per L; AND either (a) a total active joint count of at least 20 active (swollen and tender) joints; or (b) at least 4 active joints from the following list of major joints: (i) elbow, wrist, knee and/or ankle (assessed as swollen and tender); and/or (ii) shoulder and/or hip (assessed as pain in passive movement and restriction of passive movement, where pain and limitation of movement are due to active disease and not irreversible damage such as joint destruction or bony overgrowth).</p> <p>The joint count and ESR and/or CRP must be determined at the completion of the 6 month intensive DMARD trial, but prior to ceasing DMARD therapy. All measures must be no more than one month old at the time of initial application.</p> <p>If the above requirement to demonstrate an elevated ESR or CRP cannot be met, the application must state the reasons why this criterion cannot be satisfied.</p> <p>Where the baseline joint count is based on total active joints (i.e. more than 20 active joints), response will be determined according to the reduction in the total number of active joints. Where the baseline is determined on total number of major joints, the response must be demonstrated on the total number of major joints. If only an ESR or CRP is provided with the initial application, the same marker will be used to determine response</p>
<p>Administrative Advice</p>	<p>The Department of Human Services website (www.humanservices.gov.au) has details of the toxicities, including severity, which will be accepted for the following purposes: (a) exempting a patient from the requirement to undertake a minimum 3 month trial of methotrexate at a 20 mg weekly dose; (b) substituting azathioprine, cyclosporin or sodium aurothiomalate for another DMARD as part of the 6 month intensive DMARD trial; (c) exempting a patient from the requirement for a 6 month trial of intensive DMARD therapy.</p>
<p>Administrative Advice</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>

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	<p>Applications for authority to prescribe should be forwarded to: Department of Human Services Complex Drugs Reply Paid 9826 HOBART TAS 7001</p>
<p>Administrative Advice 3</p>	<p>TREATMENT OF ADULT PATIENTS WITH SEVERE ACTIVE RHEUMATOID ARTHRITIS</p> <p>The following information applies to the prescribing under the Pharmaceutical Benefits Scheme (PBS) of the biological disease modifying antirheumatic drugs (bDMARDs) for adults with severe active rheumatoid arthritis. Where the term bDMARD appears in the following notes and restrictions it refers to the tumour necrosis factor (TNF) alfa antagonists (adalimumab, certolizumab pegol, etanercept, golimumab, infliximab), the chimeric anti-CD20 monoclonal antibody (rituximab), the interleukin-6 inhibitor (tocilizumab), the T-cell co-stimulation modulator (abatacept) and the Janus-associated kinase (JAK) inhibitor (tofacitinib).</p> <p>Patients are eligible for PBS-subsidised treatment with only 1 of the above disease modifying anti-rheumatic drugs at any 1 time.</p> <p>In order to be eligible to receive PBS-subsidised treatment with rituximab, a patient must have already failed to demonstrate a response to at least 1 course of treatment with a PBS-subsidised TNF-alfa antagonist.</p> <p>A patient receiving PBS-subsidised bDMARD therapy may swap to an alternate bDMARD without having to experience a disease flare. Under these interchangeability arrangements:</p> <ul style="list-style-type: none"> - a patient may continue to receive long-term treatment with a PBS-subsidised bDMARD while they continue to show a response to therapy, - a patient cannot trial and fail, or cease to respond to, the same PBS-subsidised bDMARD more than once, and - once a patient has either failed or ceased to respond to treatment 5 times, they will not be eligible to receive further PBS-subsidised bDMARDs for the treatment of rheumatoid arthritis. <p>For patients who have failed PBS-subsidised treatment with 2 or 3 TNF-alfa antagonists prior to 1 August 2010 please contact the Department of Human Services on 1800 700 270. A patient whose most recent course of PBS-subsidised therapy was with rituximab and whose response to this treatment is sustained for more than 12 months, may apply for a further course of rituximab under the <i>First Continuing treatment restriction</i>. A patient who has failed fewer than 5 bDMARDs and who has a break in therapy of less than 24 months may commence a further course of treatment with a bDMARD without having to requalify under the Initial 1 treatment restriction. A patient who has failed fewer than 5 bDMARDs and who has had a break in therapy of longer than 24 months must requalify for treatment under the Initial 1 treatment restriction. The length of a treatment break is measured from the date the most recent treatment with PBS-subsidised bDMARD treatment is stopped to the date of the new application for treatment with a bDMARD.</p> <p>(1) How to prescribe PBS-subsidised bDMARD therapy after 1 August 2010.</p> <p>(a) Initial treatment. Applications for initial treatment should be made where:</p> <ul style="list-style-type: none"> (i) a patient has received no prior PBS-subsidised bDMARD treatment and wishes to commence such therapy, excluding rituximab (Initial 1); or (ii) a patient wishes to re-commence treatment with a bDMARD following a break in

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	<p>PBS-subsidised therapy of more than 24 months (Initial 1); or</p> <p>(iii) a patient has received prior PBS-subsidised (initial or continuing) bDMARD therapy and wishes to trial an alternate agent (Initial 2) [further details are under 'Swapping therapy' below]; or</p> <p>(iv) a patient wishes to re-commence treatment with a specific bDMARD following a break of less than 24 months in PBS-subsidised therapy with that agent (Initial 2).</p> <p>Initial applications for new or re-commencing patients (Initial 1) must include a joint count and ESR and/or CRP measured at the completion of the 6-month intensive DMARD trial, but prior to ceasing DMARD therapy.</p> <p>Initial treatment authorisations will be limited to provide a maximum of 16 weeks of therapy for abatacept, adalimumab, etanercept, golimumab, tocilizumab and tofacitinib, 18 to 20 weeks of therapy with certolizumab pegol (depending upon the dosing regimen), 22 weeks of therapy for infliximab and 2 infusions of rituximab.</p> <p>A patient must be assessed for response to any course of initial PBS-subsidised treatment (excluding rituximab) following a minimum of 12 weeks of therapy and this assessment must be submitted to the Department of Human Services no later than 4 weeks from the date that course was ceased. Rituximab patients must be assessed following a minimum of 12 weeks after the first infusion, and this assessment must be submitted to the Department of Human Services within 4 weeks.</p> <p>Where a response assessment is not submitted to the Department of Human Services within these timeframes, the patient will be deemed to have failed to respond to treatment with that bDMARD. For second and subsequent courses of PBS-subsidised bDMARD (excluding rituximab) treatment it is recommended that a patient is reviewed in the month prior to completing their current course of treatment and that where required an application is submitted to the Department of Human Services no later than 2 weeks prior to the patient completing their current treatment course.</p> <p>Abatacept patients: Patients are eligible to receive one I.V. loading dose when commencing treatment with the subcutaneous formulation. For these patients two prescriptions are required, the first prescription for the I.V. loading dose for sufficient vials for one dose based on the patient's weight with no repeats. The second prescription for the pre-filled syringes, with a maximum quantity of 4 and up to 3 repeats, must be submitted with the initial application.</p> <p>Rituximab patients: A further application may be submitted to the Department of Human Services 24 weeks after the first infusion. New baselines may be submitted with this application if appropriate.</p> <p>(b) Continuing treatment. Following the completion of an initial treatment course with a specific bDMARD (excluding rituximab), a patient may qualify to receive up to 24 weeks of continuing treatment with that drug providing they have demonstrated an adequate response to treatment. The patient remains eligible to receive continuing bDMARD treatment with the same drug in courses of up to 24 weeks providing they continue to sustain the response. It is recommended that a patient be reviewed the month prior to completing their current course of treatment to ensure uninterrupted bDMARD supply.</p> <p>Rituximab patients: A patient may qualify to receive a further course of treatment (every 24 weeks) with this agent providing they have demonstrated an adequate response to treatment following a minimum of 12 weeks after the first infusion of their most recent treatment with rituximab. The patient</p>
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	<p>remains eligible to receive a course of rituximab every 24 weeks providing they continue to demonstrate a response as specified in the restriction. Where a response assessment is not submitted to the Department of Human Services within these timeframes, the patient will be deemed to have failed to respond to treatment with that bDMARD.</p> <p>(2) Swapping therapy</p> <p>Once initial treatment with the first PBS-subsidised bDMARD is approved, a patient may swap to an alternate bDMARD without having to requalify with respect to the indices of disease severity (i.e. the erythrocyte sedimentation rate (ESR), the C-reactive protein (CRP) levels and the joint count) or the prior non-bDMARD therapy requirements, except if the patient has had a break in therapy of more than 24 months. However the requirement for concomitant treatment with methotrexate, where it applies, must be met for each bDMARD trialled.</p> <p>Patients who are not able to complete a minimum of 12 weeks of an initial treatment course will be deemed to have failed treatment with that agent.</p> <p>A patient may trial an alternate bDMARD at any time, regardless of whether they are receiving therapy (initial or continuing) with a bDMARD at the time of the application. However, they cannot swap to a particular bDMARD if they have failed to respond to prior treatment with that drug.</p> <p>Abatacept: Patients swapping from I.V. abatacept to subcutaneous abatacept will not be eligible for an I.V. loading dose when commencing treatment with the subcutaneous formulation.</p> <p>Rituximab: In order to trial rituximab, a patient must have trialled and failed to demonstrate a response to at least 1 PBS-subsidised TNF-alfa antagonist treatment.</p> <p>To ensure a patient receives the maximum treatment opportunities allowed under the interchangeability arrangements, it is important that they are assessed for response to every course of treatment approved, within the timeframes specified in the relevant restriction.</p> <p>PBS subsidy does not allow for patients to receive treatment with another PBS-subsidised biological agent during the required treatment-free period applying to patients who have demonstrated a response to their most recent course of rituximab. This means that patients who have demonstrated a response to a course of rituximab must have a PBS-subsidised biological agent therapy treatment-free period of at least 22 weeks, immediately following the second infusion, before swapping to an alternate bDMARD. Patients who fail to respond to rituximab and who qualify and wish to trial a course of an alternate bDMARD may do so without having to have any treatment-free period.</p> <p>To avoid confusion, an application for a patient who wishes to swap to an alternate bDMARD should be accompanied by the approved authority prescription or remaining repeats for the bDMARD the patient is ceasing.</p> <p>(3) Baseline measurements to determine response.</p> <p>The Department of Human Services will determine whether a response to treatment has been demonstrated based on the baseline measurements of the joint count, ESR and/or CRP submitted with the first authority application for a bDMARD. However, prescribers may provide new baseline measurements any time that an initial treatment authority application is submitted and the Department of Human Services will assess response according to these revised baseline measurements.</p>
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	<p>To ensure consistency in determining response, the same indices of disease severity used to establish baseline at the commencement of treatment with each initial treatment application must be provided used for all subsequent continuing treatment applications. Therefore, where only an ESR or CRP level is provided at baseline, an ESR or CRP level respectively must be provided used to determine response. Similarly, where the baseline active joint count is based on total active joints (i.e. more than 20 active joints), response will be determined according to the reduction in the total number of active joints. Where the baseline is determined on total number of major joints, the response must be demonstrated on the total number of major joints.</p> <p>Except as specified under the Initial 1 treatment restriction, a baseline joint count and ESR and/or CRP should be performed whilst the patient is still on treatment or within 1 month of ceasing prior treatment. Applications under the Initial 1 treatment restriction for new or re-commencing patients must include a joint count and ESR and/or CRP measured at the completion of the 6 month intensive DMARD trial, but prior to ceasing DMARD therapy.</p>
Administrative Advice	<p>Biosimilar policy</p> <p><i>Prescribing of the biosimilar brand, Riximyo, is encouraged for treatment naïve patients.</i></p> <p><i>Encouraging biosimilar prescribing for treatment naïve patients is Government policy. A viable biosimilar market is expected to result in reduced costs for biological medicines, allowing the Government to reinvest in new treatments. Further information can be found on the Biosimilar Awareness Initiative webpage (www.health.gov.au/biosimilars).</i></p>

