7.10 OSIMERTINIB, Tablet, 40mg and 80mg, Tagrisso®, AstraZeneca Pty Ltd

1 Purpose of Application

1.1 The minor resubmission requested a General Schedule, Authority Required listing for osimertinib for the treatment of patients with locally advanced or metastatic epidermal growth factor receptor (EGFR) T790M mutation positive non-small cell lung cancer (NSCLC) who have progressed on or after prior treatment with an EGFR tyrosine kinase inhibitor (TKI).

1.2 The first major submission was rejected by the PBAC at its November 2017 meeting, followed by a subsequent major resubmission that was deferred by the PBAC at its July 2018 meeting.

1.3 The current minor resubmission sought to further clarify the elements of the risk sharing arrangement (RSA) proposed by the sponsor in its pre-PBAC response for the July 2018 resubmission, and address other outstanding matters raised by the PBAC.

2 Requested listing

2.1 At its July 2018 consideration of osimertinib, the PBAC advised that the criterion 'The patients must have a WHO performance status of 2 or less' be added to the proposed restriction to maintain alignment with the restrictions of the currently PBS-listed first line tyrosine kinase inhibitors (TKIs), i.e. erlotinib and gefitinib (paragraph 7.2, osimertinib public summary document (PSD), July 2018 PBAC meeting).

2.2 The restriction proposed in the minor resubmission did not incorporate this criterion. However, the pre-PBAC response accepted the addition of the criterion "Patient must have a WHO performance status of 2 or less".

2.3 The restriction proposed by the minor resubmission has been reproduced below, with suggestions and additions proposed by the Secretariat in italics, and deletions in strikethrough.

Name, Restriction, Manner of administration and form	Max. Qty	**№.of** Rpts	Dispensed Price for Max. Qty	Proprietary Name and Manufacturer	
OSIMERTINIB 80 mg tablet, 30	1	5	$[redacted] (published) $[redacted] (effective)	Tagrisso®	AstraZeneca Pty Ltd

Category / Program	GENERAL – General Schedule (Code GE)
Prescriber type:	☐Dental ☒Medical Practitioners ☐Nurse practitioners ☐Optometrists ☐Midwives
Severity:	Locally advanced (Stage IIIB) or metastatic (Stage IV)
Condition:	Non-small cell lung cancer (NSCLC)
PBS Indication:	Locally advanced (Stage IIIB) or metastatic (Stage IV) non-small cell lung cancer
Treatment phase:	Initial *treatment*
Restriction Level / Method:	☐Restricted benefit ☒Authority Required - In Writing ☐Authority Required - Telephone ☐Authority Required - Emergency ☐Authority Required - Electronic ☐Streamlined
Clinical criteria:	The treatment must be ~~as monotherapy~~ *the sole PBS-subsidised therapy for this condition*, *AND* *Patient must have a WHO performance status of 2 or less,* AND Patient must have progressive disease following treatment with an epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor (TKI).
Population criteria:	Patient must have evidence of a T790M mutation of the EGFR gene in tumour tissue material following progression on or after an EGFR TKI.
Administrative Advice	No increase in the maximum quantity or number of units may be authorised. No increase in the maximum number of repeats may be authorised. Special Pricing Arrangements apply.

Name, Restriction, Manner of administration and form	Max. Qty	**№.of** Rpts	Dispensed Price for Max. Qty	Proprietary Name and Manufacturer	
OSIMERTINIB					
40 mg tablet, 30	1	5	$[redacted] (published) $[redacted] (effective)	Tagrisso®	AstraZeneca Pty Ltd
80 mg tablet, 30	1	5	$[redacted] (published) $[redacted] (effective)		

