

# Medical Services Advisory Committee (MSAC) Public Summary Document

## ***Application No. 1750 – Testing of tumour tissue to detect IDH1 mutations in patients with cholangiocarcinoma to determine eligibility for ivosidenib on the Pharmaceutical Benefits Scheme***

**Applicant:** Servier Laboratories (Aust.) Pty. Ltd.

**Date of MSAC consideration:** 29 November 2024

Context for decision: MSAC makes its advice in accordance with its Terms of Reference, [visit the MSAC website](#)

### **1. Purpose of application**

This streamlined codependent resubmission requested:

- Medicare Benefits Schedule (MBS) listing of *isocitrate dehydrogenase 1 (IDH1)* testing for the evaluation of Tier I IDH1 p.R132X variants for the determination of patient eligibility for treatment with ivosidenib in patients with cholangiocarcinoma (CCA); and
- Pharmaceutical Benefits Schedule (PBS) listing of ivosidenib (Tibsovo®) for the treatment of adult patients with locally advanced or metastatic cholangiocarcinoma (CCA) who have previously progressed on chemotherapy and a have confirmed *IDH1* variant.

*The Commentary Executive Summary refers to the 'PBAC resubmission' where relevant information was sourced from the resubmission commentary to the Pharmaceutical Benefits Advisory Committee (PBAC).*

### **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 supported the creation of a new Medicare Benefits Schedule (MBS) item for tumour tissue *isocitrate dehydrogenase 1 (IDH1)* variant testing to determine access to a relevant treatment under the Pharmaceutical Benefits Scheme (PBS) in patients with histologically confirmed cholangiocarcinoma. MSAC noted that PBAC had recommended ivosidenib for treatment of locally advanced or metastatic cholangiocarcinoma with an *IDH1* variant, in patients who have previously progressed on chemotherapy. At its August 2024 meeting, MSAC considered the testing was safe, the cost to the MBS was acceptable, and if it provided access to ivosidenib on the PBS, then this test would improve health outcomes for the subset of patients with cholangiocarcinoma who harbour an *IDH1* variant. MSAC acknowledged the high clinical unmet need in the defined population that would be met by access to this test noting that improved health outcomes were shown for cholangiocarcinoma patients with *IDH1* variants treated with ivosidenib. MSAC noted that PBAC considered the incremental cost-effectiveness ratio (ICER) of ivosidenib remained high at the proposed price and a further price reduction would be required.

**Table 1 MSAC's supported MBS item descriptor**

|   |
|---|
| Category 6 – Pathology Services<br>Group P7 – Genetics  |
| XXXXX<br>Detection in tumour tissue of <i>isocitrate dehydrogenase 1 (IDH1)</i> variant status, in a patient with histologically confirmed cholangiocarcinoma, to determine access to a relevant treatment under the Pharmaceutical Benefits Scheme.<br>Applicable only once per lifetime |
| Fee: \$340 Benefit: 75% = \$255.00 85% = \$289.00   |

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|--|
| <p><b>Consumer summary</b></p> <p>This was an application from Servier Laboratories Australia Pty. Ltd. requesting Medicare Benefits Schedule (MBS) listing to detect clinically significant genetic variants in the gene <i>isocitrate dehydrogenase 1 (IDH1)</i> in the cancer of patients with cholangiocarcinoma. People with these <i>IDH1</i> variants will then be eligible to access a medicine called ivosidenib on the Pharmaceutical Benefits Scheme (PBS). At the time that this application was made, ivosidenib was not listed on the PBS, so a codependent application that proposed public funding of both the test and the medicine was required.</p> <p>Cholangiocarcinoma 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 intestine. cholangiocarcinoma is a rare and aggressive form of cancer, with not many treatment options available to these patients and survival after diagnosis is usually relatively short. Significant <i>IDH1</i> genetic variants occur in the cancer of around 10% of people with cholangiocarcinoma. The presence of these <i>IDH1</i> variants in patients with cholangiocarcinoma leads to increased levels of an oncometabolite (a compound that contributes to cancer cell growth) called D-2-hydroxyglutarate (D2-HG).</p> <p>This application was for ivosidenib treatment to be funded for patients with locally advanced or metastatic cholangiocarcinoma (metastatic means that the cancer has spread beyond where it originated), who have previously tried chemotherapy, and are found to have an <i>IDH1</i> genetic variant in their cancer. The proposed genetic test would be done by a pathology laboratory on the tumour sample taken during the biopsy that was done as part of their cholangiocarcinoma diagnosis.</p> <p>MSAC recalled that it had previously accepted that <i>IDH1</i> testing was safe, effective and acceptable value for money. It would also have a modest financial impact because cholangiocarcinoma is rare and not many people would need this test and treatment. However, in August 2024, MSAC deferred its decision on listing the <i>IDH1</i> testing on the MBS as the Pharmaceutical Benefits Advisory Committee (PBAC) did not recommend listing ivosidenib on the PBS at its August 2024 meeting. In November 2024, the PBAC recommended ivosidenib for listing on the PBS as long as the cost of the drug was further reduced. Therefore, MSAC supported listing <i>IDH1</i> testing on the MBS.</p> <p><b>MSAC's advice to the Commonwealth Minister for Health and Aged Care</b><br/>MSAC supported listing <i>IDH1</i> testing on the MBS for people with cholangiocarcinoma. The testing is safe, effective, with an acceptable budget impact because cholangiocarcinoma is rare. MSAC noted PBAC recommended further price reduction for the medicine ivosidenib before it is listed on the PBS.</p> |
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### 3. Summary of consideration and rationale for MSAC's advice

