

Changes have been made to this item. Details of the corrigendum are at the end of this document.

5.27 RITUXIMAB

**Solution for I.V. infusion 100 mg in 10 mL,
Solution for I.V. infusion 500 mg in 50 mL,
Ruxience[®],
Pfizer Australia Pty Ltd**

1 Purpose of Submission

- 1.1 The Category 3 submission sought Section 100 Efficient Funding of Chemotherapy (EFC) and Highly Specialised Drug (HSD) program listings of a new brand of biosimilar medicine rituximab (Ruxience[®]) in the form of solution for I.V. infusion 100 mg in 10 mL and 500 mg in 50 mL for the same conditions as its PBS-listed reference biologic brand (Mabthera[®]) and other PBS-listed biosimilar brands (Riximyo[®] and Truxima[®]).

2 Background

- 2.1 Ruxience was registered on the Australian Register of Therapeutic Goods (ARTG) on 3 March 2021 and was determined to be biosimilar to Mabthera. Ruxience has the same registered indications as Mabthera.
- 2.2 Mabthera was delisted from the PBS at the request of the sponsor (Roche) on 1 October 2021.

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

3 Requested listing

- 3.1 The proposed Authority Required listings are for all indications for which Riximyo and Truxima are currently PBS listed:
- Non-Hodgkin's lymphoma (NHL) – EFC
 - Chronic lymphocytic leukaemia (CLL) – EFC
 - Rheumatoid arthritis (RA) – HSD
 - Granulomatosis with polyangiitis (Wegener's granulomatosis) (GPA) – HSD
 - Microscopic polyangiitis (MPA) – HSD
 - Previously untreated or Relapsed/refractory CD20 positive acute lymphoblastic leukaemia – EFC

- 3.2 The restrictions have not been reproduced due to their length. The sponsor requested restriction details and wording that is identical to the existing rituximab listings. At its September 2021 Intracycle meeting, the PBAC advised the removal of the existing administrative notes related to the biosimilar uptake drivers for the remaining PBS listed biosimilar brands of rituximab. The PBAC also recommended that the PBS listings for all listed brands of rituximab be changed to Unrestricted Benefit listings.
- 3.3 The PBAC advised the proposed Ruxience listing be made consistent with the Riximyo and Truxima listings.
- 3.4 The PBAC advised, under Section 101(4AACD) of the Act, in the Schedule of Pharmaceutical Benefits the same form and strength of Riximyo and Truxima should be treated as equivalent ('a'-flagged) to each other for the purpose of substitution for its HSD listings.
- 3.5 EFC medicines are governed by the *National Health (Efficient Funding of Chemotherapy) Special Arrangement 2011* and subsection 33(2) allows substitution of brands with the same chemotherapy drug.

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

4 Comparator

- 4.1 The submission nominated the reference biologic of rituximab, Mabthera, as the main comparator. Mabthera was delisted from the PBS on 1 October 2021. However, there is no requirement that a reference brand must be currently listed on the PBS to be used as a comparator. Based on the TGA regulatory requirements for biosimilars, a suitable reference brand must:
- be a biological medicine that has been registered in Australia based on full quality, safety and efficacy data ('the Australian reference medicine'), and
 - have been marketed in Australia for a substantial period and have a volume of marketed use so that there is likely to be a substantial body of acceptable data regarding the safety and efficacy for the approved indications

Mabthera was first registered on the ARTG in 1998 and accepted as the reference brand for the currently PBS listed biosimilar brands of rituximab. Although Mabthera was delisted from the PBS it remains registered on the ARTG. The PBAC advised Mabthera was an appropriate comparator.

- 4.2 The submission also nominated other biosimilar brands, Truxima and Riximyo, for the purpose of substitution. The PBAC advised these were appropriate.

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

5 Consideration of the evidence

Sponsor hearing

5.1 There was no hearing for this item.

Consumer comments

5.2 The PBAC noted that this item received no consumer comments.

Clinical trials

5.3 The submission presented the following clinical study reports.

Table 1. Studies presented in the submission

Study ID	Protocol/Publication Title	Publication Citation
B3281001	A Randomized, Double-Blind, Study Comparing the Pharmacokinetics and Pharmacodynamics, and Assessing the Safety of PF-05280586 and Rituximab in Subjects with Active Rheumatoid Arthritis on a Background of Methotrexate (MTX) who have had an Inadequate Response to One or More Tumor Necrosis Factor (TNF) Antagonist Therapies	Clinical Study Report date: 09 April 2018
B3281006	A Phase 3, Randomized, Double-Blind Study of PF-05280586 Versus Rituximab for the First-Line Treatment of Patients With CD20-Positive, Low Tumor Burden, Follicular Lymphoma	Clinical Study Report dates: 16 March 2018, 29 March 2018
B3281004	Extension study evaluating treatment with PF-05280586 Versus rituximab in subjects with active rheumatoid arthritis Who have participated in other pf-05280586 clinical trials	Clinical Study Report date: 06 February 2017

Source: submission

5.4 The clinical studies presented in the submission formed part of the TGA submission to register Ruxience as a biosimilar to Mabthera. The TGA Delegate Overview noted that the data presented in TGA submission demonstrated that Ruxience is biosimilar to the Australian reference product, Mabthera, with comparable pharmacokinetics, efficacy, safety, and immunogenicity.

