14.10 RITUXIMAB RESTRICTIONS
Solution for subcutaneous injection containing rituximab 1400 mg in 11.7 mL, Mabthera SC, Roche Products Pty Ltd

1. Purpose of request

1.1. The Department requested PBAC confirmation that the proposed rituximab restrictions changes meet the intended purpose of consolidation for the treatment of CD20 positive lymphoid cancers.

2. Background

2.1. At the July 2017 meeting, the PBAC recommended a new single consolidated listing for induction therapy in combination with PBS-subsidised chemotherapy for all CD20 positive lymphoid cancers to replace the applicable current restrictions for rituximab. The recommendation is applicable to all strengths of rituximab currently PBS listed. The recommendation was implemented on 1 Feb 2018.

2.2. Currently, the PBS-listed strengths of rituximab available are 100 mg and 500 mg vials for IV administration, as well as 1400mg vials for subcutaneous administration. The 100 mg and 500 mg vials (IV injections) are listed under EFC (Public/Private), whereas the 1400 mg vials (SC injections) are listed under General Schedule and S100 (CT).

2.3. PBS-listed indications are the same across all of the three strengths, except the indication for chronic lymphocytic leukaemia which is only available for 100 mg and 500 mg (IV administration). The table below highlights the restriction changes before and after 1 Feb 2018 for rituximab.

Current listing under EFC (public and private) – 100 mg and 500 mg vials	Listing from 1 Feb 2018 under EFC (public and private) – 100 mg and 500 mg vials	Restriction wording
Maintenance stage III or IV CD20 positive follicular B-cell non-Hodgkin lymphoma	RETAINED	(Maintenance therapy restriction (1 of 3) – existing restriction – no change made) **Indication**: Stage III or IV CD20 positive follicular B-cell non-Hodgkin's lymphoma **Treatment Phase**: Maintenance therapy **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, 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.
Previously untreated aggressive CD20 positive non-Hodgkin lymphoma	REMOVED	
Previously untreated symptomatic indolent CD20 positive non-Hodgkin lymphoma in combination with chemotherapy	REMOVED	
Relapsed or refractory Stage III or IV CD20 positive follicular B-cell non-Hodgkin lymphoma	RETAINED	(Maintenance therapy restriction (2 of 3) – existing restriction – no change made) **Indication**: Relapsed or refractory Stage III or IV CD20 positive follicular B-cell non-Hodgkin's lymphoma Treatment Phase: Maintenance therapy **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, AND Patient must not receive more than 8 cycles or 2 years duration of treatment, whichever comes first, under this restriction.

Relapsed or refractory low-grade B-cell non-Hodgkin lymphoma	REMOVED	
Relapsed or refractory follicular B-cell non-Hodgkin lymphoma	REMOVED	
Chronic Lymphocytic leukaemia	REMOVED	
	NEW RESTRICTION ADDED: Induction/re-induction for previously untreated or relapsed/refractory CD20 positive lymphoid cancer	(Induction/re-induction restriction) **Indication**: Previously untreated or relapsed/refractory CD20 positive lymphoid cancer. **Clinical criteria**: 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. **Prescriber Instructions**: An initial dose of rituximab must be administered with rituximab intravenous injection. Subsequent doses may be administered with either intravenous or subcutaneous rituximab. No more than 8 doses in total as per course of treatment will be allowed for lymphoma or chronic lymphocytic leukaemia. 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).
	NEW RESTRICTION ADDED: Maintenance therapy for previously untreated or relapsed/refractory CD20 positive acute lymphoblastic leukaemia	(Maintenance therapy restriction) **Indication**: Previously untreated or relapsed/refractory CD20 positive acute lymphoblastic leukaemia. **Treatment Phase:** Maintenance therapy **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.

3. Current situation

3.1. Prior to implementing the PBAC recommendation for a 1 February 2018 listing, the sponsor was given an opportunity to review the restrictions. The sponsor replied on 1 December 17 with no objections to the new restriction wordings. Upon reviewing the Summary of Changes for the 1 February 2018 listing, where individual listings are attached to specific strengths, the sponsor requested that the yellow highlighted text as shown above be removed from the restriction for the 1400mg SC strength as this strength does not have TGA approval for CLL. The sponsor further mentioned that a new strength of 1600mg for SC administration that does have TGA approval for CLL was recommended by PBAC for listing for CLL at the March 17 meeting. To date, the sponsor has requested that listing of the 1600mg not proceed.