Name, Restriction, Manner of administration and form	Max. Qty	№.of Rpts	Proprietary Manufacturer	Name and
RITUXIMAB 500 MG/50 ML I.V. INFUSION, 1 VIAL	1	0	Riximyo	Sandoz Pty Ltd

Category / Program	Section 100 – Highly Specialised Drugs Program (Public and Private Hospital)
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:	Severe active rheumatoid arthritis
Treatment phase:	Initial treatment - Initial 2 (change or re-commencement of treatment after break of less than 24 months)
Restriction Level / Method:	<input checked="" type="checkbox"/> Authority Required - In Writing
Treatment criteria:	Must be treated by a rheumatologist; OR Must be treated by a clinical immunologist with expertise in the management of rheumatoid arthritis.
Clinical criteria:	Patient must have a documented history of severe active rheumatoid arthritis, AND Patient must have failed to respond to at least 1 PBS-subsidised tumour necrosis factor (TNF) alfa antagonist, AND Patient must have received prior PBS-subsidised biological disease modifying anti-rheumatic drug (bDMARD) treatment for this condition and are eligible to receive further bDMARD

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	<p>therapy, AND Patient must not receive more than 2 infusions of rituximab under this restriction, AND The treatment must be given concomitantly with methotrexate at a dose of at least 7.5 mg weekly.</p>
Population criteria:	Patient must be aged 18 years or older.
Prescriber Instructions	<p>For the purposes of this restriction 'TNF' alfa antagonist means adalimumab, certolizumab pegol, etanercept, golimumab and infliximab.</p> <p>For the purposes of this restriction bDMARD means abatacept, adalimumab, certolizumab pegol, etanercept, golimumab, infliximab, rituximab, tocilizumab or tofacitinib.</p> <p>The authority application must be made in writing and must include: (a) completed authority prescription form(s); and (b) a completed Rheumatoid Arthritis PBS Authority Application - Supporting Information Form.</p> <p>Applications for a patient who has received PBS-subsidised treatment with rituximab and who wishes to re-commence therapy with this drug, must be accompanied by evidence of a response to the patient's most recent course of PBS-subsidised rituximab treatment, within the timeframes specified below.</p> <p>Where the most recent course of PBS-subsidised rituximab treatment was approved under either of the initial 1 or 2 treatment restrictions, the patient must have been assessed for response at least 12 weeks after the first infusion. This assessment must be submitted no later than 4 weeks from the date of the assessment.</p> <p>A patient may qualify to receive a further course of treatment (every 24 weeks) with this agent provided they have demonstrated an adequate response to treatment following a minimum of 12 weeks after the first infusion of their most recent treatment with rituximab. The demonstration of response must be submitted within 4 weeks of assessment.</p> <p>Where a response assessment is not undertaken and submitted within these timeframes, the patient will be deemed to have failed to respond to treatment with rituximab.</p> <p>A patient whose most recent course of PBS-subsidised therapy was with rituximab and whose response to this treatment is sustained for more than 12 months, may apply for a further course of rituximab under the <i>First Continuing</i> treatment restriction.</p> <p>If a patient fails to demonstrate a response to treatment with rituximab under this restriction they will not be eligible to receive further PBS-subsidised treatment with this drug for this condition.</p> <p>If a patient fails to demonstrate a response to a treatment with rituximab and who qualify to trial an alternate bDMARD according to the interchangeability arrangements for bDMARDs for the treatment of severe rheumatoid arthritis, may do so without having to have a 22 week treatment-free period.</p> <p>An adequate response to treatment is defined as: an ESR no greater than 25 mm per hour or a CRP level no greater than 15 mg per L or either marker reduced by at least 20% from baseline; AND either of the following: (a) a reduction in the total active (swollen and tender) joint count by at least 50% from baseline, where baseline is at least 20 active joints; or</p>

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	(b) a reduction in the number of the following active joints, from at least 4, by at least 50%: (i) elbow, wrist, knee and/or ankle (assessed as swollen and tender); and/or (ii) shoulder and/or hip (assessed as pain in passive movement and restriction of passive movement, where pain and limitation of movement are due to active disease and not irreversible damage such as joint destruction or bony overgrowth).
Administrative Advice	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). 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 Applications for authority to prescribe should be forwarded to: Department of Human Services Complex Drugs Reply Paid 9826 HOBART TAS 7001
Administrative Advice 3	As per "Administrative Advice 3" within the RA Initial Treatment – Initial 1 restriction above

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Manufacturer	Name and
RITUXIMAB 500 MG/50 ML I.V. INFUSION, 1 VIAL	1	0	Riximyo	Sandoz Pty Ltd

Category / Program	Section 100 – Highly Specialised Drugs Program (Public and Private Hospital)
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:	Severe active rheumatoid arthritis
Treatment phase:	<i>First continuing treatment</i>
Restriction Level / Method:	<input checked="" type="checkbox"/> Authority Required - In Writing
Treatment criteria:	Must be treated by a rheumatologist; OR Must be treated by a clinical immunologist with expertise in the management of rheumatoid arthritis.
Clinical criteria:	Patient must have a documented history of severe active rheumatoid arthritis, AND Patient must have demonstrated an adequate response to treatment with this drug, AND Patient must have received this drug as their most recent course of PBS-subsidised biological disease modifying anti-rheumatic drug (bDMARD) treatment for this condition, AND Patient must not receive more than 2 infusions of rituximab under this restriction. AND The treatment must be given concomitantly with methotrexate at a dose of at least 7.5 mg weekly.
Population criteria:	Patient must be aged 18 years or older.
Prescriber Instructions	For the purposes of this restriction bDMARD means abatacept, adalimumab, certolizumab pegol, etanercept, golimumab, infliximab, rituximab, tocilizumab or tofacitinib.

