Addenda to this Public Summary Document has been included at the end of the document.

7.05 Futibatinib, Tablet 4 mg, Lytgobi ®, Taiho Pharma Oceania Pty Ltd

1 Purpose

1.1 The early re-entry resubmission sought the PBS listing of futibatinib for the treatment of locally advanced or metastatic cholangiocarcinoma (CCA) in patients with fibroblast growth factor receptor 2 (*FGFR2*) fusion or rearrangement.

1.2 The resubmission was based on the PBAC decision to not recommend futibatinib for this indication from its March 2025 meeting. A summary of the key matters that were to be addressed in the resubmission is provided in **Table 1**.

Table 1: Summary of key matters to be addressed

Matter of concern	Response	Addressed?
Economic Model		Y/N
The submission presented an economic evaluation based on the results of the MAIC. The PBAC agreed with the ESCs that as the underlying clinical benefit used to inform the economic evaluation was uncertain, the economic model presented was likely not reflective of the true cost effectiveness of futibatinib. The PBAC noted the economic model resulted in an undiscounted life year gain of 2.48 over the 10 year time horizon of the model and considered that was implausibly large. The PBAC agreed with the ESC that the economic model should include a more conservative estimate of the modelled clinical benefit but noted the model did not include this operability. The PBAC noted that the MAIC results from Paine 2022 or Borad 2022 were more conservative, and considered that the model should be aligned with that OS HR: 0.48-0.49 (vs 0.24). (para 7.12).	The OS HR in the economic evaluation has been amended to 0.32, to align with the upper OS HR CI limit from the March 2025 submission, claiming this value represents the highest plausible value for the HR given the observed data from the submission's MAIC.	N
The PBAC noted the economic model assumed a time horizon of 10 years with no convergence of OS modelled. The PBAC agreed with the evaluation that a 10-year time horizon increased the uncertainty in the model results given the limited duration of follow-up of the two studies and the general uncertainty regarding the incremental survival. The PBAC considered that a 5-year time horizon, in line with the PBAC's consideration of ivosidenib for IDH1 positive CCA (paragraph 7.11, ivosidenib PSD, July 2024 PBAC meeting), would result in a more reliable estimate of the benefits. (para 7.13)	The time horizon of the economic evaluation has been reduced from 10 years to 7 years. The resubmission claims that OS benefit does converge in the base case of the economic model through the application of the parametric models. The resubmission stated that a 5 year time horizon, in line with ivosidenib, would not be appropriate.	N
The submission estimated treatment-specific health state utilities, with different progression free (PF) and progressive disease (PD) health state utilities based on the assumption of greater toxicity associated with FOLFOX. However, the PBAC agreed with the evaluation and the ESCs that that difference between treatment arms in post-progression utilities was not supported given both futibatinib and FOLFOX would have been ceased, and this biased the results in favour of futibatinib. The PBAC considered it would be more appropriate to apply the same utilities to the PF and PD health states in each treatment arm. (para 7.14)	Although the resubmission applied the same utilities in each arm, it applied an additional IV disutility of 0.025 to FOLFOX administrations.	N

Matter of concern	Response	Addressed?
Price		
The PBAC considered that futibatinib would be acceptably cost-effective with an ICER no more than $[redacted][1]/QALY gained (consistent with other treatments for CCA) (para 7.17)	The resubmission targeted an ICER of $[redacted][2]/QALY, arguing that this is a small and well-defined population with a high clinical need, and ICER threshold of less than $[redacted][1] per QALY is overly conservative. The Pre-PBAC response (Table 1) proposed a further price reduction to $[redacted], resulting in an ICER of $[redacted][2] for the resubmission's base case.	N
Financial Estimates		
The submission took an epidemiological approach to derive the financial estimates. The PBAC agreed with the DUSC that a number of inputs needed to be revised as outlined in paragraph 6.119. (ie: • more granular information regarding the incidence estimates available from the AIHW. • number of patients progressing to second line therapy overestimated. • number of tests per patient underestimated. • inclusion of treatment uptake rate for futibatinib patients double counts the proportion of patients who progress to second line therapy with ECOG PS 0 or 1. • treatment duration applied in the economic model and financial estimates should align.) Additionally, the PBAC considered the prevalence of FGFR2 fusion or rearrangements was likely overestimated and should be revised to account for the low prevalence (≤1%) in eCCA patients. (para 7.16)	Inputs noted by DUSC were revised as follows: • AIHW incidence utilised. • number of patients progressing to second-line therapy reduced from 60% to 50%. • number of tests increased per treated patient, and doubled test numbers to reflect testing patients in the first line treatment setting. • Treatment duration of 57.78 weeks applied (vs 12.5 months). • Reduced prevalence of *FGFR2* fusion or rearrangements from 20% to 13.86%.	Y

AIHW = Australian Institute of Health and Welfare; eCCA = extracellular cholangiocarcinoma; ECOG PS = Eastern Cooperative Oncology Group Performance Status; FGFR2 = fibroblast growth factor receptor 2; HR = hazard ratio; iCCA = intracellular cholangiocarcinoma; MAIC = matched adjusted indirect comparison; OS = overall survival; PFS = progression free survival; QALY = quality adjusted life year

The redacted values correspond to the following ranges:

[1] *$55,000 to < $75,000*

[2] *$75,000 to < $95,000*

1.3 The pre-PBAC response argued the early re-entry submission had made significant concessions compared to the previous submission and provided further arguments to support the base case economic model.

2 Background

2.1 Futibatinib was included on the ARTG on 17 April 2025 for the following indication:

"LYTGOBI monotherapy has provisional approval in Australia for the treatment of adult patients with locally advanced or metastatic intrahepatic cholangiocarcinoma with a fibroblast growth factor receptor 2 (FGFR2) fusion or rearrangement that have

progressed after at least one prior line of systemic therapy. The decision to approve this indication has been made on the basis of the favourable objective response rate and duration of response in a single arm trial. Continued approval of this indication depends on verification and description of benefit in confirmatory trials".

