3.02 ALECTINIB, Capsule 150 mg, Alecensa®, Roche Products Pty Ltd

1 Purpose

1.1 To present correspondence from ALK Positive Australia and Medical Oncology Group of Australia (MOGA) in relation to the May 2025 recommendation for alectinib for adjuvant therapy of non-small cell lung cancer (NSCLC) and advice regarding re-treatment with an anaplastic lymphoma kinase (ALK) inhibitor in the metastatic setting; and

1.2 To provide an update on the status of the pricing proposal for the May 2025 alectinib recommendation.

2 Background

Previous PBAC consideration

2.1 At its May 2025 meeting, PBAC had recommended the listing of alectinib for ALK-positive as adjuvant therapy after tumour resection.

2.2 The PBAC had considered that alectinib would be cost effective at a lower price, using the revised model parameters from the pre-PBAC response, to achieve an ICER consistent with that presented in the submission.

2.3 The PBAC had advised that consistent with other high-cost adjuvant listings (e.g. osimertinib, immune checkpoint inhibitors), re-treatment [with alectinib] in the metastatic setting should not be permitted, and furthermore use of adjuvant alectinib therapy would preclude use of any ALK TKI in the recurrent setting. The PBAC had advised it would like to increase patient access in these situations, but evidence was required to determine a cost-effective price in the re-treatment setting. This may include targeted use of TKIs to treat emerging resistance mutations. Data such as overall response rate and time on treatment would be informative, as well as expected number of patients and financial implications.

2.4 The PBAC had considered that the claim of superior clinical effectiveness was well supported by the ALINA trial in terms of a clinically meaningful benefit for disease-free survival (DFS). The PBAC had noted that there was no signal of overall survival (OS) benefit at the prespecified DFS interim. The PBAC was concerned that longer OS follow up may not establish an OS benefit given the availability of effective TKI treatments post recurrence and had requested that the committee be provided with mature OS data when available, to allow an opportunity to re-evaluate the cost-effectiveness of adjuvant alectinib.

2.5 The submission had presented a cost-utility analysis based on the DFS outcomes of the ALINA trial with extrapolation to 20 years and a base case ICER of $25,000 to < $35,000 per QALY gained. The economic model applied 2 adjustments to the extrapolated DFS, including the limitation of treatment effect where the model allowed the treatment effect of alectinib to decrease over time and a cure adjustment where the model allowed patients to be considered cured (i.e. not experience recurrence or disease-related death) if they were disease-free for a certain number of years.

2.6 The PBAC had agreed with the ESC that a 15-year time horizon was more appropriate given the precedents with atezolizumab and osimertinib and could be used to mitigate uncertainty in the estimated long-term costs and outcomes. The PBAC had also agreed with the ESC that the cure assumption was reasonable, although the survival benefit may be overestimated.

2.7 The ESC had recommended a revised base case and the pre-PBAC response, despite disagreeing with the revisions, had accepted the ESC's proposal and also updated the end-of-life costs, which PBAC had considered appropriate. The pre-PBAC response had noted the resultant revised base case was within the range of an accepted ICER for osimertinib ($35,000 to < $45,000 per QALY gained).

2.8 The PBAC had considered that although the cure assumption modelled was acceptable and consistent with osimertinib, modelled long-term benefits remained uncertain given immature survival data to support the modelled benefit and use of ALK-TKIs in the metastatic setting following adjuvant treatment, which was not adequately supported by the evidence. To further mitigate this uncertainty the PBAC had considered alectinib would be cost effective in the adjuvant treatment setting with a price reduction to maintain an ICER in the order of $25,000 to < $35,000 per QALY gained, using the revised model from the pre-PBAC response with appropriate DPMQs rather than AEMPs.

2.9 Alectinib is currently listed on the PBS as an Authority Required listing for Stage IIIB (locally advanced) or Stage IV (metastatic) NSCLC.

3 Correspondence from ALK Positive Australia and MOGA

3.1 On 8 July 2025, ALK Positive Australia wrote to the PBAC Secretariat raising concerns regarding the re-treatment restriction in the PBAC's recommendation for adjuvant alectinib, suggesting that current wording of the recommendation would leave patients with no access to the standard of care in the metastatic setting.