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	<p>An adequate response to treatment is defined as: an ESR no greater than 25 mm per hour or a CRP level no greater than 15 mg per L or either marker reduced by at least 20% from baseline; AND either of the following: (a) a reduction in the total active (swollen and tender) joint count by at least 50% from baseline, where baseline is at least 20 active joints; or (b) a reduction in the number of the following active joints, from at least 4, by at least 50%: (i) elbow, wrist, knee and/or ankle (assessed as swollen and tender); and/or (ii) shoulder and/or hip (assessed as pain in passive movement and restriction of passive movement, where pain and limitation of movement are due to active disease and not irreversible damage such as joint destruction or bony overgrowth).</p> <p><i>Where the baseline active joint count is based on total active joints (i.e. more than 20 active joints), response will be determined according to the reduction in the total number of active joints. Where the baseline is determined on total number of major joints, the response must be demonstrated on the total number of major joints. If only an ESR or CRP level is provided with the initial application, the same marker will be used to determine response.</i></p> <p>The authority application must be made in writing and must include: (a) completed authority prescription form(s); and (b) a completed Rheumatoid Arthritis PBS Authority Application - Supporting Information Form.</p> <p><i>The application for first continuing treatment with this drug must be accompanied by an assessment of response to a minimum of 12 weeks of treatment with an initial treatment course. This assessment must be submitted no later than 4 weeks from the cessation of that treatment course.</i></p> <p>A patient may qualify to receive a further course of treatment (every 24 weeks) with this agent provided they have demonstrated an adequate response to treatment following a minimum of 12 weeks after the first infusion of their most recent treatment with rituximab. The demonstration of response must be submitted within 4 weeks of assessment.</p> <p>Where a response assessment is not undertaken and submitted within these timeframes, the patient will be deemed to have failed to respond to treatment with rituximab.</p> <p>A patient whose most recent course of PBS-subsidised therapy was with rituximab and whose response to this treatment is sustained for more than 12 months, may apply for a further course of rituximab under the Continuing treatment restriction.</p> <p>If a patient fails to demonstrate a response to treatment with rituximab under this restriction will not be eligible to receive further PBS-subsidised treatment with this drug for this condition.</p>
Administrative Advice	<p>Note No increase in the maximum quantity or number of units may be authorised. Note No increase in the maximum number of repeats may be authorised.</p>

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Administrative Advice	<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 Complex Drugs Reply Paid 9826 HOBART TAS 7001</p>
Administrative Advice 3	<i>As per "Administrative Advice 3" within the RA Initial Treatment – Initial 1 restriction above</i>

Name, Restriction, Manner of administration and form	Max. Qty	Nº of Rpts	Proprietary Manufacturer	Name and
RITUXIMAB 500 MG/50 ML I.V. INFUSION, 1 VIAL	1	0	Riximyo	Sandoz Pty Ltd

Category / Program	Section 100 – Highly Specialised Drugs Program (Public and Private Hospital)
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:	Severe active rheumatoid arthritis
Treatment phase:	Subsequent continuing treatment
Restriction Level / Method:	<input checked="" type="checkbox"/> Streamlined
Treatment criteria:	Must be treated by a rheumatologist; OR Must be treated by a clinical immunologist with expertise in the management of rheumatoid arthritis.
Clinical criteria:	Patient must have a documented history of severe active rheumatoid arthritis, AND Patient must have demonstrated an adequate response to treatment with this drug, AND Patient must have received this drug as the most recent course of PBS-subsidised biological disease modifying anti-rheumatic drug (bDMARD) treatment for this condition, AND Patient must not receive more than 2 infusions of rituximab per subsequent continuing treatment course authorised under this restriction, AND The treatment must be given concomitantly with methotrexate at a dose of at least 7.5 mg weekly.
Population criteria:	Patient must be aged 18 years or older.
Prescriber Instructions	For the purposes of this restriction bDMARD means abatacept, adalimumab, certolizumab pegol, etanercept, golimumab, infliximab, rituximab, tocilizumab or tofacitinib. The authority application must be made in writing and must include: (a) completed authority prescription form(s); and (b) a completed Rheumatoid Arthritis PBS Authority Application – Supporting Information

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	<p><i>Form:</i></p> <p><i>A patient may qualify to receive a further course of treatment (every 24 weeks) with this agent provided they have demonstrated an adequate response to treatment following a minimum of 12 weeks after the first infusion of their most recent treatment with rituximab. The demonstration of response must be submitted within 4 weeks of assessment.</i></p> <p><i>Where a response assessment is not undertaken and submitted within these timeframes, the patient will be deemed to have failed to respond to treatment with rituximab.</i></p> <p><i>A patient whose most recent course of PBS subsidised therapy was with rituximab and whose response to this treatment is sustained for more than 12 months, may apply for a further course of rituximab under the Continuing treatment restriction.</i></p> <p><i>An adequate response to treatment is defined as:</i> <i>an ESR no greater than 25 mm per hour or a CRP level no greater than 15 mg per L or either marker reduced by at least 20% from baseline;</i> <i>AND either of the following:</i> <i>(a) a reduction in the total active (swollen and tender) joint count by at least 50% from baseline, where baseline is at least 20 active joints; or</i> <i>(b) a reduction in the number of the following active joints, from at least 4, by at least 50%:</i> <i>(i) elbow, wrist, knee and/or ankle (assessed as swollen and tender); and/or</i> <i>(ii) shoulder and/or hip (assessed as pain in passive movement and restriction of passive movement, where pain and limitation of movement are due to active disease and not irreversible damage such as joint destruction or bony overgrowth).</i></p> <p><i>Where the baseline active joint count is based on total active joints (i.e. more than 20 active joints), response will be determined according to the reduction in the total number of active joints. Where the baseline is determined on total number of major joints, the response must be demonstrated on the total number of major joints. If only an ESR or CRP level is provided with the initial application, the same marker will be used to determine response.</i></p> <p><i>The measurement of response to the prior course of therapy must be documented in the patient's medical notes.</i></p> <p><i>If a patient fails to demonstrate a response to treatment with rituximab under this restriction will not be eligible to receive further PBS-subsidised treatment with this drug for this condition.</i></p>
Administrative Advice	<p><i>Note No increase in the maximum quantity or number of units may be authorised.</i></p> <p><i>Note No increase in the maximum number of repeats may be authorised.</i></p>
Administrative Advice 3	<p><i>As per "Administrative Advice 3" within the RA Initial Treatment – Initial 1 restriction above</i></p>

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The PBAC noted that the grandfather arrangement included in the induction of remission restriction for severe active granulomatosis with polyangiitis (Wegeners granulomatosis) should be removed as rituximab for this indication has now been listed for more than 12 months.

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Manufacturer	Name and
RITUXIMAB 100 MG/10 ML I.V. INFUSION, 2 VIALS	1	0	Riximyo	Sandoz Pty Ltd
RITUXIMAB 500 MG/50 ML I.V. INFUSION, 1 VIAL	1	0	Riximyo	Sandoz Pty Ltd
Category / Program	Section 100 – Highly Specialised Drugs Program (Public and Private Hospital)			
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:	Severe active granulomatosis with polyangiitis (Wegeners granulomatosis)			
Treatment phase:	Induction of remission			
Restriction Level / Method:	<input checked="" type="checkbox"/> Authority Required – In Writing			
Clinical criteria:	The treatment must be for the induction of remission, AND 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, AND The treatment must be in combination with glucocorticoids, AND Patient must be at risk of end-organ damage or mortality, AND 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 The authority application must be made in writing			

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<p>Administrative Advice</p>	<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: 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>
<p>Administrative Advice</p>	<p>Biosimilar policy</p> <p><i>Prescribing of the biosimilar brand, Riximyo, is encouraged for treatment naïve patients.</i></p> <p><i>Encouraging biosimilar prescribing for treatment naïve patients is Government policy. A viable biosimilar market is expected to result in reduced costs for biological medicines, allowing the Government to reinvest in new treatments. Further information can be found on the Biosimilar Awareness Initiative webpage (www.health.gov.au/biosimilars).</i></p>

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Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Manufacturer	Name and
RITUXIMAB 100 MG/10 ML I.V. INFUSION, 2 VIALS	1	0	Riximyo	Sandoz Pty Ltd

RITUXIMAB 500 MG/50 ML I.V. INFUSION, 1 VIAL	1	0	Riximyo	Sandoz Pty Ltd
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Category / Program	Section 100 – Highly Specialised Drugs Program (Public and Private Hospital)
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:	Severe active microscopic polyangiitis
Treatment phase:	Induction of remission
Restriction Level / Method:	<input checked="" type="checkbox"/> Authority Required – In Writing
Clinical criteria:	The treatment must be for the induction of remission, AND 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, AND The treatment must be in combination with glucocorticoids, AND Patient must be at risk of end-organ damage or mortality, AND 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 therapy The authority application must be made in writing

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<p>Administrative Advice</p>	<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: 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>
<p>Administrative Advice</p>	<p>Biosimilar policy</p> <p><i>Prescribing of the biosimilar brand, Riximyo, is encouraged for treatment naïve patients.</i></p> <p><i>Encouraging biosimilar prescribing for treatment naïve patients is Government policy. A viable biosimilar market is expected to result in reduced costs for biological medicines, allowing the Government to reinvest in new treatments. Further information can be found on the Biosimilar Awareness Initiative webpage (www.health.gov.au/biosimilars).</i></p>

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Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Manufacturer	Name and
RITUXIMAB 100 MG/10 ML I.V. INFUSION, 2 VIALS	46	0	Riximyo	Sandoz Pty Ltd

RITUXIMAB 500 MG/50 ML I.V. INFUSION, 1 VIAL	44	0	Riximyo	Sandoz Pty Ltd
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Category / Program	Section 100 – Highly Specialised Drugs Program (Public and Private Hospital)
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:	Severe active granulomatosis with polyangiitis (Wegeners granulomatosis)
Treatment phase:	Re-induction of remission
Restriction Level / Method:	<input checked="" type="checkbox"/> Streamlined
Clinical criteria:	The treatment must be for the re-induction of remission, AND Patient must have previously received and responded to this drug for this condition, AND The treatment must be in combination with glucocorticoids, AND Patient must be at risk of end-organ damage or mortality, AND 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 The authority application must be made in writing
Administrative Advice	This drug is not PBS-subsidised for maintenance of remission. The authority application must be made in writing

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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>
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Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Manufacturer	Name and
RITUXIMAB 100 MG/10 ML I.V. INFUSION, 2 VIALS	46	0	Riximyo	Sandoz Pty Ltd

RITUXIMAB 500 MG/50 ML I.V. INFUSION, 1 VIAL	44	0	Riximyo	Sandoz Pty Ltd
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Category / Program	Section 100 – Highly Specialised Drugs Program (Public and Private Hospital)
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:	Severe active microscopic polyangiitis
Treatment phase:	Re-induction of remission
Restriction Level / Method:	<input checked="" type="checkbox"/> Streamlined
Clinical criteria:	The treatment must be for the re-induction of remission, AND Patient must have previously received and responded to this drug for this condition, AND The treatment must be in combination with glucocorticoids, AND Patient must be at risk of end-organ damage or mortality, AND 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. The authority application must be made in writing
Administrative Advice	This drug is not PBS-subsidised for maintenance of remission.