2.2 The PICO from the previous submission is presented below.

Table 2: Key components of the clinical issue addressed by the submission (as stated in the previous submission)

Component	Description
Population	Test: adult patients with locally advanced or metastatic CCA. Drug: adult patients with locally advanced or metastatic CCA with a *FGFR2* fusion or rearrangement that have progressed after at least one prior line of systemic therapy.
Intervention	Test: tumour tissue testing for *FGFR2* fusions or rearrangements using RNA NGS. Alternative test: tumour tissue testing for *FGFR2* gene fusions or rearrangements using FISH testing on DNA. Drug: futibatinib 20 mg (5*4 mg tablets) taken orally once daily until disease progression or unacceptable toxicity.
Comparator	Test: no testing for *FGFR2* fusions or rearrangements Drug: • primary comparator: SoC chemotherapy, represented by FOLFOX (modified FOLFOX 6 chemotherapy (oxaliplatin 85 mg/m^2, calcium folinate 50 mg*, fluorouracil 400 mg/m^2 bolus and 2400 mg/m2 continuous infusion over 46 hours; every 14 days for up to 12 cycles). • Secondary comparator: palliative care (with active symptom control).
Outcomes	Test: diagnostic yield, prognostic impact, treatment effect modification, reliability of testing, concordance between proposed testing method and clinical utility standard. Drug: PFS, OS, ORR, HRQoL, safety.
Clinical claim	Main claim: in patients with locally advanced or metastatic CCA with a *FGFR2* fusion or rearrangement, identified by tumour tissue testing, that have progressed after at least one prior line of systemic therapy, futibatinib is superior in terms of efficacy (OS, PFS and ORR) and safety, compared to FOLFOX. Secondary claim: In adult patients with locally advanced or metastatic CCA with *FGFR2* fusions or rearrangements, identified by tumour tissue testing, that have progressed after at least one prior line of systemic therapy, futibatinib is superior in terms of efficacy (OS, PFS and ORR), compared to palliative care (with ASC), with a different safety profile that is manageable.

Source: Table 1, futibatinib minutes, March 2025 PBAC meeting

DNA = deoxyribonucleic acid; CCA = cholangiocarcinoma; *FGFR2* = fibroblast growth factor receptor 2; FISH = fluorescence in situ hybridisation; HRQoL= health related quality of life; NGS = with next-generation sequencing; ORR = objective response rate: OS = overall survival; PFS = progression free survival; RNA = ribonucleic acid; SoC = standard of care

For more detail on PBAC's view, see section 5 PBAC outcome.

3 Requested listing

3.1 The resubmission accepted amendments to the PBS restriction as proposed by the Secretariat.

Name, restriction, manner of administration, form	Maximum quantity (packs)	Maximum quantity (units)	No. of repeats	Dispensed price for maximum quantity	Proprietary name and manufacturer
FUTIBATINIB 4 mg tablets, 35	4	140	5	Published: $[redacted] Effective: $[redacted]	LYGTOBI Taiho Pharma Oceania
Category / Program: ☒ GENERAL - General Schedule (Code GE)					
Prescriber type: ☒Medical Practitioners					
Restriction type: ☒Authority Required (Streamlined) [new/existing code]					
Indication: Locally advanced or metastatic cholangiocarcinoma					
Clinical criteria:					
Patient must have evidence of a fibroblast growth factor receptor 2 (*FGFR2*) fusion or rearrangement					
AND					
Clinical criteria:					
Patient must have received at least one prior line of systemic therapy					
AND					
Clinical criteria:					
Patient must have ~~a~~n *World Health Organisation (WHO) Eastern Cooperative Oncology Group (*ECOG*)* performance status score ~~of~~ no ~~greater~~ *higher* than 1 ~~at~~ *prior to* treatment initiation with this drug					
AND					
Clinical criteria:					
The treatment must be the sole PBS-subsidised therapy for this condition					
AND					
Clinical criteria:					
Patient must not have developed disease progression while being treated with this drug for this condition.					
Administrative Advice: No increase in the maximum amount 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.					
Administrative 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.*					

Source: Table 2, futibatinib minutes, March 2025 PBAC meeting.

For more detail on PBAC's view, see section 5 PBAC outcome.

4 Consideration of the evidence

Sponsor hearing

4.1 There was no hearing for this item.

Consumer comments

4.2 The PBAC noted and welcomed the input regarding the resubmission from organisations (2) via the Consumer comments facility on the PBS website. Rare

Cancers Australia described the severity of CCA, trade-offs associated with side-effects of current chemotherapy options and quality of life, and the benefits associated with futibatinib's oral administration, particularly for rural and remote patients. They noted the side-effect profile of futibatinib, but said this was manageable and the need for affordable access was a greater concern as cost and the need to travel to clinical trials were barriers to access at present. The PBAC also noted that supportive comments were received from the Pancare Foundation and the Liver Foundation in relation to the previous submission.

4.3 The Medical Oncology Group of Australia (MOGA) also expressed its support for the futibatinib submission. The PBAC noted that the MOGA presented a European Society for Medical Oncology Magnitude of Clinical Benefit Scale (ESMO-MCBS) for futibatinib of 2 (out of a maximum of 5, where 5 and 4 represent the grades with substantial improvement)[1], on the basis of objective response rate in the FOENIX-CCA2 trial.

Comparative effectiveness

4.4 The resubmission did not provide any additional clinical data.

4.5 The submission considered in March 2025 was based on FOENIX-CCA2 (n=103), an open-label, single-arm, phase 2 trial of futibatinib in patients with unresectable or metastatic *FGFR2* fusion-positive or *FGFR2* rearrangement-positive iCCA, and disease progression after one or more previous lines of systemic therapy; and ABC-06 (n=81), an open-label randomised phase 3 trial of ASC and FOLFOX in patients with locally advanced or metastatic biliary tract cancer (including CCA and gallbladder or ampullary carcinoma). These trials formed the basis of an unanchored matched adjusted indirect comparison (MAIC) of futibatinib versus FOLFOX. The PBAC noted the improvements in efficacy with futibatinib compared to FOLFOX based on the MAIC: adjusted progression free survival (PFS) hazard ratio (HR) = 0.30 (95% CI: 0.22, 0.41) and overall survival (OS) HR = 0.24 (95% CI: 0.18, 0.32[2]). However, the PBAC considered that the magnitude of clinical benefit was likely overestimated due to differences in baseline characteristics (in particular *FGFR2* status which may be a prognostic factor), and the unanchored nature of the MAIC, which confers a high risk of bias to unknown treatment effect modifiers. The PBAC noted that the adjustments applied as part of the MAIC increased the estimated PFS and OS for futibatinib, despite accounting for the FOLFOX trial patients being older and having a worse performance status compared with the patients in the futibatinib trial, which further raised

