11.02 INOTUZUMAB OZOGAMICIN, Powder for I.V. infusion 1 mg, Besponsa®, Pfizer Australia Pty Ltd

1 Purpose of Submission

1.1 The Category 3 submission requested PBAC advice on the termination of the existing shared Risk Sharing Arrangement (RSA) applying to inotuzumab ozogamicin (herein referred to as 'inotuzumab').

1.2 The PBAC was asked to advise whether the inclusion of inotuzumab in the RSA shared with blinatumomab remained appropriate given, among other matters, the stable and low utilisation of inotuzumab compared to rising blinatumomab utilisation.

2 Background

2.1 Inotuzumab is supplied via the Section 100 Efficient Funding of Chemotherapy Program for the treatment of relapsed or refractory (R/R) CD22-positive B-cell precursor acute lymphoblastic leukaemia (B-ALL). It was recommended for PBS listing on a cost-minimisation basis compared with blinatumomab (in November 2018).

2.2 At the time of its listing in May 2019, inotuzumab was required to join the existing RSA with blinatumomab, reflecting the then closely-aligned treatment settings for the two medicines. The PBAC had recommended an increase to the expenditure caps due to expected sequential use. The caps were further expanded on 1 October 2019 when the listings for both medicines were extended to Philadelphia chromosome (Ph)positive patients in the R/R setting.

2.3 The PBS listing for blinatumomab has expanded a further two times to include: newly diagnosed patients with B-ALL in complete remission with minimal residual disease (MRD) following chemotherapy (1 December 2019); and then newly diagnosed patients who are MRD-negative following induction chemotherapy (1 March 2025).[1] The shared expenditure caps were increased on both occasions (although Pfizer declined to implement the most recent increase offered for inotuzumab).

2.4 MBS items for MRD testing were introduced in July 2024, which increased identification of patients eligible for MRD-directed therapies.

[1] The current terminology for MRD is measurable residual disease.

Previous PBAC consideration

2.5 The table below outlines the relevant PBAC considerations for blinatumomab and inotuzumab, and advice regarding the RSA.

Table 1: Relevant PBAC considerations of blinatumomab and inotuzumab

Drug	Indication	Positive PBAC Recommendation	PBS listing	Key RSA advice	Key RSA history
Blinatumomab	R/R Ph negative B-ALL	November 2016	1 May 2017	Due to the highly uncertain financial estimates, the PBAC recommended financial caps based on the estimated treated population and less than 42 vials per patient. The PBAC reaffirmed that the restriction should remain silent on age. However, given the significant uncertainty around several aspects of the estimates and the high ICER, the PBAC did not consider that this was sufficient grounds for any upward revision of the expenditure cap (para 6.17, Nov 16 Public Summary Document [PSD]).	RSA established
Inotuzumab ozogamicin	R/R CD22 positive Ph negative B-ALL	November 2018	1 May 2019	The PBAC considered that inotuzumab would need to join the existing RSA terms in place for blinatumomab, and that the associated financial caps could only be increased by the number of additional treatment courses expected with sequential use permitted. The PBAC considered that the number of treatment courses with blinatumomab or inotuzumab would increase by no more than 50% with sequential use permitted (para 7.18, Nov 18 PSD)	Variation with increase in caps
Inotuzumab ozogamicin	Expanded R/R to include Ph positive B-ALL	May 2019	1 October 2019	The PBAC considered that the existing RSAs for blinatumomab and inotuzumab would need to be updated to include the estimated cost of treatment of new patients with Ph+ disease. The PBAC noted that any increase to the associated financial caps should only be based on the number of additional treatment courses expected with the extension of the existing listing to patients with Ph+ disease based on the financial estimates. The PBAC considered that the financial estimates should account for no more than 50% of patients receiving sequential therapy with these agents consistent with its previous advice (para 4.17, inotuzumab May 19 PSD & para 5.9, blinatumomab May 19 PSD).	
Blinatumomab	Expanded R/R to include Ph positive B-ALL	May 2019	1 October 2019		Variation with increase in caps