Category / Program	GENERAL – General Schedule (Code GE)
Prescriber type:	☐Dental ☒Medical Practitioners ☐Nurse practitioners ☐Optometrists ☐Midwives
Severity:	Locally advanced (Stage IIIB) or metastatic (Stage IV)
Condition:	Non-small cell lung cancer (NSCLC)
PBS Indication:	Locally advanced (Stage IIIB) or metastatic (Stage IV) non-small cell lung cancer
Treatment phase:	Continuing *treatment*
Restriction Level / Method:	☐Restricted benefit ~~☒Authority Required - In Writing~~ ☒Authority Required - Telephone ☐Authority Required - Emergency ~~☒Authority Required - Electronic~~ ☐Streamlined
Clinical criteria:	The treatment must be as ~~monotherapy~~ *the sole PBS-subsidised therapy for this condition*, AND Patient must have previously received PBS-subsidised treatment with this drug for this condition, AND Patient must not have progressive disease following PBS-subsidised treatment with this drug for this condition.
Administrative Advice	No increase in the maximum quantity or number of units may be authorised. No increase in the maximum number of repeats may be authorised. Special Pricing Arrangements apply.

Name, Restriction, Manner of administration and form	Max. Qty	№.of Rpts	Dispensed Price for Max. Qty	Proprietary Name and Manufacturer	
OSIMERTINIB					
40 mg tablet, 30	1	5	$[redacted] (published) $[redacted] (effective) $[redacted]	Tagrisso®	AstraZeneca Pty Ltd
80 mg tablet, 30	1	5	(published) $[redacted] (effective)		

Category / Program	GENERAL – General Schedule (Code GE)
Prescriber type:	☐Dental ☒Medical Practitioners ☐Nurse practitioners ☐Optometrists ☐Midwives
Severity:	Locally advanced (Stage IIIB) or metastatic (Stage IV)
Condition:	Non-small cell lung cancer (NSCLC)
PBS Indication:	Locally advanced (Stage IIIB) or metastatic (Stage IV) non-small cell lung cancer
Treatment phase:	Grandfathering *treatment*
Restriction Level / Method:	☐Restricted benefit ☒Authority Required - In Writing ☐Authority Required - Telephone ☐Authority Required - Emergency ☐Authority Required - Electronic ☐Streamlined
Clinical criteria:	Patient must have previously received non-PBS subsidised treatment with this drug for this condition prior to [listing date], AND The treatment must be as ~~monotherapy~~ *the sole PBS-subsidised therapy for this condition*, AND Patient must have progressive disease following treatment with an epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor (TKI). AND Patient must not have progressive disease following treatment with this drug for this condition.
Population criteria:	Patient must have evidence of a T790M mutation of the EGFR gene in tumour tissue material following progression on or after an EGFR TKI.
Prescribing Instructions	A patient may qualify for PBS-subsidised treatment under this restriction once only.
Administrative Advice	No increase in the maximum quantity or number of units may be authorised. No increase in the maximum number of repeats may be authorised. Special Pricing Arrangements apply.

3 Background

3.1 Osimertinib was registered by the TGA on 3 August 2016 for "the treatment of patients with locally advanced or metastatic EGFR T790M mutation-positive non-small cell lung cancer".

3.2 The November 2017 codependent submission requested:

- Pharmaceutical Benefits Schedule (PBS) listing for osimertinib in patients with locally advanced or metastatic epidermal growth factor receptor (EGFR) T790M mutation positive non-small cell lung cancer (NSCLC), who have progressed on or after treatment with an EGFR tyrosine kinase receptor (TKI); and
- Medicare Benefits Schedule (MBS) listing for EGFR T790M mutation testing in patients with locally advanced or metastatic NSCLC, to determine eligibility for access to PBS-subsidised osimertinib.

3.3 At its November 2017 consideration of the codependent submission, the PBAC decided not to recommend osimertinib. Although accepting that osimertinib is more effective than standard chemotherapy, the PBAC advised that the magnitude of incremental overall survival benefit was difficult to determine from the evidence presented in the submission, and this was an important driver of the economic evaluation. Additionally, the PBAC had concerns with other aspects of the economic model, which resulted in a high and overly optimistic estimated incremental cost effectiveness ratio at the price requested by the submission (paragraph 7.1, osimertinib Public Summary Document (PSD), November 2017 PBAC meeting).