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

[2] Note that the results presented in this section are derived from analyses conducted by the applicant for the purposes of informing the PBAC and MSAC consideration. Interpretation of the results and their application should therefore be limited to seeking to understand the basis for the PBAC and MSAC outcome and should not be used for any other purpose.

questions regarding the reliability of the MAIC. The PBAC considered that the clinical claim of superiority for futibatinib compared to FOLFOX was reasonable, but that the magnitude of benefit was highly uncertain (paragraph 7.8. futibatinib Public Summaru Document [PSD], March 2025 PBAC meeting).

4.6 Additional indirect comparisons identified during the evaluation of the submission considered in March 2025 (Paine 2022, Borad 2022), comparing futibatinib and FOLFOX for patients with *FGFR2* alterations (both arms, which accounted for the potential prognostic influence of *FGFR2* status) reported a less favourable adjusted HR for PFS (0.48-0.53 vs 0.30) and OS (0.48-0.49 vs 0.24) for futibatinib compared to chemotherapy vs those presented in the submission (see **Table 3**). The PBAC noted this supported its consideration that the MAIC likely overestimated the magnitude of clinical benefit of futibatinib (paragraph 7.8, futibatinib PSD, March 2025 PBAC meeting). The resubmission maintained that the ABC-06 trial remains the best available evidence, highlighting uncertainties due to limited details regarding methodologies and limitations of the approaches used by Paine 2022 and Borad 2022. The submission overview noted that the PBAC did not necessarily consider Paine 2022 and Borad 2022 to be better evidence; rather, they supported its consideration that the MAIC likely overestimated the magnitude of clinical benefit.

Table 3: Indirect comparison results between futibatinib and chemotherapy in FGFR2 altered patients in Paine 2022 and Borad 2022

	Unadjusted HR (95% CI, p value)	Adjusted HR (95% CI, p value)
Paine 2022		
PFS	0.40 (0.27-0.59, <0.0001)	0.48 (0.30-0.76, 0.002)
OS	0.54 (0.35-0.81, 0.003)	0.48 (0.31-0.74, 0.001)
Borad 2022		
PFS	0.40 (0.27-0.59, ≤0.01)	0.53 (0.33-0.86, ≤0.01)
OS	0.53 (0.35-0.81, ≤0.01)	0.49 (0.31-0.79, ≤0.01)
March 2025 Submission[3]		
PFS	0.43 (0.31-0.59, <0.0001)	0.30 (0.22-0.41, <0.0001)
OS	0.26 (0.18-0.37, <0.0001)	0.24 (0.18-0.32, <0.0001)

Source: Adapted from Table 2-1, Futibatinib Early Re-Entry Submission
Abbreviations: CI = confidence interval, DOR = duration of response, HR = hazard ratio, NR = not reported, ORR = objective response rate, OS = overall survival, PFS = progression free survival

Clinical Claim

4.7 The PBAC previously considered the clinical claim of superior comparative effectiveness versus the nominated comparator (FOLFOX) was reasonable; however the magnitude of effect is highly uncertain and likely overestimated due to differences

[3]Note that the results presented in this section are derived from analyses conducted by the applicant for the purposes of informing the PBAC and MSAC consideration. Interpretation of the results and their application should therefore be limited to seeking to understand the basis for the PBAC and MSAC outcome and should not be used for any other purpose.

in baseline characteristics (tumour site, *FGFR2* status), less favourable HR in other indirect comparisons, and the unanchored MAIC (paragraph 6.65, futibatinib PSD, March 2025 PBAC meeting).

4.8 The PBAC previously considered the claim of superior comparative safety compared to FOLFOX was not adequately supported by the data, but that it is theoretically plausible (paragraph 6.66, futibatinib PSD, March 2025 PBAC meeting).

Economic analysis

4.9 The previous submission presented an economic analysis based on the results of the MAIC. The PBAC previously considered that as the underlying clinical benefit used to inform the economic evaluation was uncertain, the economic model presented was likely not reflective of the true cost effectiveness of futibatinib (paragraph 7.12, futibatinib PSD, March 2025 PBAC meeting). The base case ICER in the previous submission was $95,000 to < $115,000 per QALY.

4.10 To address the PBAC's concerns regarding the cost-effectiveness of futibatinib the resubmission presented an economic evaluation with revised inputs and a reduced price for futibatinib ([redacted]% reduction in the ex-manufacturer price from $[redacted] to $[redacted] per pack). The PBAC previously considered the economic model should include a more conservative estimate of the modelled clinical benefit but noted the model did not include this operability (paragraph 7.12, futibatinib PSD, March 2025 PBAC meeting). The model provided in the resubmission was adapted to include this operability and allow alternative hazard ratios to be used.

4.11 To adapt the economic model, the resubmission started with the model provided in the previous pre-PBAC response. This model (i) corrected errors identified during the evaluation (ii) used health state utility values from the durvalumab PBAC submission for biliary tract cancer and (iii) applied an additional utility decrement for IV administration of FOLFOX. This model resulted in an ICER of $95,000 to < $115,000 per quality adjusted life year (QALY). Although the PBAC did not specifically comment on the inclusion of a utility decrement for IV administration of FOLFOX as part of its March 2025 consideration, the submission overview noted that the PBAC previously considered that that it would be more appropriate to apply the same utilities to the PF and PD health states in each treatment arm (paragraph 7.14, futibatinib PSD, March 2025 PBAC meeting). Therefore, the submission overview considered that inclusion of a disutility resulting in differing utilities between treatment arms may not be appropriate.

4.12 The economic model was adapted to allow the use of alternative hazard ratios. The adapted economic model resulted in an ICER of $95,000 to < $115,000 per QALY (which was reasonably similar to the ICER in the previous pre-PBAC response, see paragraph 4.11).