Drug	Indication	Positive PBAC Recommendation	PBS listing	Key RSA advice	Key RSA history
Blinatumomab	Newly diagnosed B-ALL in haematological complete remission with minimal residual disease (MRD) following chemotherapy	July 2019	1 December 2019	The PBAC noted that the resubmission indicated the sponsor's preference for a single set of caps for blinatumomab to encompass use in both the MRD and relapsed/refractory setting. The PBAC considered that if a single RSA subsidy cap was to be enacted, the cost of both blinatumomab and inotuzumab and a 40% decrease in use in the relapsed/refractory setting would need to be accounted for when calculating a total cap for both medicines across both settings. On this basis, the PBAC considered that an alternative arrangement which would have the same effect of maintaining overall caps for blinatumomab across both populations would also be appropriate (para 5.9, July 19 PSD).	Variation with increase in caps
Blinatumomab	Expanded newly diagnosed listing to include MRD-negative following induction chemotherapy	November 2024	1 March 2025	The PBAC advised that an RSA would be appropriate to address the uncertainty regarding the magnitude of benefit in the proposed PBS population, which is broader than the E1910 trial (e.g. in age and Ph chromosome status), and around the cost offsets associated with the reduced use of blinatumomab and inotuzumab ozogamicin in the relapsed/refractory setting. The PBAC advised that blinatumomab for MRD-negative B-ALL should join the existing RSA for blinatumomab and inotuzumab ozogamicin. The PBAC advised that the expenditure caps should be adjusted to incorporate (i) the cost offsets associated with reduced use of blinatumomab and inotuzumab ozogamicin in the relapsed/refractory setting, and (ii) the increased use of blinatumomab in the MRD-negative setting. Noting that the revised RSA would account for all populations (i.e. MRD-positive and MRD-negative and relapsed/refractory disease), the PBAC considered that a rebate for use above the expenditure caps would be reasonable (para 12.4, Nov 24 PSD).	New RSA with increase in caps (increase offer not accepted by Pfizer)

Drug	Indication	Positive PBAC Recommendation	PBS listing	Key RSA advice	Key RSA history
Blinatumomab	Recommended amendments to the newly-diagnosed listing: • to include consolidation treatment for Ph+ patients who have achieved complete haematological response to induction treatment with a TKI and corticosteroids, without requiring prior combination with chemotherapy; and • to remove the requirement for all patients to be MRD negative in order to be eligible for continuing treatment.	December 2025	TBA	The PBAC considered that the proposed changes were clinically appropriate and that the expanded listing would remain cost-effective given the expected clinical outcomes for patients. The PBAC advised that the expansion to include Ph+ patients previously treated with a TKI (who are intolerant to chemotherapy) was likely captured in previous financial estimates for blinatumomab, but that the removal of the MRD-based continuation criteria would be expected to result in a financial impact, which should be incorporated into the expenditure caps under the existing RSA, accounting for offsets in the relapsed or refractory setting (blinatumomab, Web Outcomes, December 2025 PBAC meeting).	-

Previous Departmental interactions regarding the RSA

2.6 In October 2024, the sponsor requested termination of the RSA for inotuzumab. The nominal term of the Deed had ended in April 2022 however the RSA cap from the last year of the Deed continued to apply to subsequent years (and had not been exceeded to the end of April 2024, Year 5).

2.7 In January 2025, the Department advised that the Commonwealth was not in a position to agree terminating the RSA as the PBAC had, in November 2024, recommended that the extended listing of blinatumomab be included in the existing RSA. Shortly after, the Department offered the sponsor a Deed Variation to increase the Year 6 subsidisation cap. The sponsor declined to agree the increase.

2.8 In March 2025, the Department provided a Replacement Deed to Pfizer that included the new increased subsidisation caps and reimbursement level that were agreed with the sponsor of blinatumomab to reflect its expanded listing. The sponsor declined to agree the new RSA.