3.4 At its November 2017 meeting, the MSAC deferred its advice[1] until such time as the PBAC decides to recommend the PBS listing of osimertinib for the requested population. MSAC foreshadowed its support for a new MBS item for EGFR T790M mutation testing in tumour tissue obtained after progression on or after therapy with a TKI to help determine eligibility for PBS-subsidised second-line osimertinib for the targeted treatment of patients with locally advanced (stage IIIB) or metastatic (stage IV) NSCLC. This support is subject to a PBAC recommendation to list osimertinib once PBAC's concerns regarding the medicines' cost effectiveness are resolved (paragraph 3.4, osimertinib PSD, July 2018 PBAC meeting).

3.5 At its July 2018 meeting, the PBAC deferred making a recommendation to list osimertinib, requesting further clarification from the sponsor regarding the proposed risk sharing arrangement and utilisation estimates. In deciding to defer, the PBAC acknowledged that osimertinib treatment provided a clinical benefit to some patients, but considered that the magnitude of the incremental overall survival benefit was difficult to determine from the available evidence (paragraph 7.1, osimertinib PSD, July 2018 PBAC meeting).

4 Comparator

4.1 The place in therapy and comparator was appropriately unchanged from the previous submission.

5 Consideration of evidence

Sponsor hearing

5.1 There was no hearing for this item.

Consumer comments

5.2 The PBAC noted and welcomed the input received from individuals (5) via the Consumer Comments facility on the PBS website. The comments described a range of

[1] [1] http://www.msac.gov.au/internet/msac/publishing.nsf/Content/1407-public

benefits of treatment with osimertinib, including improvements in quality of life and reduced side effects compared to chemotherapy.

5.3 The Medical Oncology Group of Australia (MOGA) also expressed its strong support for the osimertinib submission categorising it as one of the therapies of "highest priority for PBS listing". The PBAC noted that the MOGA presented a European Society for Medical Oncology Magnitude of Clinical Benefit Scale (ESMO-MCBS) of 4 (out of maximum of 5, where 5 and 4 represent the grades with substantial improvement[2]) based on a progression-free survival benefit compared with chemotherapy. The PBAC noted that the MOGA was unable to calculate the ESMO-MCBS score based on overall survival for osimertinib compared to chemotherapy as the data were immature.

Clinical Trials

5.4 The minor resubmission did not present any new clinical evidence.

Economic analysis

5.5 The economic model in the minor resubmission remained unchanged from the July 2018 resubmission.

5.6 At its July 2018 consideration of osimertinib, the PBAC had noted the resubmission's economic model was based on data from the AURA3 trial, adjusted for crossover using RPSFT (Method A). The PBAC had noted that the base case incremental cost-effectiveness ratio (ICER) presented in the resubmission ($45,000/QALY - $75,000/QALY). After accounting for osimertinib's co-dependency on the MBS listing of the EGFR T790M mutation listing, the July 2018 commentary presented a base case of $75,000/QALY - $105,000/QALY (paragraph 7.9, osimertinib PSD, July 2018 PBAC meeting).

5.7 The PBAC had also noted the ESC's advice that a multivariate sensitivity analysis assuming (i) a 5-year time horizon; (ii) no ongoing treatment effect and (iii) treatment until progression (i.e. taking into account the daily dose intensity and the ratio of time-on-treatment to PFS), and (iv) the overall survival (OS) hazard ratio (HR) generated by the rank-preserving structural failure time (RPSFT) ([redacted]) analysis, i.e. [redacted], would provide a more accurate estimate of the cost-effectiveness of osimertinib. The PBAC had further noted incorporating (i), (ii) and (iii), increased the ICER from $75,000/QALY - $105,000/QALY to $105,000/QALY - $200,000/QALY, and that the impact of changing the HR on the ICER could not be tested using the model provided (paragraph 7.10, July 2018 osimertinib PSD).

5.8 The minor resubmission provided further details on the July 2018 pre-PBAC response RSA proposal from the sponsor *(see Estimated PBS usage & financial implications for further details*).