4.13 Using the adapted economic model and (i) reducing the time horizon to 7 years and (ii) incorporating a HR for OS of 0.32 resulted in an ICER of $115,000 to < $135,000 per QALY. The resubmission reduced the price of futibatinib to result in an ICER of $75,000 to < $95,000 per QALY. The results of the economic evaluation and model traces are provided in **Table 4** and Figure 1.

4.14 The resubmission proposed a 7-year time horizon, rather than the 5-year horizon as preferred by the PBAC. The resubmission noted the 5-year time horizon was based on what was considered reasonable for ivosidenib; however, it stated that given the PBAC considers patients with *FGFR2* alterations have an improved prognosis and patients positive for *IDH1* have a poorer prognosis, it is not reasonable for the futibatinib model to have the same time horizon (i.e., 5 years).

4.15 The model in the resubmission applied an OS HR of 0.32 (compared to 0.24 in the previous model) based on the upper limit of the OS HR 95% confidence interval (CI) from the submission's MAIC, which the resubmission claimed represents the highest plausible value for the HR given the observed data. The resubmission noted this value falls within the range of the 95% CI for OS from Paine 2022 and Borad 2022 (see **Table 3**). The PBAC previously considered that the economic model should be aligned with the more conservative OS HR of 0.48-0.49 from Paine 2022 or Borad 2022 (discussed in paragraph 4.6). The Pre-PBAC response argued that the use of HRs above 0.32 result in a PFS that is higher than death and considered this is an implausible situation as it implies that deceased patients receive drug. The PBAC considered this was largely related to the structure and overall reliability of the economic model.

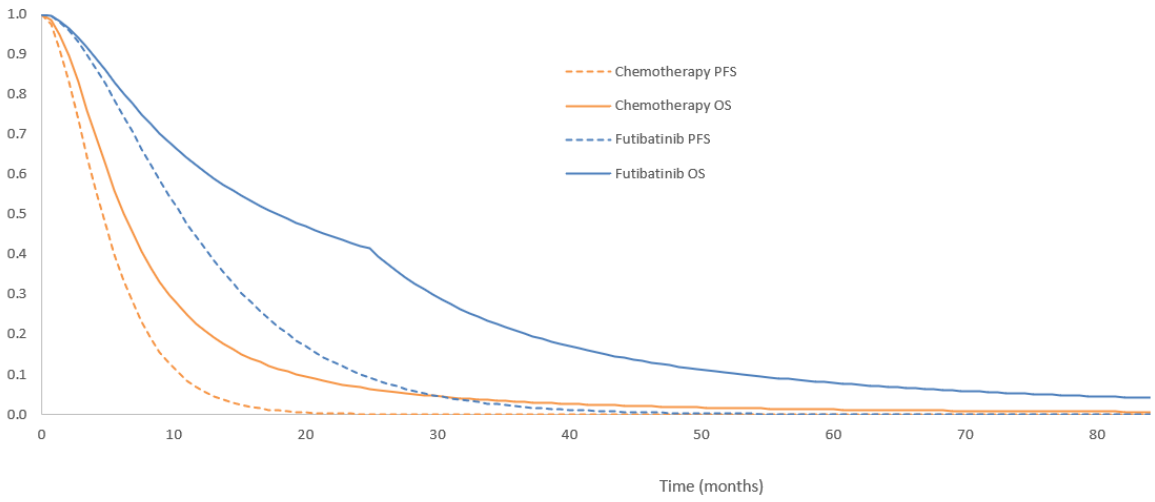
4.16 The resubmission noted the PBAC had previously recommended an ICER less than $55,000 to < $75,000 per QALY would be appropriate; however, the resubmission contended that as this is a small, well-defined population with a high clinical need, an ICER of $75,000 to < $95,000 per QALY would be more appropriate. The Pre-PBAC response offered a further reduction in the proposed EMP to $[redacted] per pack (from $[redacted] in the resubmission, and $[redacted] in the initial submission), resulting in an ICER of $75,000 to < $95,000 per QALY for the resubmission's base case.

Table 4: Results of the economic evaluation presented in the resubmission

Analyses	Incremental cost	Incremental QALY	ICER
Base case (previous submission) (paragraph 4.9)	$[redacted]	1.16	$[redacted] [1]
Model provided in previous pre-PBAC response (paragraph 4.114.11)	$[redacted]	1.22	$[redacted] [1]
Adaption of model to using HR approach (starting point in resubmission) (paragraph 4.12 4.12)	$[redacted]	1.17	$[redacted] [1]
HR (0.24 in starting point model)			
HR = 0.32 #1	$[redacted]	0.95	$[redacted] [2]
Time horizon (10 years in starting point model)			
7 years #2	$[redacted]	1.12	$[redacted] [1]
#1 + #2	$[redacted]	0.91	$[redacted] [2]
# 1 + #2 and price reduction	$[redacted]	0.91	$[redacted] [3]

Source: constructed during the evaluation from the economic model and Table 3-2 of the Futibatinib Early Re-Entry Submission
HR, hazard ration; ICER, incremental cost-effectiveness ratio; QALY, quality adjusted life year.
The redacted values correspond to the following ranges:
[1] *$95,000 to < $115,000*
[2] *$115,000 to < $135,000*
[3] *$75,000 to < $95,000*

Figure 1: Survival curves of the base case economic model



Source: economic model provided with the early re-entry resubmission

4.17 The resubmission noted that the updated OS HR used in the resubmission (0.32) resulted in approximately 4% futibatinib of patients alive at 7 years.

4.18 The revised model resulted in 1.99 life years gained (LYG) (undiscounted, over 7 years) for futibatinib compared to 2.48 LYG (undiscounted, over 10 years) in the previous submission.

4.19 Sensitivity analyses using parameters previously recommended by the PBAC are presented in Table 5. The economic model was most sensitive to the OS HR applied. The submission overview noted that a multivariate sensitivity analysis using inputs consistent with the previous PBAC recommendation resulted in an ICER of $135,000 to < $155,000per QALY gained, or $135,000 to < $155,000 using the price reduction offered in the Pre-PBAC response (see paragraph 4.16).