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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>
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Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Manufacturer	Name and
RITUXIMAB 100 MG/10 ML I.V. INFUSION, 2 VIALS	800 mg	11	Riximyo	Sandoz Pty Ltd

RITUXIMAB 500 MG/50 ML I.V. INFUSION, 1 VIAL			Riximyo	Sandoz Pty Ltd
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Category / Program	Section 100 – Efficient Funding of Chemotherapy (Public and Private Hospital)
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:	Stage III or IV CD20 positive follicular B-cell non-Hodgkin's lymphoma
Treatment phase:	Maintenance therapy
Restriction Level / Method:	<input checked="" type="checkbox"/> Streamlined
Clinical criteria:	Patient must have demonstrated a partial or complete response to induction treatment with either R-CHOP or R-CVP regimens for previously untreated follicular B-cell Non-Hodgkin's lymphoma, received immediately prior to this current Authority application, treatment with this drug for this condition AND Patient must not have received bendamustine induction therapy, AND The treatment must be maintenance therapy, AND Patient must not receive more than 12 doses or 2 years duration of treatment, whichever comes first, under this restriction.
Prescriber Instructions	A patient may only qualify for PBS-subsidised treatment under this restriction once in a lifetime.
Administrative Advice	No increase in the maximum number of repeats may be authorised.
Administrative Advice	Biosimilar policy <i>Prescribing of the biosimilar brand, Riximyo, is encouraged for treatment naïve patients.</i> <i>Encouraging biosimilar prescribing for treatment naïve patients is Government policy. A viable biosimilar market is expected to result in reduced costs for biological medicines, allowing the Government to reinvest in new treatments. Further information can be found on the Biosimilar Awareness Initiative webpage (www.health.gov.au/biosimilars).</i>

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Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Manufacturer	Name and
RITUXIMAB 100 MG/10 ML I.V. INFUSION, 2 VIALS	800 mg	7	Riximyo	Sandoz Pty Ltd

RITUXIMAB 500 MG/50 ML I.V. INFUSION, 1 VIAL			Riximyo	Sandoz Pty Ltd
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Category / Program	Section 100 – Efficient Funding of Chemotherapy (Public and Private Hospital)
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:	Relapsed or refractory Stage III or IV CD20 positive follicular B-cell non-Hodgkin's lymphoma
Treatment phase:	Maintenance therapy
Restriction Level / Method:	<input checked="" type="checkbox"/> Streamlined
Clinical criteria:	The treatment must be maintenance therapy, AND Patient must have demonstrated a partial or complete response to re-induction treatment received immediately prior to this current Authority application, <i>treatment with this drug for this condition</i> AND Patient must not receive more than 8 cycles or 2 years duration of treatment, whichever comes first, under this restriction.
Administrative Advice	No increase in the maximum number of repeats may be authorised.
Administrative advice	Biosimilar policy <i>Prescribing of the biosimilar brand, Riximyo, is encouraged for treatment naïve patients.</i> <i>Encouraging biosimilar prescribing for treatment naïve patients is Government policy. A viable biosimilar market is expected to result in reduced costs for biological medicines, allowing the Government to reinvest in new treatments. Further information can be found on the Biosimilar Awareness Initiative webpage (www.health.gov.au/biosimilars).</i>

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Manufacturer	Name and
RITUXIMAB 100 MG/10 ML I.V. INFUSION, 2 VIALS	800 mg	7	Riximyo	Sandoz Pty Ltd

RITUXIMAB 500 MG/50 ML I.V. INFUSION, 1 VIAL			Riximyo	Sandoz Pty Ltd
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Category / Program	Section 100 – Efficient Funding of Chemotherapy (Public and Private Hospital)
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:	Previously untreated or relapsed/refractory CD20 positive lymphoid cancer
Treatment phase:	Induction or re-induction therapy
Restriction Level / Method:	<input checked="" type="checkbox"/> Streamlined

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Clinical criteria:	<p>The treatment must be for induction or re-induction for CD20 positive lymphoma; OR The treatment must be for induction or re-induction for CD20 positive chronic lymphocytic leukaemia; OR The treatment must be for induction or consolidation for CD20 positive acute lymphoblastic leukaemia, AND The treatment must be in combination with chemotherapy, AND Patient must not receive more than the number of cycles of treatment recommended by standard guidelines for the partner chemotherapy under this restriction.</p>
Prescribing Instructions	<p>An initial dose of rituximab must be administered with rituximab intravenous injection. Subsequent doses may be administered with either intravenous or subcutaneous rituximab.</p> <p>No more than 8 doses in total as per course of treatment will be allowed for lymphoma or chronic lymphocytic leukaemia.</p> <p>No more than 12 doses in total as per course of treatment will be allowed for acute lymphoblastic leukaemia for induction course (including consolidation course).</p>
Administrative advice	<p>Biosimilar policy</p> <p><i>Prescribing of the biosimilar brand, Riximyo, is encouraged for treatment naïve patients.</i></p> <p><i>Encouraging biosimilar prescribing for treatment naïve patients is Government policy. A viable biosimilar market is expected to result in reduced costs for biological medicines, allowing the Government to reinvest in new treatments. Further information can be found on the Biosimilar Awareness Initiative webpage (www.health.gov.au/biosimilars).</i></p>

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Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Manufacturer	Name and
RITUXIMAB 100 MG/10 ML I.V. INFUSION, 2 VIALS	800 mg	5	Riximyo	Sandoz Pty Ltd

RITUXIMAB 500 MG/50 ML I.V. INFUSION, 1 VIAL			Riximyo	Sandoz Pty Ltd
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Category / Program	Section 100 – Efficient Funding of Chemotherapy (Public and Private Hospital)
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:	Previously untreated or Relapsed/refractory CD20 positive acute lymphoblastic leukaemia
Treatment phase:	Maintenance therapy
Restriction Level / Method:	<input checked="" type="checkbox"/> Streamlined
Clinical criteria:	The treatment must be maintenance therapy, AND The treatment must be in combination with chemotherapy, AND Patient must be in complete remission, AND Patient must not receive more than 6 doses in total under this restriction.
Administrative Advice	No increase in the maximum number of repeats may be authorised.
Administrative advice	Biosimilar policy <i>Prescribing of the biosimilar brand, Riximyo, is encouraged for treatment naïve patients.</i> <i>Encouraging biosimilar prescribing for treatment naïve patients is Government policy. A viable biosimilar market is expected to result in reduced costs for biological medicines, allowing the Government to reinvest in new treatments. Further information can be found on the Biosimilar Awareness Initiative webpage (www.health.gov.au/biosimilars).</i>

7.3 Flow-on changes to restrictions:

The changes to the note associated with the PBS listings for the medicines for the treatment of severe active rheumatoid arthritis in adults (as below) apply to all other medicines listed for this indication. At the time of the March 2018 PBAC Meeting this included abatacept, adalimumab, certolizumab pegol, etanercept, golimumab, infliximab, rituximab, tocilizumab or tofacitinib.