[2] Cherny NI, Dafni U, Bogaerts J, et al: ESMO-Magnitude of Clinical Benefit Scale version 1.1. Annals of Oncology 28:2340-2366, 2017

5.9 The minor resubmission also clarified the changes to the ICER when [redacted], as per the proposed RSA.

Table 1. Summary of RSA impact on ICER

Model Scenario	Pre- RSA ICER / QALY	RSA ICER / QALY
July 2018 submission base case	$[redacted]	$[redacted]
June 2018 ESC multivariate[a]	$[redacted]	$[redacted]
Commentary base case + 5-year time horizon	$[redacted]	$[redacted]

Source: modified from Table 5 page 3, November 2018 minor resubmission

[a] Commentary base case ($[redacted]/QALY) plus (i) a 5-year time horizon; (ii) no ongoing treatment effect and (iii) treatment until progression (i.e. taking into account the daily dose intensity and the ratio of time-on-treatment to PFS)

5.10 The minor resubmission did not explore the impact of changing the OS HR on the ICER, as per PBAC advice at its July 2018 consideration of osimertinib. The minor resubmission argued that the multivariate analysis suggested by the ESC is not well supported by the evidence and represents a 'worse case' scenario that is highly unlikely to occur in practice, and when the various assumptions suggested by ESC were applied, the economic model generated a HR for OS of [redacted] i.e. worse than the ITT ([redacted]), which is heavily confounded by [redacted]% crossover. The PBAC had previously advised that this argument was not justified, as it was inappropriate to compare the modelled HR with the ITT HRs used within the trial period, given that the validity of the proportional hazard assumption beyond the trial period was unknown (paragraph 7.11, July 2018 PBAC PSD). As the model utilises survival data for each arm, the HR is not an input parameter, and hence the impact of alternative HRs on the ICER cannot be easily determined. The PBAC noted this point was reiterated in the pre-PBAC response for the minor resubmission.

Estimated PBS usage & financial implications

5.11 The pre-PBAC response to osimertinib's July 2018 resubmission included a proposal stating that any remaining concerns regarding the cost-effectiveness of osimertinib could be mitigated through [redacted] via a risk sharing agreement.

5.12 The PBAC had advised that further information regarding the risk share agreement proposed in the pre-PBAC response would be required in the form of a minor resubmission. The PBAC advised that the resubmission should address the estimated number of treated patients (noting that the patient numbers were revised in the pre-PBAC response) together with the estimated expenditure and financial caps in each of the first five years of listing, and these estimates should appropriately account for grandfathered patients. The PBAC had also advised that the risk share arrangement should incorporate a rebate [redacted]% for expenditure above the agreed financial caps (paragraph 7.14, osimertinib PSD, July 2018 PBAC meeting).

5.13 The minor resubmission provided further details on the utilisation estimates and the proposed RSA and subsidisation caps.

5.14 The <u>major changes</u> in the minor resubmission were:

- The number of patients currently receiving treatment on the compassionate access program was updated with the latest figures ([redacted] patients).

- The first full year of listing was updated to 2019.
- The price was updated to reflect the [redacted]% rebate on the published DPMQ proposed in the July 2018 pre-PBAC response.
- The cost of osimertinib to the PBS was calculated based on the proposed [redacted] included in the RSA (rather than the cost of [redacted] packs).
- Inclusion of [redacted]% rebate above the estimated cost to the PBS.

5.15 For the estimates, the resubmission was requested to:

- Account for PBAC's advice on the restriction limiting access to patients with 2 WHO performance status of 2 or less;
- Justify why the number of grandfathered patients were changed from [redacted]; and
- Account for the amount of drug already received by grandfather patients (see paragraph 5.16).

5.16 A comparison of the utilisation estimates, proposed RSA and subsidisation caps between the July 2018 resubmission and the minor resubmission is presented in the table below.

Table 2: Comparison of the utilisation estimates, proposed RSA and subsidisation caps between the July 2018 resubmission and the minor resubmission

