Medical Services Advisory Committee (MSAC) Public Summary Document

Application No. 1779 – Testing of tumour tissue to detect FGFR2 fusions or rearrangements in people with cholangiocarcinoma, to determine eligibility for treatment with PBS subsidised futibatinib

Applicant: **Taiho Pharma Oceania Pty Ltd.**

Date of MSAC consideration: **31 July 2025**

Context for decision: MSAC makes its advice in accordance with its Terms of Reference, visit the MSAC website

1. Purpose of application

This codependent application requests:

- Medicare Benefits Schedule (MBS) listing of testing of tumour tissue to detect fibroblast growth factor receptor 2 (*FGFR2*) fusions or rearrangements in people with cholangiocarcinoma (CCA), to determine eligibility for treatment with PBS subsidised futibatinib; and

- Pharmaceutical Benefits Scheme (PBS) Authority required (streamlined) listing of futibatinib for the treatment of locally advanced or metastatic cholangiocarcinoma (CCA) in patients with *FGFR2* fusion or rearrangement.

MSAC deferred its advice at their April 2025 meeting requesting further information for outstanding issues and noting that the Pharmaceutical Benefits Advisory Committee (PBAC) did not recommend futibatinib at its March 2025 meeting. At the time, PBAC considered the issues could be addressed in an early re-entry submission. An early re-entry PBAC submission was submitted on 2 May 2025, for consideration at the July 2025 PBAC meeting.

This streamlined reapplication aimed to address the key issues identified by MSAC at its April 2025 meeting.

2. MSAC's advice to the Minister

After considering the strength of the available evidence in relation to comparative safety, clinical effectiveness, cost-effectiveness and total cost, 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. MSAC noted that the PBAC did not recommend futibatinib for PBS listing at its July 2025 meeting.

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 (the Department) was required on the appropriate MBS fee for panel testing. MSAC reiterated that the claim of codependency 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.

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This was a codependent reapplication from Taiho Pharma Oceania Pty Ltd requesting Medicare Benefits Schedule (MBS) listing of a tumour tissue test to detect fibroblast growth factor receptor 2 (*FGFR2*) gene alterations in patients with cholangiocarcinoma (CCA). The reapplication proposed that people whose tumours are identified as having *FGFR2* alterations would be eligible to access a medicine called futibatinib. The applicant has also requested listing of futibatinib on the Pharmaceutical Benefits Scheme (PBS). Applications for new drugs to be listed on the PBS are considered by the Pharmaceutical Benefits Advisory Committee (PBAC). PBAC and MSAC initially considered this application at their March 2025 and April 2025 meetings, respectively. CCA is also known as bile duct cancer. The bile ducts are a group of thin tubes starting inside the liver that carry bile from the liver and gallbladder into the small intestine. CCA is a rare and aggressive form of cancer, with not many treatment options available. Because of this, survival after diagnosis is usually relatively short, with only half of the patients alive a year after diagnosis. Therefore, there is a need to have access to more effective treatments. This genetic testing targets the *FGFR2* gene. The FGFR2 protein is associated with cell growth and differentiation, and is implicated in cancer growth. *FGFR2* alterations are mainly found in CCA and not in other cancers. MSAC noted that there are other gene targets that are relevant to CCA patients, including *IDH1*. MSAC considered that most pathology laboratories currently do not perform single gene testing and would use a multigene panel approach that included, among other genes, *IDH1* and *FGFR2*. MSAC noted that it may not be financially feasible for laboratories to provide single gene tests, and therefore it considered that the MBS item should be a gene panel test. MSAC received consultation from organisations around the MBS item fee. This consultation provided a range of prices between $300 - $1,247. MSAC considered that it was important to get an appropriate gene panel test fee otherwise patients may have to pay out of pocket. However, due to the range of feedback it was not certain what the appropriate fee should be. MSAC noted that it will work together with the Department to advice on the appropriate fees for this test and future gene panel tests which it may consider. The application originally proposed for the test to be performed once spread of the cancer (from the bile duct) was confirmed. However, during its initial consideration, MSAC advised that the test should be performed when a patient is first diagnosed with CCA. MSAC considered it appropriate to test all newly diagnosed patients because most (70%) CCA patients are diagnosed with late-stage cancer, and the cancer tends to progress very quickly. In the reapplication the applicant disagreed with this approach, stating it would increase the eligible population size by nearly 360% and that most of these patients would not go on to receive futibatinib treatment. However, MSAC reaffirmed that it is beneficial to test patients at

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diagnosis so they can receive test results and access appropriate treatment as soon as possible. MSAC considered it unreasonable to delay testing, as these patients are very unwell. CCA can be hard to diagnose as it can look similar to other cancers when examined under the microscope. In April 2025, MSAC considered that there is possibility that other cancers which are located close to the bile ducts may be thought to be CCA when in fact they are not. Therefore, MSAC considered that this may increase the number of *FGFR2* testing than expected. MSAC requested information about how this may impact the economic evaluation and financial budget. In the reapplication, the applicant stated that these patients may already be considered in the population because the data they used from the Australian Institute of Health and Welfare (AIHW) would have already included them. MSAC disagreed that the AIHW data would fully account for patients in non-CCA populations who may also access *FGFR2* testing. Therefore, MSAC considered that the reapplication did not adequately address MSAC's initial concern of the testing being performed outside of the CCA population. At its July 2025 meeting, PBAC did not recommend listing futibatinib on the PBS because the applicant had not adequately addressed the issues PBAC had flagged when it first considered the application in March 2025. The issues included uncertainties in the economic analysis such as the effect of the medicine, the size of the patient population who would be treated with futibatinib and the number of patients who have *FGFR2* alterations. MSAC acknowledged that *FGFR2* testing is safe and effective and considered that the codependency of *FGFR2* testing and futibatinib has been established. However, MSAC considered the issues from the initial application had still not been resolved in this reapplication. As such, MSAC did not support this reapplication. In addition, the PBAC did not recommend listing the codependent drug futibatinib on the PBS because of unresolved issues from the initial submission. **MSAC's advice to the Commonwealth Minister for Health, Disability and Ageing** MSAC did not support listing of *FGFR2* testing on the MBS for access to futibatinib on the PBS. Although MSAC considered the test to be safe and effective, MSAC noted several outstanding issues that had not been resolved from the initial application. MSAC considered that further information was needed to clarify the testing population and accurately determine the impact that testing at diagnosis would make to the economic and financial analyses. This meant that MSAC could not assess if the testing was good value for money or determine the total cost of testing to the health system.