Table 5: Sensitivity analyses

Analyses	Incremental cost	Incremental QALY	ICER	% change from resubmission base case
Resubmission base case	$[redacted]	0.91	$[redacted] [1]	-
Time horizon (base case 7 years)				
5 years #1	$[redacted]	0.85	$[redacted] [1]	+[redacted]%
OS HR (base case 0.32)				
0.48 #2	$[redacted]	0.59	$[redacted] [2]	+[redacted]%
Utilities (base case included disutility for FOLFOX administration)				
Disutility *removed #3*	*$[redacted]*	*0.89*	*$[redacted] [1]*	+[redacted]%
Multivariate sensitivity analyses				
#1 + #2	$[redacted]	0.56	$[redacted] [2]	+[redacted]%
#1 + #2 + #3	$[redacted]	0.54	$[redacted] [2]	+[redacted]%
#1 + #2 + #3 and Pre-PBAC price reduction [a]	$[redacted]	0.54	$[redacted] [2]	+[redacted]%

Source: economic model provided with the early re-entry resubmission
[a] Pre-PBAC response reduced the proposed AEMP to $[redacted] per pack.
The redacted values correspond to the following ranges:
[1] *$75,000 to < $95,000*
[2] *$135,000 to < $155,000*

Drug cost/patient/course

4.20 The futibatinib drug cost per patient per course in the economic model and financial estimates is presented in Table 6. The treatment duration in the resubmission's financials were not updated to reflect the revised economic model. The cost per patient per course in the economic model using the price proposed in the pre-PBAC response was $[redacted].

Table 6: Futibatinib cost per patient per course

	Futibatinib	
	Economic model	**Financial estimates**
DPMQ	$[redacted]	$[redacted]
Relative dose intensity	83.26%	83.26%
Average weeks on treatment	55.99	57.78
Cost per course per patient	$[redacted]	$[redacted]

DPMQ = dispensed price for maximum quantity

4.21 The drug cost per patient per course in the previous submission was $[redacted] in the economic model and $[redacted] in the financial estimates.

Estimated PBS usage & financial implications

4.22 The key inputs for the financial estimates are provided in **Table 7**.

Table 7: Key inputs for financial estimates

Data	Value	Comment
Eligible population		
CCA incidence	Year 1: [redacted][1] Year 2: [redacted][1] Year 3: [redacted][1] Year 4: [redacted][1] Year 5: [redacted][1] Year 6: [redacted][1]	Updated based on the more granular information available from AIHW (consistent with DUSC advice)
% patients diagnosed with advanced BTC (locally advanced, metastatic, recurrent	80%	Unchanged from previous submission
% of patients taking 1st line durvalumab	70%	Unchanged from previous submission.
% patients treated with durvalumab progressing to 2L	50%	Reduced from 60%. Consistent with previous DUSC advice.
FGFR2 aberrations/alterations	13.9%	Reduced from 20%. Consistent with previous PBAC advice.
Test utilisation		
Number of tests	14.4 tests per treated patient	Increased from 5 tests per patient treated. Amended to account for (i) yield reduced from 20% to 13.9% and (ii) to reflect numbers tested at 1st line treatment. Cost of test = $350 (unchanged from previous submission)
Treatment utilisation		
Patients electing treatment	[redacted]%	Increased from [redacted]%. Consistent with previous DUSC advice.
Duration of futibatinib treatment	57.78 weeks	Increased from 56.05 weeks. Amended to be consistent with the economic model in the previous submission; however, the mean duration of treatment in the economic model provided with the resubmission was 55.99 weeks.
Compliance	83.3%	Unchanged from previous submission.
Grandfathered patients	[redacted][2]	Treated duration = 6 months; unchanged from previous submission.

Source: compiled during the evaluation using Tables 24 and 4-1 of the March 2025 Futibatinib minutes
DUSC, drug utilisation sub-committee; FGFR2, Fibroblast Growth Factor Receptor 2; PBAC, Pharmaceutical Benefits Advisory Committee
The redacted values correspond to the following ranges:
[1] *500 to < 5,000*
[2] *< 500*

4.23 The financial estimates assumed 13.9% of patients have *FGFR2* fusion or rearrangements, calculated as a weighted proportion using data presented in **Table 8**. The resubmission stated it had assumed patients would be tested at the first line treatment setting, rather than after patients have progressed on first line treatment. The resubmission stated it had doubled the number of patients tested to reflect this;

however, the submission overview noted that the calculation[4] appeared to be based on the proportion of patients that progress to second line treatment.

Table 8: Weighted FGFR2 fusion or rearrangement

CAA type	Number of people in 2024	Proportion of CCA	% FGFR2
Intrahepatic bile duct cancer	719	47.4%	20%
Overlapping lesions of biliary tract and biliary tract, unspecified	308	20.3%	20%
Extrahepatic bile duct cancer	490	32.3%	1%
Weighted FGFR2 fusion or rearrangement:			13.9%

Source: financial table workbook from the resubmission
CCA, cholangiocarcinoma; FGFR2, Fibroblast Growth Factor Receptor 2

4.24 The submission overview identified an error in the financial estimates workbook. Given the average treatment duration for incident patients is longer than 1 year, the workbook has correctly applied this in the DTG worksheet. However, the 3a. Scripts-proposed worksheet should reflect a treatment duration of 52 weeks as the DTG worksheet has converted treated patient to patient years. As the treatment duration of grandfathered patients is less than 1 year, the DTG worksheet is not required and treatment duration can be included on the 3a. Scripts-proposed worksheet. Additionally, the submission overview considered that the treatment duration should be reduced to be consistent with the revised economic model (see paragraph 4.20).