Modelling parameter	July 2018 re-submission	November 2018 minor submission
Parameter		
Incidence of lung cancer	Incidence applied to ABS Australian population projections, series B. Incidence sourced from AIHW cancer incidence projections, 2011-2020. From 2021-2023, the incidence was extrapolated by applying a flat [redacted]% growth rate for males and [redacted]% for females each year. The growth rates were calculated from the last year of AIHW data as follows: 2020 incidence / 2019 incidence = [redacted]% (males) and [redacted]% (females).	Unchanged
Proportion of incident lung cancer population that is NSCLC	64%, sourced from the AIHW Lung cancer in Australia report.	Unchanged
Proportion of NSCLC population that is Stage IIIb/IV	59%, sourced from the AIHW Lung cancer in Australia report.	Unchanged
Proportion of Stage IIIb/IV NSCLC expressing EGFR mutation	15%, sourced from Peters et al 2014.[a]	Unchanged
Proportion treated with EGFR TKI	[redacted]%, sourced from a commissioned IMS study	Unchanged
Proportion of patients suitable for biopsy after progression on EGFR TKI therapy	82%, sourced from Socinski et al. 2017.[b]	Unchanged
Proportion of patients who are EGFR T790M positive	[redacted]%, based on average reported mutation rate from clinical trial data.[c]	Unchanged
Number of patients grandfathered from	Estimated to be [redacted] as at July 2018. Updated to [redacted] in the Pre-PBAC response.	Unchanged from the pre-PBAC response.

Modelling parameter	July 2018 re-submission	November 2018 minor submission
Compassionate Access Program		
WHO performance status of 2 or less.	Not included.	Not included. In the pre-PBAC response the sponsor agreed to the listing being restricted to patients with a WHO performance status of 2 or less.
Treated population	Pre-PBAC response increased the estimate of grandfathered patients from [redacted]. Year 1 (2019): Less than 10,000 Year 2 (2020): Less than 10,000 Year 3 (2021): Less than 10,000 Year 4 (2022): Less than 10,000 Year 5 (2023): Less than 10,000 Sourced from Pre-PBAC response, July 2018, Table 4.	Unchanged
Drug cost (at effective DPMQ)		
Duration of osimertinib treatment	[redacted] months ([redacted] packs per patient), based on time on therapy in the AURA3 trial ([redacted] months).	Rather than the cost of [redacted] packs, the treatment cost is calculated based on the proposed [redacted] included in the RSA.
Effective price	DPMQ $[redacted] Sourced from Pre-PBAC response, July 2018.	Unchanged
Drug cost to PBS/RPBS, excl. copayments (effective DPMQ)	Year 1 (2019): $[redacted] Year 2 (2020): $[redacted] Year 3 (2021): $[redacted] Year 4 (2022): $[redacted] Year 5 (2023): $[redacted] Sourced from Pre-PBAC response, July 2018, Table 4.	Unchanged
Assumed offsets for substituted medicines		
Proportion of patients not suitable for third-line therapy (osimertinib substitutes for second-line chemotherapy)	[redacted]%, sourced from commissioned IMS report. Assumed [redacted]% of substituted chemotherapy contained pemetrexed based on IMS report.	Unchanged.
Patients suitable for third-line therapy (osimertinib substitutes nivolumab)	[redacted]%, sourced from commissioned IMS report	Unchanged.
Reduction in use of premedications	Assumed less use of palonosetron, an anti-nausea medication used with each administration of chemotherapy.	Unchanged.
Reduction in cost of substituted PBS/RPBS medicines	Year 1 (2019): $[redacted] Year 2 (2020): $[redacted] Year 3 (2021): $[redacted] Year 4 (2022): $[redacted] Year 5 (2023): $[redacted] Sourced from Pre-PBAC response, July 2018.	Unchanged.
Risk sharing arrangements		

Modelling parameter	July 2018 re-submission	November 2018 minor submission
Proposed expenditure caps	A [redacted] to derive the expenditure caps. Year 1 (2019): $[redacted] Year 2 (2020): $[redacted] Year 3 (2021): $[redacted] Year 4 (2022): $[redacted] Year 5 (2023): $[redacted] Sourced from Pre-PBAC response, July 2018, Table 4.	Expenditure caps are as per the July 2018 Pre-PBAC proposal. The sponsor has [redacted]% rebate above the estimated cost to the PBS (p16 of the minor submission). This proposal is consistent with the PBAC (July 2018) recommendation that the risk share arrangement should incorporate a rebate [redacted]% for expenditure above the agreed financial caps. However, applying the same subsidisation cap to grandfathered patients is not reasonable (see paragraph 5.16).