3. Summary of consideration and rationale for MSAC's advice

MSAC noted this was a streamlined codependent application from Taiho Pharma Oceania Pty Ltd for Medicare Benefits Schedule (MBS) listing of the testing of tumour tissue to detect fibroblast growth factor receptor 2 (*FGFR2*) fusions or rearrangements in people with cholangiocarcinoma (CCA), to determine eligibility for treatment with Pharmaceutical Benefits Scheme (PBS) subsidised futibatinib.

MSAC noted that this was a reapplication. At its previous consideration in April 2025 (MSAC 1779) MSAC deferred providing its advice. MSAC acknowledged that patients with CCA typically have a poor prognosis, and that there is a high clinical need for new treatment options for this patient population. MSAC considered the claim of codependency of *FGFR2* testing and futibatinib was reasonable based on the available (albeit limited) information. MSAC considered that the test is safe and effective, however has uncertain economic and financial implications. MSAC requested that the economic and financial analyses be revised by including a more appropriate test fee and

by incorporating more accurate estimates of the number of patients who would be tested in practice.

MSAC noted that at its March 2025 meeting, the PBAC did not recommend PBS 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 advised that a resubmission, through an early re-entry pathway, should include a more realistic estimate of the clinical benefit in the economic model and revise utilisation estimates to more accurately reflect the prevalence of CCA and the number of patients with *FGFR2* fusions or rearrangements. MSAC noted that the PBAC had considered the early re-entry submission at its July 2025 meeting, where it again did not recommend PBS funding of futibatinib as the resubmission did not adequately address the outstanding issues requested as part of its March 2025 consideration.

MSAC recalled that it had supported public funding for testing of tumour tissue to detect *IDH1* mutations in patients with CCA to determine eligibility for ivosidenib, at its November 2024 meeting (MSAC 1750). MSAC noted that *FGFR2* testing is more technically complex than *IDH1* testing. *FGFR2* variants comprise a variety of fusion partners (currently more than 140), with half of them on the same chromosome or intragenic. MSAC recalled it had considered that *FGFR2* testing is not suitable to be performed using fluorescent in situ hybridisation (FISH), and considered a combined next generation sequencing (NGS) test on DNA and RNA as the most appropriate method to accurately detect *FGFR2* fusions and rearrangements. MSAC recalled that it had considered a single MBS item for a DNA and RNA NGS panel test, for *FGFR2* fusions and rearrangements and *IDH1* sequencing, would be appropriate if both tests are funded. MSAC considered single gene testing of tumour tissue may no longer be efficient or cost-effective for pathology laboratories. MSAC considered that laboratories would likely include both *IDH1* and *FGFR2* testing on a gene panel, rather than as separate single gene tests. Therefore, MSAC considered it appropriate to assess the testing methodology that would occur in clinical practice, specifically *FGFR2* testing on a gene panel, rather than single gene testing of *FGFR2*.

MSAC noted that consultation input on the appropriate fee for a gene panel item was received from multiple stakeholders, including The Royal College of Pathologists of Australasia and Public Pathology Australia. MSAC noted that the fee proposed in the inputs for a DNA and RNA NGS gene panel test including *IDH1* and *FGFR2* testing ranged from $300 to $1,247. MSAC considered a fee of $300 to be too low for a gene panel including the technically complex *FGFR2* testing. MSAC noted that at the time of the reapplication, the applicant did not have access to the stakeholder information, and used a cost of $885 based on the published fee from the Peter MacCallum Cancer Centre (PMCC). MSAC considered it uncertain whether it is feasible for other laboratories to perform the test for this fee as it was unclear whether the PMCC test fee had been cross-subsidised by other sources of funding (for example through philanthropic or research funding). However, MSAC noted that this fee is similar to the gene panel test for sarcoma (MBS 73376; fee $800). MSAC considered that it was important to find the appropriate fee for the test to avoid patients having to pay out of pocket costs. MSAC considered that there is a need to establish a standardised price guide for gene panel tests based on the sample (i.e. DNA or RNA or both) and the number of genes tested and sought further advice from the Department.

MSAC noted that because *FGFR2* would be tested as part of a gene panel, the test will likely have a higher cost than a single gene test, which may increase costs in the economic and financial evaluations. MSAC noted the applicant's position that its reapplication should only account for the incremental difference between the single gene *IDH1* test fee and the proposed gene panel fee in the economic and financial analyses. MSAC considered that this was reasonable.

MSAC recalled that during its previous consideration it recommended that all patients undergo *FGFR2* testing at the time of CCA diagnosis. MSAC noted that the reapplication stated this would

increase the proposed test population by 357% and argued that only patients who receive first line treatment in the locally advanced or metastatic disease stages should receive testing. The reapplication calculated that this population would be a 200% increase compared to that in the initial application. MSAC noted that these are very unwell patients, and considered it unreasonable to wait until patients have received first line therapy for the locally advanced or metastatic disease before testing. MSAC considered that testing at diagnosis avoids delay, saves tissue and minimises the need for re-biopsy. Therefore, MSAC re-affirmed its initial advice that testing should be done at diagnosis of CCA.