3 Current Situation

3.1 The submission requested the PBAC review the RSA on the basis that it considered it was no longer necessary or fit for purpose. The submission cited reasons including: stable and low utilisation and expenditure for inotuzumab (which it expected to decline); “no risk” of leakage due to being a Written Authority; the diverging indications between inotuzumab and blinatumomab; and the sponsor’s difficulty in determining its risk exposure in terms of a future breach in the shared caps. The Secretariat noted that inotuzumab is available through Telephone/Online Authority in the consolidation treatment phase. There are also other shared RSAs PBAC has recommended where indications may not be identical across the medicines which may encompass different stages of a disease.

3.2 The table below outlines the shared subsidisation caps for inotuzumab and blinatumomab, Commonwealth Payment over the 6 years of the shared RSA, and the percentage of the cap reached. A [redacted]% rebate applies for use exceeding the caps.

3.3 In its Pre-PBAC response, the sponsor reiterated its view that the continued inclusion of inotuzumab in the shared RSA is no longer appropriate, citing divergence in PBS listings, utilisation trends and the allocation of financial risk relative to blinatumomab.

Table 2: Commonwealth Payment vs current Risk Sharing Arrangement caps

	Year 1 (May 2019-Apr 2020)	Year 2 (May 2020-Apr 2021)	Year 3 (May 2021-Apr 2022)	Year 4 (May 2022-Apr 2023)	Year 5 (May 2023-Apr 2024)	Year 6 (May 2024-Apr 2025)
Current caps	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted][b]
Deed Commonwealth Payment – inotuzumab ozogamicin	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]
Deed Commonwealth Payment – blinatumomab	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted][a]
Actual Commonwealth Payment	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]
Market Share – inotuzumab ozogamicin	[redacted]%	[redacted]%	[redacted]%	[redacted]%	[redacted]%	[redacted]%[a]
Market Share - blinatumomab	[redacted]%	[redacted]%	[redacted]%	[redacted]%	[redacted]%	[redacted]%[redacted]
% of cap reached	[redacted]%	[redacted]%	[redacted]%	[redacted]%	[redacted]%	[redacted]%[a]

[a] February 2026 estimate, not yet finalised

[b] A new cap arrangement was proposed to Pfizer but was not accepted

3.4 The table below outlines the new subsidisation caps agreed with the sponsor of blinatumomab to reflect its expanded listing inclusive of newly diagnosed B-ALL patients who are MRD-negative following induction chemotherapy (noting that the shared caps are inclusive of sequential use with inotuzumab in the R/R setting). These arrangements were declined by Pfizer. A new rebate of [redacted]% (previously [redacted]%) applies for use exceeding the caps.

Table 3: New subsidisation caps

Year 1 (March 2025-Feb 2026)	Year 2 (March 2026-Feb 2027)	Year 3 (March 2027-Feb 2028)	Year 4 (March 2028-Feb 2029)	Year 5 (March 2029-Feb 2030)
$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]

3.5 As the sponsor declined to agree to the revised caps associated with the expanded listing of blinatumomab, inotuzumab continues to operate under the original shared RSA cap. Year 6 is estimated to have been exceeded by approximately [redacted]%. This breach results in the sponsor being liable for [redacted]% reimbursement of Commonwealth expenditure above the cap, calculated with reference to inotuzumab's market share.

3.6 Had the sponsor accepted the revised RSA terms, a breach would not have been anticipated in the March 2025 – February 2026 period. In line with the Deed terms,

the existing inotuzumab Deed continues to operate applying the final year Deed cap ($[redacted]).

3.7 The submission sought retrospective amendments to both the past May 2024 to April 2025 year of the existing Deed, as well as termination of the RSA going forward. The Secretariat noted that reimbursements for the periods elapsed have already been accrued and reflect the arrangements under the current Deed of Agreement between the Commonwealth and the sponsor.