[a]Peters, M. J., J. J. Bowden, P. Carpenter, J. Lewis and B. Solomon (2014). "Outcomes of an Australian testing programme for epidermal growth factor receptor mutations in non-small cell lung cancer." Intern Med J 44(6): 575-580.

[b]Socinski, M. A., L. C. Villaruz and J. Ross (2017). "Understanding Mechanisms of Resistance in the Epithelial Growth Factor Receptor in Non-Small Cell Lung Cancer and the Role of Biopsy at Progression." Oncologist 22(1): 3-11.

[c]Carter C and Giaccone G 2012; Sun, Ahn et al. 2013; Kuiper, Heideman et al. 2014.

[d]Mitchell et al. Lung cancer in Victoria: are we making progress? MJA 199 (10)·18 November 2013

5.17 The estimates presented in the minor resubmission take into account offsets due to substitution of later-line therapies including nivolumab. The PBS listing of osimertinib may result in displacement, rather than replacement, of these later line therapies, resulting in an underestimation of the net cost of PBS/RPBS.

5.18 The estimates presented in the minor resubmission did not account for PBAC's advice on the restriction limiting access to patients with a WHO performance status of 2 or less (paragraph 7.2, osimertinib PSD, July 2018 PBAC meeting). According to sources previously accepted by the PBAC[3], approximately 80% of Australian NSCLC patients have a WHO performance status of 2 or less (pembrolizumab PSD, March 2018 PBAC meeting). Accounting for this assumption resulted in a reduction of net PBS/RPBS expenditure (after offsets for substituted therapies) from $10 - $20 million to $10 - $20 million in the first year of listing, after accounting for grandfathered patients. The PBAC agreed with the argument in the pre-PBAC response that adjusting the estimated numbers to account for patients with a poor performance status will result in double counting as the estimates had been adjusted to account for patients unable to undergo an additional biopsy for T790M mutation testing due to poor health.

5.19 Although the resubmission appropriately applied a subsidisation cap [redacted] in the financial estimates, this cap was similarly applied to the grandfathered patients as well, i.e. without offsetting for the treatment that these patients would have already undergone, prior to accessing PBS-subsidised therapy. As such, the financial estimates need to be updated with a truncated cap for the grandfathered patients, to account for the average amount of drug that these patients have already received.

5.20 The minor resubmission did not provide any justification for the increase in the

[3] Mitchell et al. Lung cancer in Victoria: are we making progress? MJA 199 (10)·18 November 2013

number of grandfathered patients from [redacted]. The Minor Overview noted that the usual practice adopted by the Department has been to subsidise the costs for all patients who commenced treatment through a Compassionate Access Program (or similar) prior to the date of the PBAC meeting at which the submission received a positive recommendation. Patients enrolled thereafter are eligible for PBS-subsidised access to therapy, but are not accounted for in any subsidisation caps. The pre-PBAC response noted the number of grandfathered patients was updated to reflect the current number of patients on treatment through the compassionate program.

5.21 The estimated net cost to the PBS/RPBS over the first five years of listing as proposed by the minor resubmission, and adjusted for patients with WHO performance status of 2 or less, is presented in the table below.

Table 3. Estimated net cost to the PBS over the first five years of listing

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
As presented in the resubmission (i.e. without accounting for WHO performance status)						
Eligible patients (including grandfathered patients)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Total cost to PBS/RPBS	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]
Total cost to PBS/RPBS (with subsidisation cap)	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]
Total co-payment for osimertinib	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]
NET cost to PBS/RPBS (with subsidisation cap)	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]
Substituted therapies	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]
Total NET cost to PBS/RPBS after offsets (with subsidisation cap)	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]
NET cost to MBS	-$[redacted]	-$[redacted]	-$[redacted]	-$[redacted]	-$[redacted]	-$[redacted]
NET Cost health budget (with subsidisation cap)	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]
Accounting for patients with WHO performance status 2 or less						
Eligible patients with WHO PS 2 or less (including grandfathered patients)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
NET cost to PBS/RPBS (with subsidisation cap)	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]
Total NET cost to PBS/RPBS after offsets (with subsidisation cap)	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]
NET Cost health budget (with subsidisation cap)	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]

The redacted table shows that at Year 6 the estimated number of patients was less than 10,000 per year, and the net cost to the PBS would be $10 - $20 million per year.