MSAC noted that there was no specific histological marker for CCA, and therefore considered that it can be difficult to distinguish CCA and other adenocarcinomas that may metastasise to the liver, such as pancreatic cancer or cancer of unknown primary. Due to this diagnostic uncertainty, MSAC recalled that in its initial consideration it considered there to be a risk that *FGFR2* testing may be higher than expected due to testing non-CCA tumours which are presumed to be CCA. Given that most *FGFR2* fusions and rearrangements occur in patients with intrahepatic CCA (iCCA), MSAC considered that testing tumours other than iCCA may lead to a significant number of tests without any clinical benefit. MSAC noted the reapplication argued that the Australian Institute of Health and Welfare (AIHW) epidemiology data used to estimate patient numbers in the initial application would have already captured patients who may have been misdiagnosed with CCA. MSAC disagreed with this statement and considered that the AIHW data would not fully account for patients in non-CCA populations who may also access *FGFR2* testing. The reapplication did not provide any further information or risk mitigation strategies to address MSAC's concern. MSAC reiterated that there is a significant risk of the expansion of testing to populations other than CCA. MSAC acknowledged that there is significant uncertainty in the proportion of patients from these (unintended) populations who may access the test in practice, however advised that this should be taken into consideration in the economic and financial analyses of any subsequent reapplication. To manage the risk of testing expanding beyond the intended CCA population, MSAC considered it reasonable to monitor *FGFR2* test utilisation, if supported for MBS listing.

MSAC recalled that the initial application modelled 40% of testing at no cost, as this is currently provided by Omico in clinical practice. However, MSAC considered it was unlikely that Omico would continue testing for CCA at no cost if the item were MBS listed. As such, MSAC advised that the modelling be revised to include all testing at full cost. MSAC noted that the reapplication had modelled 20% of testing at no cost (reduced from the 40% modelled in the initial application). MSAC reiterated its initial advice and considered that analyses should be performed by including all testing at full cost.

While MSAC considered the test to be safe and effective, and the codependency of *FGFR2* testing and futibatinib to be established, it considered that there were still unresolved issues outstanding from its initial consideration. MSAC requested further advice from the Department on the appropriate MBS fee for gene panel testing. MSAC considered that the issues related to the testing population remained unresolved. Further, MSAC noted the PBAC did not recommend listing futibatinib on the PBS at its July 2025 meeting. Taking all this into consideration, MSAC did not support the listing of *FGFR2* testing on the MBS. MSAC considered that before the application could be reconsidered, the applicant would need to address the issues raised by MSAC, specifically:

- Include testing costs for all patients diagnosed with CCA at the point of diagnosis for all economic modelling and financial impact analysis.
- Address the issue of expansion of the testing to populations outside of the intended CCA population (e.g. pancreatic cancer and cancer of unknown primary).
- Revise the economic and financial analyses by removing the assumption that 20% of the testing will be performed at no cost

MSAC considered that these issues could be addressed in a streamlined reapplication.

4. Background

Taiho Pharma Oceania Pty Ltd submitted an integrated codependent application in October 2024 for consideration by the PBAC and MSAC at the March 2025 and April 2025 meetings, respectively.

The PBAC did not recommend futibatinib for the treatment of locally advanced or metastatic cholangiocarcinoma (CCA) in patients with *FGFR2* fusion or rearrangement at the March 2025 meeting. The PBAC considered that there was a high clinical need for treatments for patients with CCA, particularly those with locally advanced or metastatic disease, where the prognosis is generally poor. The PBAC noted that based on the available clinical evidence the magnitude of clinical benefit was highly uncertain. The PBAC considered the economic model would need to be amended to include a more conservative and realistic estimate of clinical benefit to increase the reliability of the incremental cost-effectiveness ratio (ICER). The PBAC considered futibatinib would be cost-effective with an ICER of less than $55,000 to < $75,000 per QALY. The PBAC noted the estimated number of patients that would be treated with futibatinib was uncertain and would need revision to more accurately reflect the prevalence of CCA and the number of patients with a *FGFR2* fusion or rearrangement. The PBAC considered the outstanding issues could be addressed in an early re-entry submission (Ratified Minutes).

An early re-entry PBAC submission was lodged 2 May 2025 for consideration at the July 2025 PBAC meeting. A summary of key issues addressed in the resubmission can be found in Table 1-1 of the early re-entry PBAC submission.

MSAC deferred its advice at their April 2025 meeting. MSAC noted that the PBAC did not recommend futibatinib at its March 2025 meeting, and requested further information regarding the testing population, test methodology, cost effectiveness and financial analysis. MSAC considered that a streamlined reapplication could proceed via the direct MSAC assessment pathway. The MSAC summary outcomes is below:

"MSAC acknowledged that patients with CCA typically have a poor prognosis, and that there is a high clinical need for new treatment options for this patient population. MSAC considered the claim of codependency of *FGFR2* testing and futibatinib was reasonable based on the available (albeit limited) information. MSAC considered that *FGFR2* testing should occur in the whole CCA population at diagnosis to prevent any delays in treatment decisions as it is a rapidly progressing cancer and the tumour samples for testing are small. MSAC considered a combined next generation sequencing (NGS) test on DNA and RNA as the most appropriate method to ensure that *FGFR2* fusions and rearrangements are accurately detected, with NGS on RNA or DNA as the next preferred method should a combination test be unavailable. MSAC considered that Fluorescence In Situ Hybridisation (FISH) was not an appropriate testing option as it is less robust (compared to, and superseded by, NGS testing) in detecting tumours with *FGFR2* fusions and rearrangements. MSAC considered that a single MBS item for a DNA and RNA NGS panel test for *FGFR2* fusions and rearrangements and *IDH1* sequencing (Application 1750 supported by MSAC in November 2024 for the whole CCA population) would be appropriate if both tests are funded. MSAC considered an appropriate fee for the panel needed to be determined. MSAC considered there is a risk that test may be used outside of the intended CCA population for other cancers as it can be difficult to differentiate CCA and other cancer in nearby organs (e.g. pancreatic cancers and cancers of unknown primary). MSAC requested further information on the cost effectiveness of a panel test and potential financial impact of testing if testing were to occur in these (unintended) populations in practice. MSAC considered that updated economic and financial analyses should be presented to MSAC via the direct MSAC assessment pathway."