3.2. The PBAC noted that ALL (shown in blue highlighted) is also not a TGA approved indication for 1400 mg nor 100 mg and 500 mg, however the sponsor did not dispute its inclusion for all the three strengths.

4. Matters considered by the PBAC

4.1. The PBAC considered the following matters:

a) The PBAC was asked to confirm if its intention is to have a new simple and consolidated restriction for CD20 positive lymphoid cancer, and if so whether all three strengths should be listed for CLL. Or alternatively, if the CLL indication should be removed from the 1400mg SC strength as requested by the sponsor.
b) If the CLL indication is removed for the 1400mg strength due to not being registered for this indication and as requested by the sponsor, should the ALL indications be removed for all strengths?
c) If the PBAC decides to retain the CLL listing for the 1400mg SC strength, if the sponsor decides to proceed to listing with the 1600mg SC strength, should text be added to the restriction to note that the 1600mg strength is indicated for CLL such as 'The 1600 mg vial for subcutaneous injection is indicated for CLL' or leave treatment choice up to the treating physician's discretion?

5. PBAC outcome

5.1. The PBAC confirmed that its intent was to simplify and consolidate the evidence-based rituximab restriction for CD20 positive lymphoid cancers. The PBAC recommended that the chronic lymphocytic leukaemia indication

be removed from the 1400mg SC strength as requested by the sponsor because it is not the standard dose for CLL.

5.2. The PBAC recommended that the ALL indication be retained for all strengths as this in in line with the above stated intention for a simple and consolidated evidence-based restriction for CD20 positive lymphoid cancers.

5.3. The PBAC further recommended that upon the 1600mg vial listing proceeding, that the text 'The 1600 mg vial for subcutaneous injection is indicated for CLL' be added to the listing.

5.4. The PBAC noted that this submission is not eligible for an Independent Review as it received a positive recommendation.

Outcome:
Recommended

6. Recommended listing

6.1. Amend the current restrictions under S85 and S100 (CT) for the 1400 mg strength as follows:

Category / Program	GENERAL – General Schedule (Code GE) Schedule 100 Chemotherapy (CT)
Prescriber type:	☐Dental ☒Medical Practitioners ☐Nurse practitioners ☐Optometrists ☐Midwives
PBS Indication:	Previously untreated or relapsed/refractory CD20 positive lymphoid cancer
Treatment phase:	Induction or re-induction therapy
Restriction Level / Method:	☐Restricted benefit ☐Authority Required - In Writing ☐Authority Required - Telephone ☒Streamlined
Clinical criteria:	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. .

Prescriber Instructions	An initial dose of rituximab must be administered with rituximab intravenous injection. Subsequent doses may be administered with either intravenous or subcutaneous rituximab. No more than 8 doses in total as per course of treatment will be allowed for lymphoma ~~or chronic lymphocytic leukaemia~~. 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).

6.2. Amend the restrictions (recommended by not yet listed) under S85 and S100 (CT) for the 1600 mg strength as follows:

Category / Program	GENERAL – General Schedule (Code GE) Schedule 100 Chemotherapy (CT)
Prescriber type:	☐Dental ☒Medical Practitioners ☐Nurse practitioners ☐Optometrists ☐Midwives
PBS Indication:	Previously untreated or relapsed/refractory CD20 positive lymphoid cancer
Treatment phase:	Induction or re-induction therapy
Restriction Level / Method:	☐Restricted benefit ☐Authority Required - In Writing ☐Authority Required - Telephone ☒Streamlined
Clinical criteria:	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. .
Prescriber Instructions	An initial dose of rituximab must be administered with rituximab intravenous injection. Subsequent doses may be administered with either intravenous or subcutaneous rituximab. No more than 8 doses in total as per course of treatment will be allowed for lymphoma or chronic lymphocytic leukaemia. 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).
Administrative advice	*The 1600 mg vial for subcutaneous injection is indicated for CLL*