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

6 PBAC outcome

6.1 The PBAC recommended the Section 85 Authority Required (written) listing of osimertinib and is satisfied that osimertinib provides, for some patients, a significant improvement in efficacy and a reduction in toxicity over platinum-based doublet chemotherapy. The PBAC's recommendation for listing was based on, among other matters, its assessment, as described above, that the cost-effectiveness of osimertinib would be acceptable at the capped cost per patient proposed in the minor resubmission.

6.2 The PBAC noted the strong support from consumers and the MOGA for osimertinib and considered there is an unmet clinical need for treatment options as patients with EGFR mutation positive NSCLC develop acquired resistance to first-line EGFR TKI therapy.

6.3 The PBAC recalled it deferred making a recommendation for osimertinib at its July 2018 meeting to request additional information from the sponsor regarding the proposed risk sharing arrangement and utilisation estimates. The PBAC also requested updated cost-effectiveness ratios for the July 2018 Commentary base case and the ESC multivariate sensitivity analysis, and the impact of changing the overall survival hazard ratio on the cost-effectiveness be explored.

6.4 The PBAC recalled at its July 2018 consideration that it advised that the criterion "Patients must have a WHO performance status of 2 or less" be added to the restriction. The PBAC noted that the sponsor agreed to this addition in their pre-PBAC response.

6.5 The PBAC noted the financial estimates presented in the minor resubmission were not reduced to specifically account for excluding patients with a poor performance status. The PBAC also noted the argument in the pre-PBAC response that further reduction of the patient estimates would double-count patients with a poor performance status as the estimates had been adjusted to account for patients unable to undergo an additional biopsy for T790M mutation testing due to poor health. The PBAC considered an additional reduction in patient numbers to specifically account for patients with a WHO performance status of 2 or less being excluded from the PBS listing was not required as this would result in double counting.

6.6 The PBAC noted the financial estimates in the minor resubmission were revised from that presented in the July 2018 submission to account for:

- The number of patients currently receiving treatment on the compassionate access program ([redacted] patients).
- The first full year of listing being updated from 2018 to 2019.
- The proposed [redacted]% rebate on the published DPMQ.
- The proposed [redacted].

6.7 The PBAC also noted the sponsor agreed to [redacted]% rebate for use above the proposed expenditure caps.

6.8 The PBAC noted the cost-effectiveness ratios presented in Table 1 of this Overview which incorporated the [redacted] for osimertinib. The PBAC noted the sponsor's argument in the minor resubmission and pre-PBAC response that the structure of the economic model is such that impact of changing the overall survival hazard ratio on the cost-effectiveness could not be reliably explored. The PBAC considered the multivariate sensitivity analyses presented in the minor resubmission adequately addressed the uncertainty with the cost-effectiveness estimates.

6.9 The PBAC considered the proposed RSA and expenditure caps with [redacted]% rebate of any expenditure over the caps based on projected utilisation were appropriate, and adequately addressed its previous concerns regarding the utilisation and cost-effectiveness of osimertinib.

6.10 The PBAC noted the subsidisation cap [redacted] was applied to the grandfathered patients without offsetting for the treatment that these patients would have already received prior to accessing PBS-subsidised therapy. The PBAC considered the financial estimates and subsequent caps should be updated and reduced to account for the amount of drug that the grandfathered patients have already received.