A summary of key matters of MSAC concern and how this reapplication addresses these concerns is provided in Table 1.

Table 1 Summary of key matters of MSAC concern

Component	Matter of concern	How the current assessment report addresses it
Testing population	MSAC considered that *FGFR2* testing should occur in the whole CCA population at diagnosis to prevent any delays in treatment decisions as it is a rapidly progressing cancer and the tumour samples for testing are small.	Although testing population has been revised, it did not include the whole CCA population at diagnosis as advised by MSAC.
Test methodology	MSAC considered a combined next generation sequencing (NGS) test on DNA and RNA as the most appropriate method to ensure that *FGFR2* fusions and rearrangements are accurately detected, with NGS on RNA or DNA as the next preferred method should a combination test be unavailable. MSAC considered that a single MBS item for a DNA and RNA NGS panel test for *FGFR2* fusions and rearrangements and *IDH1* sequencing (Application 1750 supported by MSAC in November 2024 for the whole CCA population) would be appropriate if both tests are funded. MSAC considered an appropriate fee for the panel needed to be determined.	The applicant noted that MSAC is seeking public consultation to inform an appropriate fee, and this advice was not available at the time of lodgement of this reapplication.
Cost effectiveness of testing	MSAC requested further information on the cost effectiveness of a panel test.	As the appropriate fee has not yet been determined the model has been updated to facilitate decision making.
Financial impact of testing	MSAC considered there is a risk of test leakage outside of the intended CCA population as it can be difficult to differentiate CCA and other cancer in nearby organs (e.g. pancreatic cancers and cancers of unknown primary). MSAC requested further information on the potential financial impact of testing if testing were to occur in these (unintended) populations in practice.	The budget impact model has been updated to test the impact of testing.

Abbreviations: CCA = cholangiocarcinoma; *FGFR2* = fibroblast growth factor receptor 2Assessment; MSAC = Medical Services Advisory Committee; NGS = next generation sequencing

MSAC application 1750 (Testing of tumour tissue to detect isocitrate dehydrogenase 1 [*IDH1*] mutations in patients with CCA to determine eligibility for ivosidenib on the PBS) was considered at the July 2024 PBAC/MSAC meetings. The PBAC did not recommend ivosidenib at the July 2024 meeting. MSAC deferred its decision at the July 2024 meeting due to PBAC not recommending ivosidenib at the time. This application was considered again by PBAC and MSAC at the November

2024 meetings and was supported by both committees. Ivosidenib was listed on the PBS and *IDH1* testing listed on the MBS on 1 July 2025.

5. Prerequisites to implementation of any funding advice

LYTGOBI (futibatinib) has been granted provisional registration by the TGA in the Australian Register of Therapeutic Goods (ARTG). The indication is:

"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."

The PBAC considered it would be appropriate for futibatinib to be listed for patients with locally advanced or metastatic CCA who have previously progressed on systemic therapy and who have evidence of an *FGRF2* fusion or rearrangement. The PBAC agreed with the ESCs that it can be difficult to differentiate between intrahepatic and extrahepatic CCA and it was likely futibatinib would provide benefit in the small population of patients with non-iCCA who have an *FGFR2* fusion or rearrangement.

FGFR2 fusions or rearrangements testing is expected to be conducted in specialist laboratories who must hold the appropriate accreditation and registration for this testing procedure to receive MBS funding for the proposed test. Laboratories will need to participate in the relevant Royal College of Pathologist of Australasia (RCPA) Quality Assurance Program (QAP). Testing must be conducted, and the results interpreted and reported by suitably qualified and trained pathologists.

Many laboratories in Australia currently offer National Association of Testing Authorities (NATA) accredited testing for *FGFR2* fusions, supported by an established external quality assessment program.

6. Proposal for public funding

In its initial consideration, the ESCs proposed the following MBS item descriptor if a single gene test for *FGFR2* is supported (Table 2).

Table 2 - MBS item descriptor for single gene *FGFR2* testing as per ESCs advice

Category 6 – Pathology Services	
Proposed item descriptor XXXXX	Group P7 - Genetics
A nucleic acid-based test of tumour tissue for FGFR2 fusions or rearrangements in a patient with cholangiocarcinoma requested by, or on behalf of, a specialist or consultant physician to determine access to a relevant treatment under the Pharmaceutical Benefits Scheme (PBS) Applicable only once per lifetime.	
Fee: $682.35 Benefit: 75% = $511.80 85% = $580.00	

The ESCs proposed the following MBS item descriptor if panel testing is supported (Table 3).

Table 3 - MBS item descriptor for panel testing including *FGFR2* and *IDH1* testing as per ESCs advice

Category 6 – Pathology Services	
Proposed item descriptor XXXXX	Group P7 - Genetics
A nucleic acid-based multi-gene panel test of tumour tissue from a patient with cholangiocarcinoma requested by, or on behalf of, a specialist or consultant physician, if the test is: (a) To detect at least IDH1 variant status[a], and (b) To detect the fusion or rearrangement status of at least FGFR2 (c) To determine access to a relevant treatment under the Pharmaceutical Benefits Scheme (PBS) Applicable only once per lifetime.	
Fee: $TBC Benefit: 75% = $TBC 85% = $TBC	

[a]Note that this would only be included if *IDH1* testing is MBS listed.