3.2 ALK Positive Australia was particularly concerned regarding the impact on priority populations including Aboriginal and Torres Strait Islander peoples, and those living in rural and remote areas. ALK Positive Australia stated that this restriction may further entrench existing inequities in cancer treatment for these groups.

3.3 ALK Positive Australia stated that this restriction did not reflect the biology of ALK-positive NSCLC, that it departed from current PBS practice, and it is not in line with international standards.

3.4 ALK Positive Australia requested the PBAC to:

- clarify whether re-treatment will be entirely excluded under the proposed listing,
- consider a more flexible approach by permitting access to a next line ALK inhibitor following recurrence,
- continue dialogue with clinicians and patient advocates to ensure that long-term outcomes for people with ALK positive NSCLC are not compromised.

3.5 On 14 October 2025, the PBAC Secretary wrote to ALK Positive Australia advising its letter was discussed at the PBAC Executive meeting in August 2025, and that the PBAC Executive had noted ALK Positive Australia's request and matters raised concerning patient access in the metastatic setting.

3.6 On 17 October 2025, the PBAC Secretary wrote to MOGA requesting input on the re-treatment of ALK-positive NSCLC following adjuvant alectinib.

3.7 MOGA indicated it strong support for expanding the availability of third/subsequent-generation ALK TKIs on the PBS to include use in the metastatic or recurrent setting following adjuvant alectinib. Input from MOGA included that:

- There is a clear clinical rationale for re-treatment – the use of lorlatinib upon recurrence after adjuvant alectinib is biologically and clinically equivalent to patients progressing on first line alectinib and aligns with the current PBS listing of lorlatinib.
- The evidence for use of lorlatinib in this setting comes from a phase II study that included a subgroup of 198 patients with ALK-positive, metastatic NSCLC previously treated with ≥1 ALK inhibitor. The overall response rate with lorlatinib among these patients was 47 percent and median progression free survival of 11 months.
- Based on the updated results of the ALINA study, the recurrence rate at 4 years was 25% therefore MOGA estimated the number of patients needing to access an ALK TKI subsequent to adjuvant alectinib would be very modest (likely fewer than 50 patients/year).
- Restricting access to ALK TKIs post-adjuvant therapy would place Australian patients at a significant disadvantage, and recurrence after adjuvant treatment should be managed in accordance with metastatic disease paradigms.

4 Current situation with alectinib pricing proposal

4.1 At the time of the March 2026 PBAC meeting, negotiations with Roche Products Pty Ltd had stalled as the sponsor had not accepted the economic model changes

recommended by PBAC and instead insisted that the economic model must also remove re-treatment for 'consistency' with the PBS recommendation regarding the restriction. This does not factor in the PBAC's advice that the recommended model parameters were intended to address the uncertainty with the overall survival and subsequent ALK use.

4.2 The Pre-PBAC Response put forward two pricing proposals for PBAC consideration: (1) inclusive of subsequent retreatment and (2) precluding subsequent retreatment. The AEMPs were $[redacted] and $[redacted] respectively, and the estimated net R/PBS impacts were $30 million to < $40 million and $20 million to < $30 million respectively.

5 PBAC Outcome

5.1 The PBAC reaffirmed its recommendation that alectinib be made available for the treatment of anaplastic lymphoma kinase (ALK)-positive non-small cell lung cancer (NSCLC) (tumours ≥4 cm or node positive) as adjuvant therapy after tumour resection. Based on the additional input received from consumer and clinical groups, the PBAC provided additional advice that: (1) reaffirmed that re-treatment with alectinib in the locally advanced/metastatic setting would not be permitted following treatment with alectinib as adjuvant therapy after tumour resection; however (2) adjuvant alectinib may be followed by use of another ALK TKI in the locally advanced/metastatic setting. The PBAC maintained that the listing would be cost-effective with the updates to the economic model that it had previously recommended (paragraphs 7.9 to 7.11, 6.01 alectinib Public Summary Document [PSD], May 2025 PBAC meeting).