<p>Administrative Advice 3</p>	<p>TREATMENT OF ADULT PATIENTS WITH SEVERE ACTIVE RHEUMATOID ARTHRITIS</p> <p>The following information applies to the prescribing under the Pharmaceutical Benefits Scheme (PBS) of the biological disease modifying antirheumatic drugs (bDMARDs) for adults with severe active rheumatoid arthritis. Where the term bDMARD appears in the following notes and restrictions it refers to the tumour necrosis factor (TNF) alfa antagonists (adalimumab, certolizumab pegol, etanercept, golimumab, infliximab), the chimeric anti-CD20 monoclonal antibody (rituximab), the interleukin-6 inhibitor (tocilizumab), the T-cell co-stimulation modulator (abatacept) and the Janus-associated kinase (JAK) inhibitor (tofacitinib).</p> <p>Patients are eligible for PBS-subsidised treatment with only 1 of the above disease modifying anti-rheumatic drugs at any 1 time.</p> <p>In order to be eligible to receive PBS-subsidised treatment with rituximab, a patient must have already failed to demonstrate a response to at least 1 course of treatment with a PBS-subsidised TNF-alfa antagonist.</p> <p>A patient receiving PBS-subsidised bDMARD therapy may swap to an alternate bDMARD without having to experience a disease flare. Under these interchangeability arrangements:</p> <ul style="list-style-type: none"> - a patient may continue to receive long-term treatment with a PBS-subsidised bDMARD while they continue to show a response to therapy, - a patient cannot trial and fail, or cease to respond to, the same PBS-subsidised bDMARD more than once, and - once a patient has either failed or ceased to respond to treatment 5 times, they will not be eligible to receive further PBS-subsidised bDMARDs for the treatment of rheumatoid arthritis. <p>For patients who have failed PBS-subsidised treatment with 2 or 3 TNF-alfa antagonists prior to 1 August 2010 please contact the Department of Human Services on 1800 700 270. A patient whose most recent course of PBS-subsidised therapy was with rituximab and whose response to this treatment is sustained for more than 12 months, may apply for a further course of rituximab under the <i>First Continuing treatment restriction</i>. A patient who has failed fewer than 5 bDMARDs and who has a break in therapy of less than 24 months may commence a further course of treatment with a bDMARD without having to requalify under the Initial 1 treatment restriction. A patient who has failed fewer than 5 bDMARDs and who has had a break in therapy of longer than 24 months must requalify for treatment under the Initial 1 treatment restriction. The length of a treatment break is measured from the date the most recent treatment with PBS-subsidised bDMARD treatment is stopped to the date of the new application for treatment with a bDMARD.</p> <p>(1) How to prescribe PBS-subsidised bDMARD therapy after 1 August 2010.</p> <p>(a) Initial treatment.</p>
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	<p>Applications for initial treatment should be made where:</p> <ul style="list-style-type: none">(i) a patient has received no prior PBS-subsidised bDMARD treatment and wishes to commence such therapy, excluding rituximab (Initial 1); or(ii) a patient wishes to re-commence treatment with a bDMARD following a break in PBS-subsidised therapy of more than 24 months (Initial 1); or(iii) a patient has received prior PBS-subsidised (initial or continuing) bDMARD therapy and wishes to trial an alternate agent (Initial 2) [further details are under 'Swapping therapy' below]; or(iv) a patient wishes to re-commence treatment with a specific bDMARD following a break of less than 24 months in PBS-subsidised therapy with that agent (Initial 2). <p>Initial applications for new or re-commencing patients (Initial 1) must include a joint count and ESR and/or CRP measured at the completion of the 6-month intensive DMARD trial, but prior to ceasing DMARD therapy.</p> <p>Initial treatment authorisations will be limited to provide a maximum of 16 weeks of therapy for abatacept, adalimumab, etanercept, golimumab, tocilizumab and tofacitinib, 18 to 20 weeks of therapy with certolizumab pegol (depending upon the dosing regimen), 22 weeks of therapy for infliximab and 2 infusions of rituximab.</p> <p>A patient must be assessed for response to any course of initial PBS-subsidised treatment (excluding rituximab) following a minimum of 12 weeks of therapy and this assessment must be submitted to the Department of Human Services no later than 4 weeks from the date that course was ceased. Rituximab patients must be assessed following a minimum of 12 weeks after the first infusion, and this assessment must be submitted to the Department of Human Services within 4 weeks.</p> <p>Where a response assessment is not submitted to the Department of Human Services within these timeframes, the patient will be deemed to have failed to respond to treatment with that bDMARD. For second and subsequent courses of PBS-subsidised bDMARD (excluding rituximab) treatment it is recommended that a patient is reviewed in the month prior to completing their current course of treatment and that where required an application is submitted to the Department of Human Services no later than 2 weeks prior to the patient completing their current treatment course.</p> <p>Abatacept patients: Patients are eligible to receive one I.V. loading dose when commencing treatment with the subcutaneous formulation. For these patients two prescriptions are required, the first prescription for the I.V. loading dose for sufficient vials for one dose based on the patient's weight with no repeats. The second prescription for the pre-filled syringes, with a maximum quantity of 4 and up to 3 repeats, must be submitted with the initial application.</p> <p>Rituximab patients: A further application may be submitted to the Department of Human Services 24 weeks after the first infusion initial PBS-subsidised treatment. New baselines may be submitted with this application if appropriate.</p> <p>(b) Continuing treatment. Following the completion of an initial treatment course with a specific bDMARD (excluding rituximab), a patient may qualify to receive up to 24 weeks of continuing treatment with that drug providing they have demonstrated an adequate response to treatment. The patient remains eligible to receive continuing bDMARD treatment with the same drug in courses of up to 24 weeks providing they continue to sustain the response. It is recommended that a patient be reviewed the month prior to completing their current course of treatment to ensure uninterrupted bDMARD supply.</p>
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	<p>Rituximab patients: A patient may qualify to receive a further course of treatment (every 24 weeks) with this agent providing they have demonstrated an adequate response to treatment following a minimum of 12 weeks after the first infusion of their most recent treatment with rituximab. The patient remains eligible to receive a course of rituximab every 24 weeks providing they continue to demonstrate a response as specified in the restriction. Where a response assessment is not submitted to the Department of Human Services within these timeframes, the patient will be deemed to have failed to respond to treatment with that bDMARD.</p> <p>(2) Swapping therapy</p> <p>Once initial treatment with the first PBS-subsidised bDMARD is approved, a patient may swap to an alternate bDMARD without having to requalify with respect to the indices of disease severity (i.e. the erythrocyte sedimentation rate (ESR), the C-reactive protein (CRP) levels and the joint count) or the prior non-bDMARD therapy requirements, except if the patient has had a break in therapy of more than 24 months. However the requirement for concomitant treatment with methotrexate, where it applies, must be met for each bDMARD trialed.</p> <p>Patients who are not able to complete a minimum of 12 weeks of an initial treatment course will be deemed to have failed treatment with that agent.</p> <p>A patient may trial an alternate bDMARD at any time, regardless of whether they are receiving therapy (initial or continuing) with a bDMARD at the time of the application. However, they cannot swap to a particular bDMARD if they have failed to respond to prior treatment with that drug.</p> <p>Abatacept: Patients swapping from I.V. abatacept to subcutaneous abatacept will not be eligible for an I.V. loading dose when commencing treatment with the subcutaneous formulation.</p> <p>Rituximab: In order to trial rituximab, a patient must have trialed and failed to demonstrate a response to at least 1 PBS-subsidised TNF-alfa antagonist treatment.</p> <p>To ensure a patient receives the maximum treatment opportunities allowed under the interchangeability arrangements, it is important that they are assessed for response to every course of treatment approved, within the timeframes specified in the relevant restriction.</p> <p>PBS subsidy does not allow for patients to receive treatment with another PBS-subsidised biological agent during the required treatment-free period applying to patients who have demonstrated a response to their most recent course of rituximab. This means that patients who have demonstrated a response to a course of rituximab must have a PBS-subsidised biological agent therapy treatment-free period of at least 22 weeks, immediately following the second infusion, before swapping to an alternate bDMARD. Patients who fail to respond to rituximab and who qualify and wish to trial a course of an alternate bDMARD may do so without having to have any treatment-free period.</p> <p>To avoid confusion, an application for a patient who wishes to swap to an alternate bDMARD should be accompanied by the approved authority prescription or remaining repeats for the bDMARD the patient is ceasing.</p> <p>(3) Baseline measurements to determine response.</p> <p>The Department of Human Services will determine whether a response to treatment has been</p>
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	<p>demonstrated based on the baseline measurements of the joint count, ESR and/or CRP submitted with the first authority application for a bDMARD. However, prescribers may provide new baseline measurements any time that an initial treatment authority application is submitted and the Department of Human Services will assess response according to these revised baseline measurements.</p> <p>To ensure consistency in determining response, the same indices of disease severity used to establish baseline at the commencement of treatment with each initial treatment application must be provided used for all subsequent continuing treatment applications. Therefore, where only an ESR or CRP level is provided at baseline, an ESR or CRP level respectively must be provided used to determine response. Similarly, where the baseline active joint count is based on total active joints (i.e. more than 20 active joints), response will be determined according to the reduction in the total number of active joints. Where the baseline is determined on total number of major joints, the response must be demonstrated on the total number of major joints.</p> <p>Except as specified under the Initial 1 treatment restriction, a baseline joint count and ESR and/or CRP should be performed whilst the patient is still on treatment or within 1 month of ceasing prior treatment. Applications under the Initial 1 treatment restriction for new or re-commencing patients must include a joint count and ESR and/or CRP measured at the completion of the 6 month intensive DMARD trial, but prior to ceasing DMARD therapy.</p>
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The split to the rituximab for RA continuing restriction into First Continuing and Subsequent Continuing restrictions has flow-on implications for the current PBS listing for the reference brand of rituximab (MabThera), as listed below.

Name, Restriction, Manner of administration and form	Max. Qty	№.of Rpts	Proprietary Manufacturer	Name and
RITUXIMAB 500 MG/50 ML I.V. INFUSION, 1 VIAL	1	0	Mabthera	Roche Products Pty Ltd

Category / Program	Section 100 – Highly Specialised Drugs Program (Public and Private Hospital)
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:	Severe active rheumatoid arthritis
Treatment phase:	Initial treatment - Initial 1 (patient recommencing treatment after a break of more than 24 months)
Restriction Level / Method:	<input checked="" type="checkbox"/> Authority Required - In Writing
Treatment criteria:	Must be treated by a rheumatologist; OR Must be treated by a clinical immunologist with expertise in the management of rheumatoid arthritis.
Clinical criteria:	Patient must have severe active rheumatoid arthritis, AND Patient must have failed to respond to at least 1 PBS-subsidised tumour necrosis factor (TNF) alfa antagonist, AND Patient must have received no PBS-subsidised treatment with a biological disease modifying anti-rheumatic drug (bDMARD) for this condition in the previous 24 months,