At its April 2025 meeting, MSAC considered that a single MBS item for a DNA and RNA NGS panel test for *FGFR2* fusions and rearrangements and *IDH1* sequencing (Application 1750 supported by MSAC in November 2024 for the whole CCA population) would be appropriate if both tests are funded. The applicant acknowledged MSAC's desire to future proof the MBS item descriptor. However, the applicant noted that testing at the point of CCA diagnosis will result in additional cost to the MBS, much of which will be attributable to testing in patients who will never be assessed for eligibility for treatment in the second line advanced setting (futibatinib and/or ivosidenib), including those who elect no treatment at all in the advanced disease setting.

Given the higher cost of testing estimated under the proposed MBS item descriptor to identify one patient eligible for futibatinib, the applicant proposed that the descriptor be narrowed and the cost effectiveness of testing all patients with CCA be reconsidered if targeted treatments become available in the earlier phases of disease.

In preparing the initial submission, the applicant identified a range of MBS fees listed for NGS. This included:

- Item 73437 for a DNA and RNA-based multi-gene panel test of tumour tissue from a patient with a new diagnosis of non-small cell lung cancer has a fee of $1,247.00.
- Item 73439 for an RNA-based multi-gene panel test of tumour tissue from a patient with a new diagnosis of non-small cell lung cancer has a fee of $682.55.
- Item 73376 for the analysis of tumour tissue from a patient with sarcoma for the analysis of four or more genes has a fee of $800, or item 73374 for the analysis of tumour tissue from a patient with sarcoma for the analysis of one gene has a fee of $340.
- Item 73433 for an NGS test for NTRK fusions by DNA or RNA in tumour tissue from a patient with a locally advanced or metastatic solid tumour has a fee of $1,000.00.

The applicant noted that the published private cost of reporting a single gene is $350 at Peter MacCallum Cancer Centre.

In the initial submission, the applicant proposed a fee of $350 per test in the base case of the economic and financial analyses given testing was proposed using RNA only and reporting limited to *FGFR2* fusions or rearrangements.

Single gene test fee

The ESCs considered that if an RNA testing gene panel alone is supported, a fee comparable to MBS item 73439 for fusion testing in lung cancer would be appropriate ($682.35).

Panel testing fee

The PBS listing of ivosidenib and MBS listing (item 73319) for *IDH1* testing occurred on 1 July 2025. Based on this, panel testing is considered the most likely scenario. Whilst MSAC has sought public consultation to inform an appropriate fee, this advice was not available at the time of lodgement of this reapplication. The applicant has undertaken targeted consultation to inform the additional analyses presented in this reapplication.

At its February 2025 meeting, the ESCs considered that the MBS item fee for panel testing should be aligned to other established MBS items for panel testing, such as item 73437 for sequence and fusion testing in lung carcinoma (MBS fee $1,247.00). However, the applicant argued that this item has a benefit reflective of testing at least 4 genes and may not be entirely relevant to this reapplication.

The applicant noted that only two targets are included in the proposed CCA panel. The applicant noted from targeted consultation that an appropriate fee would likely be less than the lung panel and in the vicinity of $800-$900. The applicant noted that the private cost of an NGS DNA and RNA panel is currently $885 at Peter MacCallum Cancer Centre.

The applicant considered that it would be appropriate to only apply the incremental cost of testing required to detect *FGFR2* fusion or rearrangement in this reapplication.

The MSAC 1750 PSD indicates that the proposed fee for *IDH1* testing is $340.

Based on the information above, this reapplication assumed an incremental cost of $885-$340 = $545 in the base case for *FGFR2* testing, when included on a panel test with *IDH1* testing.

7. Population

Testing in locally advanced or metastatic disease

The applicant noted that the test population was increased by 200% in the PBAC early re-entry submission to account for testing earlier in the algorithm (i.e. all patients who receive first line treatment in the locally advanced or metastatic disease stages receive testing).

The applicant noted that including locally advanced or metastatic patients who elect no first-line treatment results in a 286% increase in testing, and including all patients at the first diagnosis of CCA as previously proposed by MSAC (i.e. either early stage or advanced disease) would result in a 357% increase in testing. The applicant considered that these are not reasonable scenarios as, at this point in time, they do not reflect clinical practice.

The applicant considered it appropriate to only apply the cost of testing according to the proposed clinical algorithm, which is aligned with key clinical guidelines (which recommend that testing occur in the advanced stage of disease), the inclusion criteria of FOENIX-CCA2 and the timing of testing in current Australian clinical practice. The applicant noted that they had received advice from clinical experts at the Advisory Board (cited in the initial submission) and targeted consultation during the preparation of this reapplication which stated that, in practice, testing will occur in patients with locally advanced or metastatic disease who are electing first-line treatment (i.e. in most cases durvalumab + GemCis) for the sole purpose of guiding second line targeted treatment.

Given the rare nature of this cancer and fusion/rearrangement, the applicant considered the test cost was at a disadvantage, compared to other more common diseases and cancers with biomarkers. The applicant therefore considered it unreasonable for the cost of any additional testing beyond that proposed in Section 13 and 14 to be borne by the test in this reapplication.

The applicant therefore considered it was appropriate that the updated economic and financial analyses used the 200% increase to the test population.

Testing of patients with pancreatic cancer and cancer of unknown primary

The applicant contended that the MSAC's request to include additional testing of patients with pancreatic cancer and cancer of unknown primary would be double counting. The applicant considered that if differentiating the site of the primary tumour is as problematic as suggested, it could reasonably be expected that these patients were already captured in the AIHW epidemiology data used to estimate patient numbers in the original submission.

The applicant therefore considered it was appropriate that the updated economic and financial analyses did not further adjust testing to account for potential misdiagnoses, as these patients were assumed to already be included.

Diagnostic yield

The diagnostic yield was reduced from 20% to 13.9 in the early re-entry submission to PBAC in the assessment of the financial impact. Yield of 13.9% was included in the MSAC reapplication and was also considered in the economic model.

8. Comparator

There was no change to the drug or test comparator compared to the initial submission.