5.2 The PBAC recalled that it had previously considered it would like to increase patient access to ALK TKI treatment in the metastatic setting following adjuvant alectinib treatment, but had not received adequate evidence to support such a recommendation. The PBAC therefore welcomed the input provided by ALK Positive Australia and Medical Oncology Group of Australia (MOGA), noting the equity issues raised, the clinical rationale and expected outcomes of re-treatment with an ALK TKI following adjuvant alectinib treatment, the supporting evidence provided by MOGA, and the potential modest financial impact given expected clinical outcomes with adjuvant treatment.

5.3 In view of the substantial equity issues associated with preventing re-treatment, while still recognising the uncertainties with respect to overall survival (OS) and subsequent ALK use, the PBAC considered it would be cost-effective to allow treatment with another ALK TKI in the locally advanced/metastatic setting under the economic parameters it had previously recommended.

5.4 The PBAC noted the pre-PBAC response had modelled an estimated net financial impact of $30 million to < $40 million to the R/PBS, inclusive of downstream costs associated with distant recurrence. The PBAC recalled it had previously agreed with the ESC that adjuvant use of alectinib may result in a reduced need for treatment in the later line setting and yet the potential cost savings had not been accounted for in

the analyses (paragraphs 7.12, 6.01 alectinib PSD, May 2025 PBAC meeting). The PBAC noted that the revised approach had not been evaluated and would be subject to finalisation during the post-PBAC processes, including the required alignment with previously recommended changes to the model (paragraphs 7.12 and 7.13, 6.01 alectinib PSD, May 2025 PBAC meeting).

5.5 In terms of the restrictions, the PBAC advised that its previously recommended flow-ons to later line ALK TKIs to preclude re-treatment (paragraphs 8.2 and 8.3, 6.01 alectinib PSD, May 2025 PBAC meeting) would not be required, however flow-ons to later line alectinib would be required to preclude alectinib re-treatment.

5.6 The PBAC again requested that the committee be provided with mature OS data when available, to allow an opportunity to re-evaluate the cost-effectiveness of adjuvant alectinib (paragraphs 7.6, 6.01 alectinib PSD, May 2025 PBAC meeting).

Outcome:
Advice provided

6 Recommended listing

6.1 Add new adjuvant listing:

MEDICINAL PRODUCT medicinal product pack		**PBS item code**	**Max. qty packs**	**Max. qty units**	**№.of Rpts**	**Available brands**
ALECTINIB						
alectinib 150 mg capsule, 4 x 56		NEW	1	224	3	Alecensa
Concept ID (for internal Dept. use)		**Category / Program:** ☒ GENERAL - General Schedule (Code GE)				
		Prescriber type: ☒Medical Practitioners				
		Restriction type: ☒Authority Required (immediate assessment) - Telephone/Online PBS Authorities				
Prescribing rule level		**Administration advice:** Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 888 333.				
		Administrative Advice: No increase in the maximum quantity or number of units may be authorised.				
		Administrative Advice: No increase in the maximum number of repeats may be authorised.				
		Administrative Advice: Special Pricing Arrangements apply.				
Restriction Summary [new1] / Treatment of Concept: [new1A]						
		Episodicity: Resected				
		Severity: [blank]				
		Condition: Non-small cell lung cancer (NSCLC)				
		Indication: Resected non-small cell lung cancer (NSCLC)				
		Treatment Phase: Adjuvant therapy				
		Clinical criteria:				
		Patient must be both: (i) initiating treatment, (ii) untreated with an Anaplastic Lymphoma Kinase-Tyrosine Kinase Inhibitor (ALK-TKI) for non-small cell lung cancer; OR				
		Patient must be continuing existing PBS-subsidised treatment with this drug; OR				