5.5 *As a Category 3 submission, no evaluation of the clinical evidence was undertaken.*

Clinical claim

5.6 The submission claimed that Ruxience was:

- biosimilar to Mabthera
- non-inferior in terms of comparative effectiveness and safety to Mabthera.

5.7 The PBAC considered that Ruxience was biosimilar to Mabthera based on the TGA approval.

Pricing consideration

5.8 The submission requested listing Ruxience on a cost-minimisation basis to Mabthera at a 1:1 unit equivalence for Ruxience to Mabthera. The submission considered Ruxience is expected to substitute directly with Mabthera 100 mg vial and 500 mg vial. The submission also considered Ruxience will directly replace Riximyo and Truxima on the PBS and would not change the overall use of rituximab on the PBS.

- 5.9 The submission stated there would be no change in the utilisation of other pharmaceuticals, medical devices or other related products or services that would already be used in conjunction with rituximab.
- 5.10 The proposed approved ex-manufacturer price (AEMP) for Ruxience is the same as the AEMP of Truxima and Riximyo listed in the PBS in August 2021. The submission presented no economic or financial analysis.

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

6 PBAC Outcome

- 6.1 The PBAC recommended the listing of a new brand of biosimilar medicine rituximab (Ruxience) in the form of solution for I.V. infusion 100 mg in 10 mL and 500 mg in 50 mL under the same conditions as the currently listed biosimilar brands (Riximyo and Truxima). The PBAC's recommendation for listing was based on, among other matters, its assessment that the cost-effectiveness of Ruxience would be acceptable if it were cost-minimised to Riximyo and Truxima for the following indications:
- Non-Hodgkin's lymphoma (NHL) – EFC
 - Chronic lymphocytic leukaemia (CLL) – EFC
 - Rheumatoid arthritis (RA) – HSD
 - Granulomatosis with polyangiitis (Wegener's granulomatosis) (GPA) – HSD
 - Microscopic polyangiitis (MPA) – HSD
 - Previously untreated or Relapsed/refractory CD20 positive acute lymphoblastic leukaemia – EFC.
- 6.2 The PBAC advised the equi-effective doses are a 1:1 ratio of Ruxience with the relevant strengths of Riximyo and Truxima.
- 6.3 The PBAC advised that the listing of Ruxience should be consistent with the other biosimilar brands of rituximab, inclusive of the changes it advised for these listings at the September 2021 PBAC Intracycle meeting. These changes were to remove the existing administrative notes related to the biosimilar uptake drivers for the remaining PBS listed biosimilar brands of rituximab and for all listed brands of rituximab to be changed to Unrestricted Benefit listings
- 6.4 The PBAC advised, under Section 101(4AACD) of the Act, in the Schedule of Pharmaceutical Benefits that the same form and strength of Ruxience, Riximyo and Truxima should be treated as equivalent ('a'-flagged) to each other for the purpose of substitution for those pharmaceutical benefits listed within the *National Health (Highly Specialised Drugs Program) Special Arrangement 2021*.

- 6.5 The PBAC noted the submission did not provide any estimated financial implications to the PBS. The PBAC considered that Ruxience would substitute for use within the existing rituximab market and consequently the listing would be nil net cost to the government.
- 6.6 The PBAC noted that its recommendation was on a cost-minimisation basis and advised that, because Ruxience is not expected to provide a substantial and clinically relevant improvement in efficacy, or reduction of toxicity over Riximyo and Truxima, or not expected to address a high and urgent unmet clinical need given the presence of an alternative therapy, the criteria prescribed by the *National Health (Pharmaceuticals and Vaccines – Cost Recovery) Regulations 2009* for Pricing Pathway A were not met.
- 6.7 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 rituximab brand (Ruxience) for the following listings:
- Non-Hodgkin’s lymphoma (NHL) – EFC
 - Chronic lymphocytic leukaemia (CLL) – EFC
 - Previously untreated or Relapsed/refractory CD20 positive acute lymphoblastic leukaemia – EFC.
- 7.2 Add new rituximab brand (Ruxience) with schedule equivalence ('a' flag) for the same indications as Riximyo and Truxima for the following listings:
- Rheumatoid arthritis (RA) – HSD
 - Granulomatosis with polyangiitis (Wegener’s granulomatosis) (GPA) – HSD
 - Microscopic polyangiitis (MPA) – HSD.

MEDICINAL PRODUCT medicinal product pack	Proprietary Name, Manufacturer
RITUXIMAB Solution for I.V. infusion 100 mg in 10 mL, Solution for I.V. infusion 500 mg in 50 mL	Ruxience, Pfizer Australia Pty Ltd

This restriction may be subject to further review. Should there be any changes made to the restriction the Sponsor will be informed.

8 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised through the Pharmaceutical Benefits Scheme (PBS) in Australia. It considers applications regarding the listing of medicines on the PBS and provides advice about other matters relating to the operation of the PBS in this context. A PBAC decision in relation to PBS listings does not necessarily represent a final PBAC view about the merits of the medicine or the circumstances in which it should be made available through the PBS. The PBAC welcomes applications containing new information at any time.

9 Sponsor's Comment

The sponsor had no comment.

10 Corrigendum

The following changes were made:

Change made	Date of revision
Paragraph 3.1, 6.1 and 7.1: Transcription error where an indication was missed. It was carried over from sponsor submission. The indication was 'Previously untreated or Relapsed/refractory CD20 positive acute lymphoblastic leukaemia – EFC'.	April 2022