9. Summary of consultation input

The Department received consultation input on the potential test fees from three organisations (The Royal College of Pathologists of Australasia [RCPA], Public Pathology Australia [PPA], and QIAGEN).

The organisations were asked to advise on the appropriate costs for testing *FGFR2* fusions and rearrangements and *IDH1* variants in tumour tissue from a patient with suspected CCA using the following methodologies:

1. A DNA and RNA next generation sequencing (NGS) multigene panel test (with at least 2 genes)
2. A DNA NGS multigene panel test (with at least 2 genes)
3. A RNA NGS multigene panel test (with at least 2 genes)

They were also asked to advise on the appropriate cost for testing *FGFR2* fusions and rearrangements as a single gene test using the following methodologies:

1. DNA and RNA NGS
2. DNA NGS
3. RNA NGS

The input received is summarized in Table 4 below.

Table 4 Summary of consultation input on test costs for application 1779

Test Type	PPA	RCPA	QIAGEN
DNA + RNA NGS Multigene Panel (≥2 genes)	$1247	$1247	$300–480[1]
DNA NGS Multigene Panel (≥2 genes)	~$400	$682.35	$165–325[1]
RNA NGS Multigene Panel (≥2 genes)	~$850	$682.35	$175–300[1]
RNA + DNA Single Gene	Not provided	$1247	$275-480[1]
DNA NGS Single Gene	$200	Not provided	$165–325[1]
RNA NGS Single Gene	$850	$682.35	$175–300[1]

[1] Cost per sample

Given MSAC identified there may be clinical uncertainty in assigning a morphological diagnosis of CCA at the time of diagnosis and that the test population may, in practice include a proportion of those with pancreatic cancer or cancer of unknown primary, RCPA and PPA were asked to advise on an estimate of the proportion and number of patients with pancreatic cancers and cancer of unknown primary who may be suspected of having CCA and tested for *FGFR2* fusions or rearrangements.

RCPA stated that there is significant uncertainty, but the number is likely very small especially after multidisciplinary team (MDT) review. They suggested that requiring a final MDT diagnosis of CCA could help reduce uncertainty and recommended using World Health Organization terminology of “intrahepatic cholangiocarcinoma” and “carcinoma of the extrahepatic bile ducts” to clearly distinguish between intrahepatic and extrahepatic CCA. RCPA noted that the clinical trials that supported funding for *FGFR2* testing likely included a small proportion of patients who may not have had true CCA, and this uncertainty may already be reflected in the clinical and cost-effectiveness estimates.

PPA provided an estimate for South Australia, noting around 100 cases of CCA are diagnosed annually, with approximately 200 cases entering the differential diagnosis between CCA and pancreatic cancer. They noted that SA Pathology captures about 60% of these cases, therefore they estimate around 200 patients would be tested for *FGFR2* fusions on the MBS each year.

10. Characteristics of the evidence base

Refer to PBAC public summary document and Section 11 and 12 below.

There were no changes to the evidence base for the test component compared to the initial submission.

11. Comparative safety

There were no changes to the claim of comparative safety for the drug or test component compared to the initial submission.

12. Comparative effectiveness

The early re-entry submission to PBAC altered the overall survival hazard ratio (to 0.32 from 0.24) based on the PBAC advice from its March 2025 meeting. This increased the overall survival associated with FOLFOX treatment and increased the ICER. No changes occurred to the futibatinib PFS or OS curves.

13. Economic evaluation

The base case in the original submission resulted in an ICER of $95,000 to < $115,000/quality adjusted life year (QALY) and the cost of testing to identify one patient treated with futibatinib of $1,050.

At its March 2025 meeting, the PBAC noted uncertainty within the economic evaluation of futibatinib. PBAC noted the model resulted in an undiscounted life year gain of 2.48 over a 10-year horizon, which it considered implausibly large. The PBAC recommended the model should use more conservative overall survival hazard ratios, noting Paine 2022, and Borad 2022 (HR: 0.48–0.49 vs the model's 0.24) to better reflect realistic outcomes. Additionally, the PBAC suggested shortening the time horizon to 5 years to reduce uncertainty and align with application 1750 for ivosidenib in *IDH1*-positive CCA.

The applicant noted three key inputs were changed in the PBAC early re-entry submission. These did not impact the test component.

- The change in the OS HR to 0.32 was accompanied by a structural change to permit use of HRs in the model.
- The time horizon was reduced from 10 to 7 years.
- The effective approved ex-manufacturer price (AEMP) of futibatinib was reduced from $**Redacted** per pack to $**Redacted**.

These input changes resulted in an ICER of $75,000 to < $95,000 /QALY in the resubmission to PBAC. The cost of testing to identify one patient treated with futibatinib was $1,050. Further details were provided in the PBAC early re-entry submission.

There was also a reduction in the diagnostic yield to 13.9% from 20% in the financial and economic estimates.

The applicant noted that including the diagnostic yield of 13.9% down from 20% in the economic model increased the ICER to $75,000 to < $95,000 and the cost of testing to identify one patient treated with futibatinib to $1,511.

The applicant noted that in its previous consideration, the MSAC had proposed the following four additional changes to the test component:

1. Increase test cost (range of $682.35 to $1,247, from $350)
2. Reduce Omico testing where MBS does not pay from 40% to 0%
3. Include testing at the point of CCA diagnosis (equivalent to an additional 357% of tests versus base case)
4. Increase testing population by taking into consideration the patients with pancreatic cancer and cancer of unknown primary who may access the test

The applicant noted that using the upper thresholds of MSAC changes above, the cost of testing to identify one patient who will have futibatinib increased to $32,040.

The applicant considered that the $32,040 cost of testing per futibatinib treated patient represented Redacted% of the calculated drug cost in the model and Redacted% of the total costs of the futibatinib arm. The applicant considered that this was not reflective of a plausible clinical scenario that was described in the earlier sections of the reapplication.