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	<p>AND Patient must not have failed previous PBS-subsidised treatment with rituximab for this condition, and have not already failed, or ceased to respond to, PBS-subsidised bDMARD treatment for this condition 5 times, AND</p> <ul style="list-style-type: none"> • Patient must have failed, in the 24 months immediately prior to the date of the application, to achieve an adequate response to a trial of at least 6 months of intensive treatment with disease modifying anti-rheumatic drugs (DMARDs) which must include at least 3 months continuous treatment with each of at least 2 DMARDs, one of which must be methotrexate at a dose of at least 20 mg weekly and one of which must be: (i) hydroxychloroquine at a dose of at least 200 mg daily; or (ii) leflunomide at a dose of at least 10 mg daily; or (iii) sulfasalazine at a dose of at least 2 g daily; OR • Patient must have failed, in the 24 months immediately prior to the date of the application, to achieve an adequate response to a trial of at least 6 months of intensive treatment with DMARDs which, if methotrexate is contraindicated according to the Therapeutic Goods Administration (TGA)-approved Product Information or cannot be tolerated at a 20 mg weekly dose, must include at least 3 months continuous treatment with each of at least 2 of the following DMARDs: (i) hydroxychloroquine at a dose of at least 200 mg daily; and/or (ii) leflunomide at a dose of at least 10 mg daily; and/or (iii) sulfasalazine at a dose of at least 2 g daily; OR • Patient must have failed, in the 24 months immediately prior to the date of the application, to achieve an adequate response to a trial of at least 6 months of intensive treatment with DMARDs which, if 3 or more of methotrexate, hydroxychloroquine, leflunomide and sulfasalazine are contraindicated according to the relevant TGA-approved Product Information or cannot be tolerated at the doses specified above, must include at least 3 months continuous treatment with each of at least 2 DMARDs, with one or more of the following DMARDs being used in place of the DMARDs which are contraindicated or not tolerated: (i) azathioprine at a dose of at least 1 mg/kg per day; and/or (ii) cyclosporin at a dose of at least 2 mg/kg/day; and/or (iii) sodium aurothiomalate at a dose of 50 mg weekly, <p>AND Patient must not receive more than 2 infusions of rituximab under this restriction, AND The treatment must be given concomitantly with methotrexate at a dose of at least 7.5 mg weekly.</p>
Population criteria:	Patient must be aged 18 years or older.
Prescriber Instructions	<p>For the purposes of this restriction 'TNF' alfa antagonist means adalimumab, certolizumab pegol, etanercept, golimumab and infliximab.</p> <p>For the purposes of this restriction bDMARD means abatacept, adalimumab, certolizumab pegol, etanercept, golimumab, infliximab, rituximab, tocilizumab or tofacitinib.</p> <p>If methotrexate is contraindicated according to the TGA-approved product information or cannot be tolerated at a 20 mg weekly dose, the application must include details of the contraindication or intolerance including severity to methotrexate. The maximum tolerated dose of methotrexate must be documented in the application, if applicable.</p> <p>The application must include details of the DMARDs trialed, their doses and duration of treatment, and all relevant contraindications and/or intolerances including severity.</p> <p>The requirement to trial at least 2 DMARDs for periods of at least 3 months each can be met using single agents sequentially or by using one or more combinations of DMARDs.</p> <p>If the requirement to trial 6 months of intensive DMARD therapy with at least 2 DMARDs</p>

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	<p>cannot be met because of contraindications and/or intolerances of a severity necessitating permanent treatment withdrawal to all of the DMARDs specified above, details of the contraindication or intolerance including severity and dose for each DMARD must be provided in the authority application.</p> <p>The authority application must be made in writing and must include: (1) completed authority prescription form(s); and (2) a completed Rheumatoid Arthritis PBS Authority Application - Supporting Information Form; and (3) a signed patient acknowledgement.</p> <p>Assessment of a patient's response to an initial course of treatment must be made at least 12 weeks after the first infusion so that there is adequate time for a response to be demonstrated. This assessment, which will be used to determine eligibility for continuing treatment, must be submitted to the Department of Human Services within 4 weeks of the date it was conducted. Where a response assessment is not undertaken and submitted to the Department of Human Services within these timeframes, the patient will be deemed to have failed to respond to treatment with rituximab.</p> <p>A patient whose most recent course of PBS-subsidised therapy was with rituximab and whose response to this treatment is sustained for more than 12 months, may apply for a further course of rituximab under the <i>First</i> Continuing treatment restriction.</p> <p>If a patient who fails to demonstrate a response to treatment with rituximab under this restriction they will not be eligible to receive further PBS-subsidised treatment with this drug for this condition.</p> <p>A patient who fails to demonstrate a response to rituximab treatment and who qualifies to trial an alternate bDMARD according to the interchangeability arrangements for bDMARDs for the treatment of severe rheumatoid arthritis, may do so without having to have a 22 week treatment-free period.</p> <p>The following criteria indicate failure to achieve an adequate response and must be demonstrated in all patients at the time of the initial application: an elevated erythrocyte sedimentation rate (ESR) greater than 25 mm per hour or a C-reactive protein (CRP) level greater than 15 mg per L; AND either (a) a total active joint count of at least 20 active (swollen and tender) joints; or (b) at least 4 active joints from the following list of major joints: (i) elbow, wrist, knee and/or ankle (assessed as swollen and tender); and/or (ii) shoulder and/or hip (assessed as pain in passive movement and restriction of passive movement, where pain and limitation of movement are due to active disease and not irreversible damage such as joint destruction or bony overgrowth).</p> <p>The joint count and ESR and/or CRP must be determined at the completion of the 6 month intensive DMARD trial, but prior to ceasing DMARD therapy. All measures must be no more than one month old at the time of initial application.</p> <p>If the above requirement to demonstrate an elevated ESR or CRP cannot be met, the application must state the reasons why this criterion cannot be satisfied.</p> <p>Where the baseline joint count is based on total active joints (i.e. more than 20 active joints), response will be determined according to the reduction in the total number of active joints. Where the baseline is determined on total number of major joints, the response must be demonstrated on the total number of major joints. If only an ESR or CRP is provided with the initial application, the same marker will be used to determine response</p>
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<p>Administrative Advice</p>	<p>The Department of Human Services website (www.humanservices.gov.au) has details of the toxicities, including severity, which will be accepted for the following purposes:</p> <p>(a) exempting a patient from the requirement to undertake a minimum 3 month trial of methotrexate at a 20 mg weekly dose;</p> <p>(b) substituting azathioprine, cyclosporin or sodium aurothiomalate for another DMARD as part of the 6 month intensive DMARD trial;</p> <p>(c) exempting a patient from the requirement for a 6 month trial of intensive DMARD therapy.</p>
<p>Administrative Advice</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 Complex Drugs Reply Paid 9826 HOBART TAS 7001</p>
<p>Administrative Advice 3</p>	<p>TREATMENT OF ADULT PATIENTS WITH SEVERE ACTIVE RHEUMATOID ARTHRITIS</p> <p>The following information applies to the prescribing under the Pharmaceutical Benefits Scheme (PBS) of the biological disease modifying antirheumatic drugs (bDMARDs) for adults with severe active rheumatoid arthritis. Where the term bDMARD appears in the following notes and restrictions it refers to the tumour necrosis factor (TNF) alfa antagonists (adalimumab, certolizumab pegol, etanercept, golimumab, infliximab), the chimeric anti-CD20 monoclonal antibody (rituximab), the interleukin-6 inhibitor (tocilizumab), the T-cell co-stimulation modulator (abatacept) and the Janus-associated kinase (JAK) inhibitor (tofacitinib).</p> <p>Patients are eligible for PBS-subsidised treatment with only 1 of the above disease modifying anti-rheumatic drugs at any 1 time.</p> <p>In order to be eligible to receive PBS-subsidised treatment with rituximab, a patient must have already failed to demonstrate a response to at least 1 course of treatment with a PBS-subsidised TNF-alfa antagonist.</p> <p>A patient receiving PBS-subsidised bDMARD therapy may swap to an alternate bDMARD without having to experience a disease flare. Under these interchangeability arrangements:</p> <ul style="list-style-type: none"> - a patient may continue to receive long-term treatment with a PBS-subsidised bDMARD while they continue to show a response to therapy, - a patient cannot trial and fail, or cease to respond to, the same PBS-subsidised bDMARD more than once, and - once a patient has either failed or ceased to respond to treatment 5 times, they will not be eligible to receive further PBS-subsidised bDMARDs for the treatment of rheumatoid arthritis. <p>For patients who have failed PBS-subsidised treatment with 2 or 3 TNF-alfa antagonists prior to 1 August 2010 please contact the Department of Human Services on 1800 700 270. A patient whose most recent course of PBS-subsidised therapy was with rituximab and whose response to this treatment is sustained for more than 12 months, may apply for a further course of rituximab under the <i>First Continuing treatment</i> restriction. A patient who has failed fewer than 5 bDMARDs and who has a break in therapy of less than 24 months may</p>