3.8 The submission stated that, "the proposed increases to the shared RSA caps have been implemented without consultation with Pfizer, and that Pfizer does not have visibility of the uptake assumptions, cost offsets, or the confidential effective price of blinatumomab which would be required to determine the risk of exceeding the proposed SCs [subsidisation caps] over the 5-year Replacement Deed term. Pfizer is also not in a position to accurately assess or validate any future reimbursement which may be due if the annual CP [Commonwealth Payment] under the Deed were to exceed the RSA" (p1).

3.9 The Secretariat noted that the increases to the blinatumomab caps were negotiated and implemented in line with standard practice.

Consumer Comments

3.10 There were no consumer comments for this item.

4 PBAC Outcome

4.1 The PBAC provided advice regarding the sponsor's request to terminate the Risk Sharing Arrangement (RSA) for inotuzumab ozogamicin for the treatment of acute lymphoblastic leukaemia (ALL). The PBAC advised that it is reasonable to reconsider the current arrangements of the RSA in the context of the divergence in PBS listings and utilisation patterns between inotuzumab ozogamicin and blinatumomab since the RSA was established.

4.2 The PBAC noted that inotuzumab ozogamicin has remained restricted to the relapsed or refractory setting and that utilisation and Commonwealth expenditure for inotuzumab ozogamicin has remained low and relatively stable over time. In contrast, the PBAC noted that blinatumomab has undergone additional PBS listing expansions, including newly diagnosed and MRD-directed populations, with corresponding increases in utilisation and expenditure. The PBAC considered that the growth in expenditure under the shared RSA was largely attributable to blinatumomab rather than inotuzumab ozogamicin.

4.3 The PBAC considered that in the context of low, stable utilisation and a declining share of use within the RSA, that the available financial data reflected the current and likely ongoing place of inotuzumab ozogamicin in the market. The PBAC advised that there

was minimal risk of utilisation outside of the current eligible population (or risk to the cost-effectiveness of inotuzumab ozogamicin).

4.4 The PBAC recalled that inotuzumab ozogamicin was originally recommended for PBS listing on a cost-minimisation basis against blinatumomab and that the RSA expenditure caps had been increased to include inotuzumab ozogamicin and sequential use of blinatumomab and inotuzumab ozogamicin. The PBAC noted that no new clinical uncertainties or changes to the PBS restriction had been identified for inotuzumab ozogamicin since listing.

4.5 The PBAC considered that the original rationale for including inotuzumab ozogamicin in a shared RSA with blinatumomab, which was to manage uncertain financial estimates and a high ICER, had diminished over time. The PBAC noted that increases from the expanded blinatumomab populations (i.e. newly diagnosed B-ALL) had been included in the same RSA with the expectation of realising offsets in the relapsed/refractory setting, and managing total financial implications of targeted therapies in ALL. However, the PBAC acknowledged the submission's contention that inotuzumab ozogamicin utilisation was limited in the context of the broader indications within the RSA and that usage in the relapsed/refractory setting had remained relatively stable.

4.6 The PBAC therefore advised that termination of the RSA for inotuzumab ozogamicin would be reasonable. In providing this advice, the PBAC considered that inotuzumab ozogamicin would continue to be cost-effective in the approved PBS population in the absence of an RSA. The PBAC considered that this advice is open to reconsideration should the sponsor of inotuzumab ozogamicin apply to have the eligible PBS population expanded.

4.7 The PBAC noted that as there are no changes to the patient cohort, restriction or pricing components for inotuzumab ozogamicin, and the market for inotuzumab ozogamicin remains stable, there are no additional financial implications.

4.8 The PBAC advised that its advice related to future arrangements only and did not extend to retrospective amendment of obligations under the existing Deed.

Outcome:
Advice provided

5 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.

6 Sponsor's Comment

Pfizer welcomes the PBAC's advice that termination of the RSA for inotuzumab ozogamicin is reasonable in the context of the divergence in PBS listings and utilisation patterns since the RSA was established. Risk sharing arrangements should be open to review, and where they are no longer fit-for-purpose (such as where utilisation, PBS listings, or other factors have evolved) their continuation should be reconsidered to ensure they remain proportionate and justified.