The applicant proposed the below updated values, consistent with Sections 6 and 7:

1. An updated panel test cost of $885, with $545 attributable to *FGFR2* testing
2. An increase in testing population to include testing at the point of first line treatment in the locally advanced and metastatic stage (i.e. 200% additional versus base case)
3. No increase in testing population to include pancreatic cancer and cancer of unknown primary, as the applicant considered these patients were already included in the epidemiology estimates derived from AIHW
4. Reduction in diagnostic yield to 13.9%, consistent with the early re-entry submission to PBAC. The Department noted that the economic model assumed that 13.9% of tested patients would be eligible for futibatinib treatment. The Department considered that this did not reflect testing at initial diagnosis of CCA. As, if all patients diagnosed with CCA have testing at diagnosis, the diagnostic yield would be lower.
5. The applicant also noted that the average proportion of testing undertaken by Omico or within a public hospital (ie. non-MBS testing) was revised to 20%. The applicant noted they had received advice through targeted consultation during the preparation of this reapplication that suggested a number of patients with CCA undergo testing as inpatients due to the severity of their condition. The applicant considered it a reasonable assumption that government funded Omico testing would not be eligible for an MBS service.

With these updated values the ICER was $95,000 to < $115,000/QALY and a test cost of $6,273.38 to identify one patient treated with futibatinib.

Table 5 presents the results of the economic evaluation using the updated values described above.

Table 5: Cost results from the economic model – updated base case

	Total costs ($)	PF	PD	AE	EOL	Drug acquisition	Drug admin.	Test costs
Futibatinib	$Redacted	$2,215	$787	$802	$45,990	$Redacted	$0	$6,273
Chemotherapy	$59,608	$1,412	$299	$1,577	$49,990	$2,740	$3,590	$0
Incremental cost	**$Redacted**	**$803**	**$488**	**-$774**	**-$3,999**	**$Redacted**	**-$3,590**	**$6,273**
% of incremental cost		**Redacted%**	**Redacted%**	**-Redacted%**	**-Redacted%**	**Redacted%**	**-Redacted%**	**Redacted%**

Abbreviations: AE = adverse events, EOL = end of life costs, PD = progressed disease state, PF = progression free state

The incremental cost of futibatinib treatment becomes Redacted and incremental QALYs are constant at 0.91. As such, the ICER ($/QALY) is $95,000 to < $115,000.

14. Financial/budgetary impacts

Using the values described in Section 13 of this reapplication, the applicant estimated costs to MBS of *FGFR2* testing as $0 to < $10 million in year 1, increasing to $0 to < $10 million in year 6 (Table 6).

Table 6: MBS costs of *FGFR2* testing – updated base case

Description	2025	2026	2027	2028	2029	2030
Resubmission to PBAC (already doubled the population)	$Redacted[1]	$Redacted[1]	$Redacted[1]	$Redacted[1]	$Redacted[1]	$Redacted[1]
Change test cost to $545	$Redacted[1]	$Redacted[1]	$Redacted[1]	$Redacted[1]	$Redacted[1]	$Redacted[1]
Include OMICO testing to 20%	$Redacted[1]	$Redacted[1]	$Redacted[1]	$Redacted[1]	$Redacted[1]	$Redacted[1]
All changes	**$Redacted[1]**	**$Redacted[1]**	**$Redacted[1]**	**$Redacted[1]**	**$Redacted[1]**	**$Redacted[1]**

Abbreviations: PBAC = Pharmaceutical Benefits Advisory Committee
The redacted values correspond to the following ranges:
[1]$0 to < $10 million

The Department provided sensitivity analyses on the financial estimates. These are shown below in Table 7.

Table 7 Department conducted sensitivity analysis

Description	2025	2026	2027	2028	2029	2030
Total incident population[a]	**Redacted[2]**	**Redacted[2]**	**Redacted[2]**	**Redacted[2]**	**Redacted[2]**	**Redacted[2]**
Patients diagnosed with locally advanced, metastatic CCA (80%)[a]	**Redacted[2]**	**Redacted[2]**	**Redacted[2]**	**Redacted[2]**	**Redacted[2]**	**Redacted[2]**
Number of patients tested in the original submission[b]	**Redacted[1]**	**Redacted[1]**	**Redacted[1]**	**Redacted[1]**	**Redacted[1]**	**Redacted[1]**
Number of patients tested in reapplication[c]	**Redacted[2]**	**Redacted[2]**	**Redacted[2]**	**Redacted[2]**	**Redacted[2]**	**Redacted[2]**
Cost to MBS of *FGFR2* testing if testing is done at diagnosis[d]	**$Redacted[3]**	**$Redacted[3]**	**$Redacted[3]**	**$Redacted[3]**	**$Redacted[3]**	**$Redacted[3]**
Cost to MBS of *FGFR2* testing if testing is done at locally advanced, metastatic CCA[d]	**$Redacted[3]**	**$Redacted[3]**	**$Redacted[3]**	**$Redacted[3]**	**$Redacted[3]**	**$Redacted[3]**
Cost to MBS of *FGFR2* testing if tested at diagnosis and test price increases to $1247[e]	**$Redacted[3]**	**$Redacted[3]**	**$Redacted[3]**	**$Redacted[3]**	**$Redacted[3]**	**$Redacted[3]**

[a] Information sourced from PBAC early re-entry submission
[b] The original submission did not present an estimate of number of patients tested. During the evaluation the implied estimates were calculated based on the submission's estimate of number of units of testing presented in the financial workbook, which was estimated by multiplying the number of patient years of futibatinib treatment in the incident population (12.5 months; 1.04 patient years per patient treated) by 500% (based on an assumed 20% prevalence).
[c] 200% increase from original submission
[d] Calculated by Incident rate x test price ($545, at 80% MBS rebate). Note that this does not include costs to the MBS for optical coherence tomography nor cost offsets to the MBS from reduction in FOLFOX administration.
[e] Calculated by Incident rate x test price ($1247, at 80% MBS rebate). Note that this does not include costs to the MBS for optical coherence tomography nor cost offsets to the MBS from reduction in FOLFOX administration.
The redacted values correspond to the following ranges:
[1]< 500
[2]500 to < 5,000
[3]$0 to < $10 million

15. Other relevant information

Table 8 below is the estimated utilisation data and financial impact analysis from application 1750 for *IDH1* testing in CCA.