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	<p>commence a further course of treatment with a bDMARD without having to requalify under the Initial 1 treatment restriction. A patient who has failed fewer than 5 bDMARDs and who has had a break in therapy of longer than 24 months must requalify for treatment under the Initial 1 treatment restriction. The length of a treatment break is measured from the date the most recent treatment with PBS-subsidised bDMARD treatment is stopped to the date of the new application for treatment with a bDMARD.</p> <p>(1) How to prescribe PBS-subsidised bDMARD therapy after 1 August 2010.</p> <p>(a) Initial treatment. Applications for initial treatment should be made where:</p> <ul style="list-style-type: none">(i) a patient has received no prior PBS-subsidised bDMARD treatment and wishes to commence such therapy, excluding rituximab (Initial 1); or(ii) a patient wishes to re-commence treatment with a bDMARD following a break in PBS-subsidised therapy of more than 24 months (Initial 1); or(iii) a patient has received prior PBS-subsidised (initial or continuing) bDMARD therapy and wishes to trial an alternate agent (Initial 2) [further details are under 'Swapping therapy' below]; or(iv) a patient wishes to re-commence treatment with a specific bDMARD following a break of less than 24 months in PBS-subsidised therapy with that agent (Initial 2). <p>Initial applications for new or re-commencing patients (Initial 1) must include a joint count and ESR and/or CRP measured at the completion of the 6-month intensive DMARD trial, but prior to ceasing DMARD therapy.</p> <p>Initial treatment authorisations will be limited to provide a maximum of 16 weeks of therapy for abatacept, adalimumab, etanercept, golimumab, tocilizumab and tofacitinib, 18 to 20 weeks of therapy with certolizumab pegol (depending upon the dosing regimen), 22 weeks of therapy for infliximab and 2 infusions of rituximab.</p> <p>A patient must be assessed for response to any course of initial PBS-subsidised treatment (excluding rituximab) following a minimum of 12 weeks of therapy and this assessment must be submitted to the Department of Human Services no later than 4 weeks from the date that course was ceased. Rituximab patients must be assessed following a minimum of 12 weeks after the first infusion, and this assessment must be submitted to the Department of Human Services within 4 weeks.</p> <p>Where a response assessment is not submitted to the Department of Human Services within these timeframes, the patient will be deemed to have failed to respond to treatment with that bDMARD. For second and subsequent courses of PBS-subsidised bDMARD (excluding rituximab) treatment it is recommended that a patient is reviewed in the month prior to completing their current course of treatment and that where required an application is submitted to the Department of Human Services no later than 2 weeks prior to the patient completing their current treatment course.</p> <p>Abatacept patients: Patients are eligible to receive one I.V. loading dose when commencing treatment with the subcutaneous formulation. For these patients two prescriptions are required, the first prescription for the I.V. loading dose for sufficient vials for one dose based on the patient's weight with no repeats. The second prescription for the pre-filled syringes, with a maximum quantity of 4 and up to 3 repeats, must be submitted with the initial application.</p> <p>Rituximab patients: A further application may be submitted to the Department of Human Services 24 weeks after the first infusion. New baselines may be submitted with this application if appropriate.</p>
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	<p>(b) Continuing treatment. Following the completion of an initial treatment course with a specific bDMARD (excluding rituximab), a patient may qualify to receive up to 24 weeks of continuing treatment with that drug providing they have demonstrated an adequate response to treatment. The patient remains eligible to receive continuing bDMARD treatment with the same drug in courses of up to 24 weeks providing they continue to sustain the response. It is recommended that a patient be reviewed the month prior to completing their current course of treatment to ensure uninterrupted bDMARD supply.</p> <p>Rituximab patients: A patient may qualify to receive a further course of treatment (every 24 weeks) with this agent providing they have demonstrated an adequate response to treatment following a minimum of 12 weeks after the first infusion of their most recent treatment with rituximab. The patient remains eligible to receive a course of rituximab every 24 weeks providing they continue to demonstrate a response as specified in the restriction. Where a response assessment is not submitted to the Department of Human Services within these timeframes, the patient will be deemed to have failed to respond to treatment with that bDMARD.</p> <p>(2) Swapping therapy</p> <p>Once initial treatment with the first PBS-subsidised bDMARD is approved, a patient may swap to an alternate bDMARD without having to requalify with respect to the indices of disease severity (i.e. the erythrocyte sedimentation rate (ESR), the C-reactive protein (CRP) levels and the joint count) or the prior non-bDMARD therapy requirements, except if the patient has had a break in therapy of more than 24 months. However the requirement for concomitant treatment with methotrexate, where it applies, must be met for each bDMARD trialled.</p> <p>Patients who are not able to complete a minimum of 12 weeks of an initial treatment course will be deemed to have failed treatment with that agent.</p> <p>A patient may trial an alternate bDMARD at any time, regardless of whether they are receiving therapy (initial or continuing) with a bDMARD at the time of the application. However, they cannot swap to a particular bDMARD if they have failed to respond to prior treatment with that drug.</p> <p>Abatacept: Patients swapping from I.V. abatacept to subcutaneous abatacept will not be eligible for an I.V. loading dose when commencing treatment with the subcutaneous formulation.</p> <p>Rituximab: In order to trial rituximab, a patient must have trialled and failed to demonstrate a response to at least 1 PBS-subsidised TNF-alfa antagonist treatment.</p> <p>To ensure a patient receives the maximum treatment opportunities allowed under the interchangeability arrangements, it is important that they are assessed for response to every course of treatment approved, within the timeframes specified in the relevant restriction.</p> <p>PBS subsidy does not allow for patients to receive treatment with another PBS-subsidised biological agent during the required treatment-free period applying to patients who have demonstrated a response to their most recent course of rituximab. This means that patients who have demonstrated a response to a course of rituximab must have a PBS-subsidised biological agent therapy treatment-free period of at least 22 weeks, immediately following the second infusion, before swapping to an alternate bDMARD. Patients who fail to respond to rituximab and who qualify and wish to trial a course of an alternate bDMARD may do so</p>
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	<p>without having to have any treatment-free period.</p> <p>To avoid confusion, an application for a patient who wishes to swap to an alternate bDMARD should be accompanied by the approved authority prescription or remaining repeats for the bDMARD the patient is ceasing.</p> <p>(3) Baseline measurements to determine response.</p> <p>The Department of Human Services will determine whether a response to treatment has been demonstrated based on the baseline measurements of the joint count, ESR and/or CRP submitted with the first authority application for a bDMARD. However, prescribers may provide new baseline measurements any time that an initial treatment authority application is submitted and the Department of Human Services will assess response according to these revised baseline measurements.</p> <p>To ensure consistency in determining response, the same indices of disease severity used to establish baseline at the commencement of treatment with each initial treatment application must be provided used for all subsequent continuing treatment applications. Therefore, where only an ESR or CRP level is provided at baseline, an ESR or CRP level respectively must be provided used to determine response. Similarly, where the baseline active joint count is based on total active joints (i.e. more than 20 active joints), response will be determined according to the reduction in the total number of active joints. Where the baseline is determined on total number of major joints, the response must be demonstrated on the total number of major joints.</p> <p>Except as specified under the Initial 1 treatment restriction, a baseline joint count and ESR and/or CRP should be performed whilst the patient is still on treatment or within 1 month of ceasing prior treatment. Applications under the Initial 1 treatment restriction for new or re-commencing patients must include a joint count and ESR and/or CRP measured at the completion of the 6 month intensive DMARD trial, but prior to ceasing DMARD therapy.</p>
<p>Administrative Advice</p>	<p>Biosimilar policy</p> <p><i>Prescribing of the biosimilar brand, Riximyo, is encouraged for treatment naïve patients.</i></p> <p><i>Encouraging biosimilar prescribing for treatment naïve patients is Government policy. A viable biosimilar market is expected to result in reduced costs for biological medicines, allowing the Government to reinvest in new treatments. Further information can be found on the Biosimilar Awareness Initiative webpage (www.health.gov.au/biosimilars).</i></p>

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Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Manufacturer	Name and
RITUXIMAB 500 MG/50 ML INJECTION, 1 VIAL	1	0	MabThera	Roche Products Pty Ltd

Category / Program	Section 100 – Highly Specialised Drugs Program (Public and Private Hospital)
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:	Severe active rheumatoid arthritis
Treatment phase:	Initial treatment - Initial 2 (change or re-commencement of treatment after break of less than 24 months)
Restriction Level / Method:	<input checked="" type="checkbox"/> Authority Required - In Writing
Treatment criteria:	Must be treated by a rheumatologist; OR Must be treated by a clinical immunologist with expertise in the management of rheumatoid arthritis.
Clinical criteria:	Patient must have a documented history of severe active rheumatoid arthritis, AND Patient must have failed to respond to at least 1 PBS-subsidised tumour necrosis factor (TNF) alfa antagonist, AND Patient must have received prior PBS-subsidised biological disease modifying anti-rheumatic drug (bDMARD) treatment for this condition and are eligible to receive further bDMARD therapy, AND Patient must not receive more than 2 infusions of rituximab under this restriction, AND The treatment must be given concomitantly with methotrexate at a dose of at least 7.5 mg weekly.
Population criteria:	Patient must be aged 18 years or older.
Prescriber Instructions	For the purposes of this restriction 'TNF' alfa antagonist means adalimumab, certolizumab pegol, etanercept, golimumab and infliximab. For the purposes of this restriction bDMARD means abatacept, adalimumab, certolizumab pegol, etanercept, golimumab, infliximab, rituximab, tocilizumab or tofacitinib. The authority application must be made in writing and must include: (a) completed authority prescription form(s); and (b) a completed Rheumatoid Arthritis PBS Authority Application - Supporting Information Form. Applications for a patient who has received PBS-subsidised treatment with rituximab and who wishes to re-commence therapy with this drug, must be accompanied by evidence of a response to the patient's most recent course of PBS-subsidised rituximab treatment, within the timeframes specified below. Where the most recent course of PBS-subsidised rituximab treatment was approved under either of the initial 1 or 2 treatment restrictions, the patient must have been assessed for response at least 12 weeks after the first infusion. This assessment must be submitted no later than 4 weeks from the date of the assessment. A patient may qualify to receive a further course of treatment (every 24 weeks) with this agent