[4] (1/13.863%) x (1/50%) = 14.4

Table 9: Estimated use and financial implications

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Estimated patient numbers						
Total incident population	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
Patients diagnosed with locally advanced, metastatic CCA (80%)	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
1st line treatment (durvalumab) for CCA (70%)	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
Progress to 2L ECOG PS 0 or 1 (50%)	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]
FGFR alterations (13.9%); initiating patients	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]
Grandfathered patients	[redacted][2]	-	-	-	-	-
Estimated financial implications of futibatinib to the PBS/RPBS						
Scripts	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
Cost to PBS/RPBS less copayments	$[redacted][3]	$[redacted][3]	$[redacted][3]	$[redacted][3]	$[redacted][3]	$[redacted][3]
Estimated financial implications for reduction in FOLFOX use to the PBS/RPBS						
Cost to PBS/RPBS less copayments	-$[redacted][3]	-$[redacted][3]	-$[redacted][3]	-$[redacted][3]	-$[redacted][3]	-$[redacted][3]
Estimated financial implications of the *FGFR2* testing to the MBS						
Cost to MBS less co-payments (80% rebate)	$[redacted][3]	$[redacted][3]	$[redacted][3]	$[redacted][3]	$[redacted][3]	$[redacted][3]
Estimated financial implications of the Optical Coherence tomography (ophthalmological monitoring) to the MBS						
Cost to MBS less co-payments (80% rebate)	$[redacted][3]	$[redacted][3]	$[redacted][3]	$[redacted][3]	$[redacted][3]	$[redacted][3]
Estimated financial implications for FOLFOX associated costs to the MBS						
Cost to MBS less co-payments (80% rebate)	-$[redacted][3]	-$[redacted][3]	-$[redacted][3]	-$[redacted][3]	-$[redacted][3]	-$[redacted][3]
Net financial implications						
Net cost to PBS/RPBS	$[redacted][3]	$[redacted][3]	$[redacted][3]	$[redacted][3]	$[redacted][3]	$[redacted][3]
Net cost to MBS	$[redacted][3]	$[redacted][3]	$[redacted][3]	$[redacted][3]	$[redacted][3]	$[redacted][3]
Net cost to PBS/RPBS/MBS	$[redacted][3]	$[redacted][3]	$[redacted][3]	$[redacted][3]	$[redacted][3]	$[redacted][3]

Source: financial table workbook from the resubmission
ECOG PS, Eastern Cooperative Oncology Group Performance Status; FGFR, Fibroblast growth factor receptor
The redacted values correspond to the following ranges:
[1] *500 to < 5,000*
[2] *< 500*
[3] *$0 to < $10 million*

4.25 The total net cost to the PBS/RPBS of listing futibatinib was estimated to be $0 to < $10 million in Year 1, increasing to $0 to < $10 million in Year 6, and a total of $30 million to < $40 million in the first six years of listing.

4.26 The pre-PBAC response provided revised financial estimates that corrected the errors identified in paragraph 4.24 and incorporated the revised price. The pre-PBAC response noted this reduced the cost to the R/PBS over 6 years to $30 million to < $40 million.

For more detail on PBAC's view, see section 5 PBAC outcome.

5 PBAC Outcome

5.1 The PBAC did not recommended futibatinib for the treatment of patients with locally advanced or metastatic cholangiocarcinoma who have previously progressed on systemic therapy and have a fibroblast growth factor receptor 2 fusion or rearrangement. The PBAC considered the early re-entry resubmission did not adequately address the outstanding issues requested as part of its March 2025 PBAC consideration. In particular, the PBAC considered the revised economic model remained highly optimistic. The PBAC considered the ICER was high and uncertain and that futibatinib was not cost-effective at the price proposed in the pre-PBAC response.

5.2 The PBAC recalled that it previously considered there is a high clinical need for more effective therapies for CAA and noted that consumer input received for the March 2025 and July 2025 meetings supported the availability of futibatinib.

5.3 In terms of the restriction, the PBAC noted that the requested changes were made and considered that the proposed restriction was reasonable.

5.4 To address the PBAC's previous concerns regarding the cost-effectiveness of futibatinib the resubmission presented an economic evaluation with revised inputs and a reduced price for futibatinib. The PBAC recalled it previously considered the clinical benefit associated with the submission's matched adjusted indirect comparison (MAIC) to be uncertain, and considered that the economic model should include a more conservative estimate of the modelled clinical benefit (i.e. using more conservative hazard ratios, HRs). The PBAC noted the overall survival (OS) HR was amended to 0.32 (from 0.24), rather than the more conservative value of 0.48-0.49, as previously requested. The PBAC noted the model estimated an additional 1.99 life years gained (undiscounted) over the 7 year time horizon and considered this was highly optimistic. The PBAC noted changing the HR to 0.48 increased the ICER from $75,000 to < $95,000 to $135,000 to < $155,000 per QALY (using the price proposed in the submission).

5.5 The PBAC recalled that it previously considered it would be appropriate to apply the same health state utility values to the progression free (PF) and progressed disease (PD) health states in each treatment arm. The PBAC noted that while the resubmission's model applied the same utilities (from the durvalumab PBAC submission) to each arm, an additional "chemotherapy administration" utility decrement was applied to the chemotherapy arm, which the PBAC considered was not adequately supported.

5.6 The PBAC noted that the time horizon in the resubmission was updated to 7 years (from 10 years), rather than 5 years as previously requested by the PBAC to align with

its previous consideration of ivosidenib. The PBAC considered 7 years to be overly optimistic and maintained that 5 years would be more appropriate.

5.7 The PBAC noted that using the PBAC's preferred inputs of OS HR of 0.48 (vs 0.32 in resubmission), 5 year time horizon (vs 7 years in resubmission) and same utilities between arms (vs additionally disutility in chemotherapy arm) increased the resubmission's base case ICER from $75,000 to < $95,000 per QALY, to $135,000 to < $155,000 per QALY, or $135,000 to < $155,000 per QALY with the price reduction proposed in the Pre-PBAC response. The PBAC noted this is well above the ICER of $55,000 to < $75,000, per QALY which it previously considered to be acceptable.

5.8 The PBAC considered that the utilisation estimates proposed in the pre-PBAC response (with errors corrected) addressed the Committee's previous concerns and were reasonable.

5.9 The PBAC considered any resubmission needs to address the outstanding issues related to the economic evaluation. The resubmission may be lodged at any future standard due date for PBAC submissions using the standard re-entry pathway.

5.10 The PBAC noted that this submission is eligible for an Independent Review.

Outcome:
Not recommended

6 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.

7 Sponsor's Comment

The sponsor had no comment.