Table 8 - Estimated use and financial implications to the MBS

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Estimated extent of use of IDH1 testing						
Total CCA incidence	**Redacted[2]**	**Redacted[2]**	**Redacted[2]**	**Redacted[2]**	**Redacted[2]**	**Redacted[2]**
Number of patients tested (uptake of 90%)	**Redacted[2]**	**Redacted[2]**	**Redacted[2]**	**Redacted[2]**	**Redacted[2]**	**Redacted[2]**
Number of patients likely to receive a positive test result (9.15% positive rate)	**Redacted[1]**	**Redacted[1]**	**Redacted[1]**	**Redacted[1]**	**Redacted[1]**	**Redacted[1]**
Estimated financial implications of the IDH1 testing to the MBS						
Cost to MBS less copayments (80% of the proposed MBS fee)	**$Redacted[3]**	**$Redacted[3]**	**$Redacted[3]**	**$Redacted[3]**	**$Redacted[3]**	**$Redacted[3]**
Cost to MBS less copayment (85% of the proposed MBS fee)[a]	**$Redacted[3]**	**$Redacted[3]**	**$Redacted[3]**	**$Redacted[3]**	**$Redacted[3]**	**$Redacted[3]**
Estimated financial implications for ECG monitoring to the MBS						
Cost to MBS less copayments (80% benefit, MBS item 11704)	**$Redacted[3]**	**$Redacted[3]**	**$Redacted[3]**	**$Redacted[3]**	**$Redacted[3]**	**$Redacted[3]**
Cost to MBS less copayment (85% of the proposed MBS fee)[a]	**$Redacted[3]**	**$Redacted[3]**	**$Redacted[3]**	**$Redacted[3]**	**$Redacted[3]**	**$Redacted[3]**
Net financial implications						
Net cost to MBS	**$Redacted[3]**	**$Redacted[3]**	**$Redacted[3]**	**$Redacted[3]**	**$Redacted[3]**	**$Redacted[3]**
Net cost to MBS, assuming 85% benefit[a]	**$Redacted[3]**	**$Redacted[3]**	**$Redacted[3]**	**$Redacted[3]**	**$Redacted[3]**	**$Redacted[3]**

Source: Table 4-19 and Table 4-20, p181 of the submission.
CCA = cholangiocarcinoma; ECG = electrocardiogram; IDH1 = isocitrate dehydrogenase 1
[a] Additional analyses performed during the evaluation, by assuming 85% benefit as for out of hospital services.

The redacted values correspond to the following ranges:
[1] < 500
[2] 500 to < 5,000
[3] $0 to < $10 million

As noted in the PSD for 1750, the listing of *IDH1* testing for CCA patients was estimated to result in a net cost of *$0 to < $10 million* in Year 1 to *$0 to < $10 million* in Year 6 to the MBS. At its June 2024 meeting the ESCs noted that an epidemiological approach was utilised to estimate the number of patients who would receive treatment based on the CCA incidence data from the Australian Institute of Health and Welfare (AIHW) and historical growth rate. The ESCs agreed with the commentary that the Applicant Developed Assessment Report (ADAR) had overestimated the number of patients likely to be treated with ivosidenib. Consequently, the MBS costs for electrocardiograms (ECGs) to monitor patients receiving ivosidenib were likely to be lower than estimated. The ESCs noted the ADAR's overestimation was accepted by the applicant in its pre-ESC response. The ESCs noted that sensitivity analyses indicated the financial results were largely stable under the scenarios tested. However, the ESCs also considered that potential increases in testing could occur due to a "diagnostic expansion'. The ESCs considered that if the MBS fee for the proposed item were raised from aligning with other *IDH1* testing to instead aligned with other comparable MBS items, this would also increase the net financial cost to the MBS. Similarly, if the testing were implemented as a gene panel test to futureproof testing for patients with CCA, then this would likely be at a higher cost than $340 per test.

At its August 2024 meeting, MSAC noted ESC's concern about possible diagnostic expansion leading to *IDH1* testing intended for patients with CCA also being conducted in patients with

primary distal common bile duct or head of pancreas, and metastatic pancreatobiliary cancer or carcinoma of unknown primary site. MSAC noted the pre-MSAC response argued that this was unlikely, as a diagnosis of CCA is required to have occurred before genetic testing of the tumour tissue. MSAC agreed with ESC that these cancers had similar profiles to CCA, and noted that *IDH1* variants are more common in intrahepatic CCA than in extrahepatic CCA. MSAC considered that, even if there was leakage through diagnostic expansion, the additional service volume would be extremely small. MSAC considered it would be appropriate for all patients with a tumour in their bile ducts to receive this testing (including when it is uncertain whether the CCA is the primary tumour), and that this would not have any material effect on the financial cost or the cost-effectiveness of testing. Overall, MSAC advised the financial cost of *IDH1* testing to the MBS was acceptable. However, given the remaining uncertainty around test volumes, MSAC considered if it were to support this testing, it would be appropriate to review service volumes following implementation.

16. Applicant comments on MSAC's Public Summary Document

Taiho remains committed to working with MSAC to facilitate access to testing of tumour tissue to detect *FGFR2* fusions or rearrangements in people with CCA, to determine eligibility for treatment with PBS subsidised futibatinib.

17. Further information on MSAC

MSAC Terms of Reference and other information are available on the MSAC Website: visit the MSAC website