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	<p>provided they have demonstrated an adequate response to treatment following a minimum of 12 weeks after the first infusion of their most recent treatment with rituximab. The demonstration of response must be submitted within 4 weeks of assessment.</p> <p>Where a response assessment is not undertaken and submitted within these timeframes, the patient will be deemed to have failed to respond to treatment with rituximab.</p> <p>A patient whose most recent course of PBS-subsidised therapy was with rituximab and whose response to this treatment is sustained for more than 12 months, may apply for a further course of rituximab under the <i>First Continuing</i> treatment restriction.</p> <p>If a patient fails to demonstrate a response to treatment with rituximab under this restriction they will not be eligible to receive further PBS-subsidised treatment with this drug for this condition.</p> <p>If a patient fails to demonstrate a response to a treatment with rituximab and who qualify to trial an alternate bDMARD according to the interchangeability arrangements for bDMARDs for the treatment of severe rheumatoid arthritis, may do so without having to have a 22 week treatment-free period.</p> <p>An adequate response to treatment is defined as: an ESR no greater than 25 mm per hour or a CRP level no greater than 15 mg per L or either marker reduced by at least 20% from baseline; AND either of the following: (a) a reduction in the total active (swollen and tender) joint count by at least 50% from baseline, where baseline is at least 20 active joints; or (b) a reduction in the number of the following active joints, from at least 4, by at least 50%: (i) elbow, wrist, knee and/or ankle (assessed as swollen and tender); and/or (ii) shoulder and/or hip (assessed as pain in passive movement and restriction of passive movement, where pain and limitation of movement are due to active disease and not irreversible damage such as joint destruction or bony overgrowth).</p>
Administrative Advice	<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 Complex Drugs Reply Paid 9826 HOBART TAS 7001</p>
Administrative Advice 3	<p>As per "Administrative Advice 3" within the RA Initial Treatment – Initial 1 restriction above</p>

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Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Manufacturer	Name and
RITUXIMAB 500 MG/50 ML INJECTION, 1 VIAL	1	0	MabThera	Roche Products Pty Ltd

Category / Program	Section 100 – Highly Specialised Drugs Program (Public and Private Hospital)
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:	Severe active rheumatoid arthritis
Treatment phase:	<i>First continuing treatment</i>
Restriction Level / Method:	<input checked="" type="checkbox"/> Authority Required - In Writing
Treatment criteria:	Must be treated by a rheumatologist; OR Must be treated by a clinical immunologist with expertise in the management of rheumatoid arthritis.
Clinical criteria:	Patient must have a documented history of severe active rheumatoid arthritis, AND Patient must have demonstrated an adequate response to treatment with this drug, AND Patient must have received this drug as their most recent course of PBS-subsidised biological disease modifying anti-rheumatic drug (bDMARD) treatment for this condition, AND Patient must not receive more than 2 infusions of rituximab under this restriction. AND The treatment must be given concomitantly with methotrexate at a dose of at least 7.5 mg weekly.
Population criteria:	Patient must be aged 18 years or older.
Prescriber Instructions	For the purposes of this restriction bDMARD means abatacept, adalimumab, certolizumab pegol, etanercept, golimumab, infliximab, rituximab, tocilizumab or tofacitinib. An adequate response to treatment is defined as: an ESR no greater than 25 mm per hour or a CRP level no greater than 15 mg per L or either marker reduced by at least 20% from baseline; AND either of the following: (a) a reduction in the total active (swollen and tender) joint count by at least 50% from baseline, where baseline is at least 20 active joints; or (b) a reduction in the number of the following active joints, from at least 4, by at least 50%: (i) elbow, wrist, knee and/or ankle (assessed as swollen and tender); and/or (ii) shoulder and/or hip (assessed as pain in passive movement and restriction of passive movement, where pain and limitation of movement are due to active disease and not irreversible damage such as joint destruction or bony overgrowth). <i>Where the baseline active joint count is based on total active joints (i.e. more than 20 active joints), response will be determined according to the reduction in the total number of active joints. Where the baseline is determined on total number of major joints, the response must be demonstrated on the total number of major joints. If only an ESR or CRP level is provided with the initial application, the same marker will be used to determine response.</i> The authority application must be made in writing and must include: (a) completed authority prescription form(s); and (b) a completed Rheumatoid Arthritis PBS Authority Application - Supporting Information

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	<p>Form.</p> <p><i>The application for first continuing treatment with this drug must be accompanied by an assessment of response to a minimum of 12 weeks of treatment with an initial treatment course. This assessment must be submitted no later than 4 weeks from the cessation of that treatment course.</i></p> <p>A patient may qualify to receive a further course of treatment (every 24 weeks) with this agent provided they have demonstrated an adequate response to treatment following a minimum of 12 weeks after the first infusion of their most recent treatment with rituximab. The demonstration of response must be submitted within 4 weeks of assessment.</p> <p>Where a response assessment is not undertaken and submitted within these timeframes, the patient will be deemed to have failed to respond to treatment with rituximab.</p> <p>A patient whose most recent course of PBS subsidised therapy was with rituximab and whose response to this treatment is sustained for more than 12 months, may apply for a further course of rituximab under the Continuing treatment restriction.</p> <p>If a patient fails to demonstrate a response to treatment with rituximab under this restriction will not be eligible to receive further PBS-subsidised treatment with this drug for this condition.</p>
Administrative Advice	<p>Note No increase in the maximum quantity or number of units may be authorised. Note No increase in the maximum number of repeats may be authorised.</p>
Administrative Advice	<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 Complex Drugs Reply Paid 9826 HOBART TAS 7001</p>
Administrative Advice 3	<p>As per "Administrative Advice 3" within the RA Initial Treatment – Initial 1 restriction above</p>

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Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Manufacturer	Name and
RITUXIMAB 500 MG/50 ML INJECTION, 1 VIAL	1	0	MabThera	Roche Products Pty Ltd

Category / Program	Section 100 – Highly Specialised Drugs Program (Public and Private Hospital)
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:	Severe active rheumatoid arthritis
Treatment phase:	Subsequent continuing treatment
Restriction Level / Method:	<input checked="" type="checkbox"/> Authority Required - In Writing
Treatment criteria:	Must be treated by a rheumatologist; OR Must be treated by a clinical immunologist with expertise in the management of rheumatoid arthritis.
Clinical criteria:	Patient must have a documented history of severe active rheumatoid arthritis, AND Patient must have demonstrated an adequate response to treatment with this drug, AND Patient must have received this drug as the most recent course of PBS-subsidised biological disease modifying anti-rheumatic drug (bDMARD) treatment for this condition, AND Patient must not receive more than 2 infusions of rituximab <i>per subsequent continuing treatment course authorised</i> under this restriction, AND The treatment must be given concomitantly with methotrexate at a dose of at least 7.5 mg weekly.
Population criteria:	Patient must be aged 18 years or older.
Prescriber Instructions	For the purposes of this restriction bDMARD means abatacept, adalimumab, certolizumab pegol, etanercept, golimumab, infliximab, rituximab, tocilizumab or tofacitinib. The authority application must be made in writing and must include: (a) completed authority prescription form(s); and (b) a completed Rheumatoid Arthritis PBS Authority Application - Supporting Information Form. A patient may qualify to receive a further course of treatment (every 24 weeks) with this agent provided they have demonstrated an adequate response to treatment following a minimum of 12 weeks after the first infusion of their most recent treatment with rituximab. The demonstration of response must be submitted within 4 weeks of assessment. Where a response assessment is not undertaken and submitted within these timeframes, the patient will be deemed to have failed to respond to treatment with rituximab. A patient whose most recent course of PBS-subsidised therapy was with rituximab and whose response to this treatment is sustained for more than 12 months, may apply for a further course of rituximab under the <i>Subsequent Continuing treatment</i> restriction. An adequate response to treatment is defined as: an ESR no greater than 25 mm per hour or a CRP level no greater than 15 mg per L or either marker reduced by at least 20% from baseline;

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	<p>AND either of the following:</p> <p>(a) a reduction in the total active (swollen and tender) joint count by at least 50% from baseline, where baseline is at least 20 active joints; or</p> <p>(b) a reduction in the number of the following active joints, from at least 4, by at least 50%:</p> <p>(i) elbow, wrist, knee and/or ankle (assessed as swollen and tender); and/or</p> <p>(ii) shoulder and/or hip (assessed as pain in passive movement and restriction of passive movement, where pain and limitation of movement are due to active disease and not irreversible damage such as joint destruction or bony overgrowth).</p> <p><i>Where the baseline active joint count is based on total active joints (i.e. more than 20 active joints), response will be determined according to the reduction in the total number of active joints. Where the baseline is determined on total number of major joints, the response must be demonstrated on the total number of major joints. If only an ESR or CRP level is provided with the initial application, the same marker will be used to determine response.</i></p> <p><i>All applications for subsequent continuing treatment with this product must include a measurement of response to the prior course of therapy. This assessment must be submitted no later than 4 weeks from the cessation of that treatment course.</i></p> <p><i>Where a response assessment is not undertaken and submitted within these timeframes, the patient will be deemed to have failed to respond to treatment with this drug.</i></p> <p>If a patient fails to demonstrate a response to treatment with rituximab under this restriction will not be eligible to receive further PBS-subsidised treatment with this drug for this condition.</p>
Administrative Advice	<p>Note No increase in the maximum quantity or number of units may be authorised.</p> <p>Note No increase in the maximum number of repeats may be authorised.</p>
Administrative Advice	<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 Complex Drugs Reply Paid 9826 HOBART TAS 7001</p>
Administrative Advice 3	<p>As per “Administrative Advice 3” within the RA Initial Treatment – Initial 1 restriction above</p>

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

The sponsor had no comment.