Addendum to the July 2025 PBAC Public Summary Document:

8 Purpose

8.1 At its July 2025 meeting, the PBAC did not recommended futibatinib for the treatment of patients with locally advanced or metastatic cholangiocarcinoma who have previously progressed on systemic therapy and have a fibroblast growth factor receptor 2 (*FGFR2*) fusion or rearrangement. The PBAC considered the early re-entry resubmission did not adequately address the outstanding issues requested as part of its March 2025 PBAC consideration. In particular, the PBAC considered the revised economic model remained highly optimistic. The PBAC considered the ICER was high and uncertain and that futibatinib was not cost-effective at the price proposed in the pre-PBAC response.

8.2 Following the post-PBAC meeting with the Chair, the sponsor provided a proposal for consideration by the PBAC (see paragraphs 10.1 - 10.4 for details).

8.3 At its July 2025 meeting, the MSAC did not support testing of tumour tissue to detect *FGFR2* fusions or rearrangements in people with cholangiocarcinoma (CCA), to determine eligibility for treatment with PBS subsidised futibatinib. The MSAC recalled that it deferred providing advice on the proposed testing in April 2025. MSAC had advised revising the economic and financial analyses by including an updated test fee, testing the whole CCA population at diagnosis and accounting for testing conducted outside of the intended CCA population. MSAC considered that while the current reapplication for the test incorporated a higher test fee to reflect the costs associated with a panel test, it did not appropriately address MSAC's previous concerns and advice that testing should be performed in all newly diagnosed patients with CCA. MSAC also considered that further advice from the Department of Health, Disability and Ageing was required on the appropriate MBS fee for panel testing. MSAC reiterated that the claim of co-dependency of FGFR2 testing and futibatinib was reasonable. MSAC considered that the outstanding issues relating to the testing component could be addressed as a streamlined application.

8.4 The sponsor has since provided further information to be considered at the November 2025 MSAC meeting, and informed the PBAC that the resubmission included assumptions that potentially had an impact on the economic analyses provided in the post-PBAC proposal (see paragraph 10.5).

9 Requested listing

9.1 The PBAC previously considered the restriction appropriate (see section 3 and paragraph 5.3).

10 Economic evaluation

10.1 The sponsor's proposal proposed an ex-manufacturer price (EMP) of $[redacted] per pack (compared to $[redacted] proposed in the July 2025 resubmission).

10.2 The proposal stated that the economic model addressed the key issues raised previously:

- OS HR of futibatinib vs FOLFOX is 0.48 (paragraph 5.4).
- No disutility applied for FOLFOX administration (paragraph 5.5).
- Time horizon is 5 years (paragraph 5.6).
- The ICER is below $75,000/QALY (paragraph 5.7).

10.3 The economic model in the July 2025 resubmission was adapted to allow alternative hazard ratios to be used (see paragraph 4.10). The proposal noted that the approach used to implement this operability moved the futibatinib OS curve below the futibatinib PFS curve, leading to an implausible situation where OS was less than PFS, and deceased patients in the model continued to incur drug cost. To keep the futibatinib curves plausible, the July 2025 resubmission moved the futibatinib OS and PFS curves; however, this resulted in a delinking of the model results from the clinical trial data. To address this issue, the proposal proposed moving the FOLFOX curves to the right to reflect a greater response to treatment in an *FGFR2*+ population than the KM curves in the 'all comers' population, and applying an OS HR of 0.48 (as preferred previously by the PBAC).

Table 10: Results of the economic evaluation presented in the proposal

Analyses	Incremental cost	Incremental QALY	ICER
Using revised model provided in proposal	$[redacted]	0.62	$[redacted][1]

Source: sponsor's proposal
ICER, incremental cost effectiveness ratio; QALY, quality adjusted life years.
The redacted value corresponds to the following range:
[1] *$65,000 to < $75,000*

10.4 The proposal noted that the undiscounted life years gained from the revised model was reduced to 0.85 from 1.99 (paragraph 5.4, futibatinib Public Summary Document [PSD], July 2025 PBAC meeting).

10.5 The sponsor noted that the proposal provided to MSAC (see paragraph 8.4) included the following assumptions that potentially had an impact on the economic analyses for PBAC (i) cost of testing for all patients diagnosed with CCA (rather than testing at advanced/ metastatic disease) and (ii) changes to the cost of testing, including removing assumption regarding Omico testing accounting for a panel test.

10.6 The model in the proposal for PBAC consideration included a test yield of 20%. Decreasing the yield to 10.1% to account for testing in an earlier CCA population had

a small impact on the ICER (+[redacted]%). The model in the proposal for PBAC consideration assumed an MBS fee of $350 with 40% of patients tested at no cost via Omico. Removing testing by Omico had a small impact on the ICER (+[redacted]%).

11 Cost per patient per course

11.1 The cost per patient per course is $[redacted] (based on a treatment duration of 56 weeks).

12 Estimated PBS usage & financial implications

12.1 The PBAC previously considered that the utilisation estimates proposed in the pre-PBAC response (with errors corrected) were reasonable (see paragraph 5.8).

13 PBAC Outcome

13.1 The PBAC deferred making a recommendation for the listing of futibatinib for the treatment of patients with locally advanced or metastatic cholangiocarcinoma (CCA) who have previously progressed on systemic therapy and have a fibroblast growth factor receptor 2 (FGFR2) fusion or rearrangement. The PBAC was of a mind to recommend futibatinib, but noted MBS listing of testing of tumour tissue to detect FGFR2 fusions or rearrangements was not recommended by MSAC in July 2025 and would be reconsidered at the November 2025 MSAC meeting. The PBAC recalled it did not recommend futibatinib in March 2025 or July 2025 due to outstanding issues related to inputs into the economic model and its cost-effectiveness at the proposed price, but considered that these issues have been addressed in the proposal provided by the sponsor which included a price reduction, and additional modelling of Kaplan Meier (KM) curves to better address previous concerns.

13.2 The PBAC recalled that it previously considered there is a high clinical need for more effective therapies for CAA and noted that consumer input received for the March 2025 and July 2025 meetings supported the availability of futibatinib (see paragraph 5.2).