6.11 The PBAC recommended that the Early Supply Rule should not apply.

6.12 The PBAC advised that osimertinib is not suitable for prescribing by nurse practitioners.

6.13 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 item:

Name, Restriction, Manner of administration and form	Max. Qty	**№.of** Rpts	Proprietary Name and Manufacturer	
OSIMERTINIB 80 mg tablet, 30	1	5	Tagrisso®	AstraZeneca Pty Ltd

Category / Program	GENERAL – General Schedule (Code GE)
Prescriber type:	☐ Dental ☒ Medical Practitioners ☐ Nurse practitioners ☐ Optometrists ☐ Midwives
Severity:	Locally advanced (Stage IIIB) or metastatic (Stage IV)
Condition:	Non-small cell lung cancer (NSCLC)
PBS Indication:	Locally advanced (Stage IIIB) or metastatic (Stage IV) non-small cell lung cancer
Treatment phase:	Initial treatment
Restriction Level / Method:	☐ Restricted benefit ☒ Authority Required - In Writing ☐ Authority Required - Telephone ☐ Authority Required - Emergency ☐ Authority Required - Electronic ☐ Streamlined
Clinical criteria:	The treatment must be the sole PBS-subsidised therapy for this condition, AND Patient must have a WHO performance status of 2 or less, AND Patient must have progressive disease following treatment with an epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor (TKI).
Population criteria:	Patient must have evidence of a T790M mutation of the EGFR gene in tumour tissue material following progression on or after an EGFR TKI.
Administrative Advice	No increase in the maximum quantity or number of units may be authorised. No increase in the maximum number of repeats may be authorised. Special Pricing Arrangements apply.

Name, Restriction, Manner of administration and form	Max. Qty	**№.of** Rpts	Proprietary Name and Manufacturer	
OSIMERTINIB				
40 mg tablet, 30	1	5	Tagrisso®	AstraZeneca Pty Ltd
80 mg tablet, 30	1	5		

Category / Program	GENERAL – General Schedule (Code GE)
Prescriber type:	☐Dental ☒Medical Practitioners ☐Nurse practitioners ☐Optometrists ☐Midwives
Severity:	Locally advanced (Stage IIIB) or metastatic (Stage IV)
Condition:	Non-small cell lung cancer (NSCLC)
PBS Indication:	Locally advanced (Stage IIIB) or metastatic (Stage IV) non-small cell lung cancer
Treatment phase:	Continuing treatment
Restriction Level / Method:	☐Restricted benefit ☐Authority Required - In Writing ☒Authority Required - Telephone ☐Authority Required - Emergency ☐Authority Required - Electronic ☐Streamlined
Clinical criteria:	The treatment must be as the sole PBS-subsidised therapy for this condition, AND Patient must have previously received PBS-subsidised treatment with this drug for this condition, AND Patient must not have progressive disease following PBS-subsidised treatment with this drug for this condition.
Administrative Advice	No increase in the maximum quantity or number of units may be authorised. No increase in the maximum number of repeats may be authorised. Special Pricing Arrangements apply.

Name, Restriction, Manner of administration and form	Max. Qty	№.of Rpts	Proprietary Name and Manufacturer	
OSIMERTINIB				
40 mg tablet, 30	1	5	Tagrisso®	AstraZeneca Pty Ltd
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Category / Program	GENERAL – General Schedule (Code GE)
Prescriber type:	☐Dental ☒Medical Practitioners ☐Nurse practitioners ☐Optometrists ☐Midwives
Severity:	Locally advanced (Stage IIIB) or metastatic (Stage IV)
Condition:	Non-small cell lung cancer (NSCLC)
PBS Indication:	Locally advanced (Stage IIIB) or metastatic (Stage IV) non-small cell lung cancer
Treatment phase:	Grandfathering treatment
Restriction Level / Method:	☐Restricted benefit ☒Authority Required - In Writing ☐Authority Required - Telephone ☐Authority Required - Emergency ☐Authority Required - Electronic ☐Streamlined
Clinical criteria:	Patient must have previously received non-PBS subsidised treatment with this drug for this condition prior to [listing date], AND The treatment must be as the sole PBS-subsidised therapy for this condition, AND Patient must have progressive disease following treatment with an epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor (TKI). AND Patient must not have progressive disease following treatment with this drug for this condition.
Population criteria:	Patient must have evidence of a T790M mutation of the EGFR gene in tumour tissue material following progression on or after an EGFR TKI.
Prescribing Instructions	A patient may qualify for PBS-subsidised treatment under this restriction once only.
Administrative Advice	No increase in the maximum quantity or number of units may be authorised. No increase in the maximum number of repeats may be authorised. Special Pricing Arrangements apply.

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.