	Patient must be both: (i) transitioning from existing non-PBS to PBS-subsidised supply of this drug, (ii) untreated with ALK-TKI at the time this drug was initiated.
	AND
	Clinical criteria
	The condition must be/have been at least one of: (i) node positive, (ii) at least 4 cm in size,
	AND
	Clinical criteria
	The treatment must be for the purpose of adjuvant therapy following surgical resection,
	AND
	Clinical criteria
	The treatment must be commenced within 26 weeks of surgery,
	AND
	Clinical criteria
	Patient must have evidence of an anaplastic lymphoma kinase (ALK) gene rearrangement in tumour material, defined as either: (i) 15% (or greater) positive cells by fluorescence in situ hybridisation (FISH) testing, (ii) positive next generation sequencing (NGS) testing,
	AND
	Clinical criteria
	Patient must have/have had a WHO performance status of no greater than 1 at treatment initiation with this drug,
	AND
	Clinical criteria
	The treatment must be the sole PBS-subsidised systemic anti-cancer therapy for this condition,
	AND
	Treatment criteria:
	Patient must be undergoing treatment that does not occur beyond the following, whichever comes first: (i) the first instance of disease progression/recurrence, (ii) 24 months of combined non-PBS and PBS-subsidised treatment for this condition from the first administered dose; mark any remaining repeat prescriptions with the words 'cancelled' where (i)/(ii) has occurred.

6.2 Flow-on changes to the alectinib listing in advanced or metastatic setting:

MEDICINAL PRODUCT medicinal product pack	**PBS item code**	**Max. qty packs**	**Max. qty units**	**№.of Rpts**	**Available brands**
ALECTINIB					
alectinib 150 mg capsule, 4 x 56	11226W	1	224	3	Alecensa

Concept ID (for internal Dept. use)		**Category / Program:** ☒ GENERAL - General Schedule (Code GE)
		Prescriber type: ☒Medical Practitioners
		Restriction type: ☒Authority Required (immediate assessment) - Telephone/Online PBS Authorities
Prescribing rule level		**Administration advice:** Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 888 333.
		Administrative Advice: No increase in the maximum quantity or number of units may be authorised.
		Administrative Advice: No increase in the maximum number of repeats may be authorised.
		Administrative Advice: Special Pricing Arrangements apply.
Restriction Summary 15802 / Treatment of Concept: 15759		

	Indication: Stage IIIB (locally advanced) or Stage IV (metastatic) non-small cell lung cancer (NSCLC)
	Treatment Phase: Initial treatment
	Clinical criteria:
	Patient must not have previously received PBS-subsidised treatment with alectinib as adjuvant therapy in resected NSCLC
	AND
	Clinical criteria:
	~~The treatment must be as monotherapy~~ *The treatment must be the sole PBS-subsidised systemic anti-cancer therapy for this condition*
	AND
	Clinical criteria:
	The condition must be non-squamous type non-small cell lung cancer (NSCLC) or not otherwise specified type NSCLC
	AND
	Clinical criteria:
	Patient must have a WHO performance status of 2 or less
	AND
	Clinical criteria:
	Patient must have evidence of an anaplastic lymphoma kinase (ALK) gene rearrangement in tumour material, defined as either: (i) 15% (or greater) positive cells by fluorescence in situ hybridisation (FISH) testing, (ii) positive next generation sequencing (NGS) testing
Restriction Summary 7346 / Treatment of Concept: 7346	
	Indication: Stage IIIB (locally advanced) or Stage IV (metastatic) non-small cell lung cancer (NSCLC)
	Treatment Phase: Continuing treatment
	Clinical criteria:
	~~The treatment must be as monotherapy~~ *The treatment must be the sole PBS-subsidised systemic anti-cancer therapy for this condition*
	AND
	Clinical criteria:
	Patient must have previously received PBS-subsidised treatment with this drug for this ~~condition~~ *indication (i.e. for stage IIIB/IV NSCLC)*
	AND
	Clinical criteria:
	Patient must not develop disease progression while receiving PBS-subsidised treatment with this drug for this condition

6.3 No flow-on changes to any other ALK-TKIs advanced or metastatic setting.

These restrictions may be subject to further review. Should there be any changes made to the restriction the sponsor will be informed.

7 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

Roche welcomes the PBAC's recommendation that alectinib, as adjuvant treatment, may be followed by use of another ALK TKI in the locally advanced/metastatic setting and is committed to finalising the listing to ensure subsidised patient access at the earliest opportunity.

We extend our sincere thanks to ALK Positive Australia and the MOGA for their vital input regarding re-treatment, which successfully addressed critical clinical rationale and patient equity concerns.

Roche sees significant value in how this outcome was achieved with open, constructive dialogue. For future outcomes, we support establishing more responsive collaborative frameworks to minimise the delay in timely access for patients.