13.3 The PBAC recalled that it previously considered that the proposed restriction was reasonable (see paragraph 5.3).

13.4 The PBAC recalled it previously considered that the July 2025 resubmission did not adequately address its previous concerns regarding cost-effectiveness of futibatinib. The PBAC considered that its previous concerns were addressed in the proposal (paragraph 10.2):

- The OS HR of futibatinib vs FOLFOX was updated to the more conservative value of 0.48 (from 0.32 in the July 2025 resubmission, or 0.24 in the

March 2025 submission), and to account for the uncertain clinical benefit associated with the submission's matched adjusted indirect comparison (MAIC), as previously preferred by the PBAC (paragraph 5.4). The PBAC considered that the sponsor's proposal to move the FOLFOX curves to the right to reflect a greater response to treatment in an FGFR2+ population than the KM curves in the 'all comers' population was reasonable (see paragraph 10.3).

- No disutility applied for FOLFOX administration (paragraph **Error! Reference source not found.**).
- Time horizon of 5 years (from 7 years in the July 2025 resubmission or 10 years in the March 2025 submission, paragraph 5.6).
- Reduction in the proposed ex-manufacturer price (EMP) to $[redacted] per pack (compared to $[redacted] proposed in the July 2025 resubmission, see paragraph 10.1).

The revised inputs and price resulted in an ICER of $65,000 to < $75,000/QALY (Table 10). The PBAC recalled that it had previously considered that an ICER below $75,000/QALY would be acceptably cost effective (paragraph 5.7).

13.5 The PBAC noted changes in the inputs provided to the MSAC for consideration at its November 2025 meeting, including changes to the population and costs for testing (paragraph 10.5), and considered that futibatinib remained cost effective with the revised inputs.

13.6 The PBAC recalled that it previously considered that the utilisation estimates proposed in the pre-PBAC response (with errors corrected) were reasonable (see paragraph 5.8). The PBAC noted the financial estimates need to be updated to include the revised price.

13.7 The PBAC noted that this submission is not eligible for an Independent Review.

Outcome:
Deferred

Addendum to the November 2025 PBAC Public Summary Document:

14 Background

14.1 At its November 2025 meeting, the PBAC deferred making a recommendation for the listing of futibatinib for the treatment of patients with locally advanced or metastatic cholangiocarcinoma (CCA) who have previously progressed on systemic therapy and have a fibroblast growth factor receptor 2 (*FGFR2*) fusion or rearrangement. The PBAC was of a mind to recommend futibatinib, but noted Medicare Benefits Schedule (MBS) listing of testing of tumour tissue to detect *FGFR2* fusions or rearrangements was not recommended by Medicare Services Advisory Committee (MSAC) in July 2025 and would be reconsidered at the November 2025 MSAC meeting.

MSAC consideration – November 2025

14.2 At its November 2025 meeting, the MSAC supported the creation of a new MBS item for testing of tumour tissue to detect *FGFR2* fusions or rearrangements in people with CCA to determine eligibility for treatment with PBS subsidised futibatinib.

15 PBAC Outcome

15.1 The PBAC recommended the listing of futibatinib for the treatment of patients with locally advanced or metastatic CCA who have previously progressed on systemic therapy and have a *FGFR2* fusion or rearrangement. The PBAC noted MSAC had supported creation of a new MBS item for testing of tumour tissue to detect *FGFR2* fusions or rearrangements in people with CCA to determine eligibility for treatment with PBS subsidised futibatinib.

15.2 The PBAC noted the restriction criteria recommended in March 2025 remained appropriate; however, there may be some patients who are currently receiving futibatinib via non-PBS subsidised pathways, who wish to transition to PBS-subsidised treatment and amendments to the criteria to allow this would be reasonable.

15.3 The PBAC noted it had previously considered the proposed price was acceptable (see paragraphs 13.1, 13.4 and 13.5), and the utilisation estimates were reasonable (see paragraph 13.6).

15.4 The PBAC recommended that futibatinib should not be treated as interchangeable on an individual patient basis with any other drugs.

15.5 The PBAC advised that futibatinib is suitable for prescribing by medical practitioners only.

15.6 The PBAC found that the criteria prescribed by the *National Health (Pharmaceuticals and Vaccines – Cost Recovery) Regulations 2022* for Pricing Pathway A were not met. Specifically the PBAC found that in the circumstances of its recommendation for futibatinib:

a) The treatment is not expected to provide a substantial and clinically relevant improvement in efficacy, or reduction of toxicity over alternative therapies, as the magnitude of benefit was highly uncertain;

b) The treatment is not expected to address a high and urgent unmet clinical need as other treatments for CCA are available;

c) It was not necessary to make a finding in relation to whether it would be in the public interest for the subsequent pricing application to be progressed under Pricing Pathway A because one or more of the preceding tests had failed.

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

Outcome:
Recommended

16 Recommended listing

16.1 Add new item:

MEDICINAL PRODUCT **medicinal product pack**	**PBS item code**	**Max. qty packs**	**Max. qty units**	**№.of Rpts**	**Available brands**
FUTIBATINIB					
futibatinib 4mg tablet, 35	NEW MP	4	140	5	Lytgobi®
Restriction Summary [new1] / Treatment of Concept: [new1A]					
Category / Program: ☒ GENERAL - General Schedule (Code GE)					
Prescriber type: ☒Medical Practitioners					
Restriction type: ☒Authority Required (Streamlined) [new/existing code]					
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.					
Episodicity: Locally advance or metastatic					
Condition: Cholangiocarcinoma					
Indication: Locally advanced or metastatic cholangiocarcinoma					
Clinical criteria:					
Patient must have evidence of a fibroblast growth factor receptor 2 (FGFR2) fusion or rearrangement at treatment initiation					
AND					
Clinical criteria:					
Patient must have/have had received at least one prior line of systemic therapy prior to treatment initiation					
AND					
Clinical criteria:					
Patient must have/ have had a World Health Organisation (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 therapy for this condition					
AND					
Clinical criteria:					
Patient must not have developed disease progression while being treated with this drug for this condition.					

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

17 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.

18 Sponsor's Comment

The sponsor had no comment.