MSAC noted that this was a streamlined codependent application from Servier Laboratories (Aust.) Pty. Ltd. requesting MBS listing of testing to detect *isocitrate dehydrogenase 1 (IDH1)* genetic variants in the tumours of adult patients with locally advanced or metastatic cholangiocarcinoma (CCA) who have previously progressed on chemotherapy, and PBS listing of ivosidenib (Tibsovo®) for the treatment of those patients whose tumours are found to have an *IDH1* genetic variant.

MSAC noted that this codependent application claimed that the IDH1 inhibitor ivosidenib (Tibsovo®) is a highly targeted therapeutic candidate for treating patients with CCA who have a clinically significant *IDH1* variant. MSAC noted that testing for *IDH1* variants is required to determine eligibility for ivosidenib if listed on the Pharmaceutical Benefits Scheme (PBS).

MSAC recalled at its August 2024 meeting, it had considered *IDH1* genetic testing to be comparatively safe, would have an acceptable financial cost to the MBS, and if testing provided access to ivosidenib on the PBS then it would improve health outcomes for patients with *IDH1* variants. MSAC further recalled that the Pharmaceutical Benefits Advisory Committee (PBAC) did not recommend the initial submission at its July 2024 meeting because of the high incremental cost-effectiveness ratio (ICER) at the proposed price and the optimistic assumptions used in the economic model. The PBAC considered that these issues could be addressed in an early re-entry submission. Consequently, MSAC deferred its decision for public funding of *IDH1* genetic testing in patients with CCA at its August 2024 meeting.

MSAC noted that the PBAC at its November 2024 meeting recommended listing ivosidenib on the PBS, with a further price reduction.

MSAC noted that CCA accounts for 3% of gastrointestinal cancers, which are broadly classified as intrahepatic (iCCA) or extrahepatic (eCCA) cancers. The prognosis for CCA is poor due to the aggressive nature of the disease (typically advanced at diagnosis) and lack of effective treatment options. MSAC noted the low 5-year survival rate for patients with locally advanced or metastatic CCA. MSAC noted that *IDH1* genetic variations are predominantly somatic and occur in around 10% of CCA cases. The variants are mostly heterozygous missense variants at the arginine residue *IDH1*:R132 in the catalytic site, consistent with a direct gain of function impact on the enzyme function. Ivosidenib inhibits isocitrate dehydrogenase enzyme activity and reduces production of the oncometabolite D2-HG.

MSAC noted the population, intervention, comparator and outcome (PICO) that had been ratified by the PICO Advisory Subcommittee.

MSAC noted the consultation feedback, which was supportive of testing to enable a more personalised treatment approach. Feedback raised concerns about access to testing and access to appropriate medical and non-medical interventions. MSAC noted Pancare and the Cholangiocarcinoma Foundation Australia emphasized the need for supporting patients undergoing the testing, including providing genetic counselling and psychological support. However, MSAC considered that this was likely unnecessary as almost all variations identified are somatic. MSAC noted the Royal College of Pathologists of Australasia (RCPA) feedback highlighted the application mentioned 'tissue' in the item descriptor, and that this could potentially include specimen types unsuitable for genetic testing (such as cytology specimens).

MSAC noted that most contemporary *IDH1* tumour testing is performed as part of a gene panel test (using next generation sequencing) rather than as a single gene test.

MSAC noted that *IDH1* genetic testing is currently performed for other tumours, notably gliomas, which has the same test fee of \$340. MSAC noted the MBS item descriptor. MSAC agreed with ESC advice from its June 2024 meeting, that specific reference to *IDH1*:p.R132 variants was not required, and that the descriptor should refer to 'relevant treatment listed under the Pharmaceutical Benefits Scheme' instead of specifying the drug class. MSAC also considered it appropriate that the test be pathologist-determinable. MSAC noted ESC's concern about possible diagnostic expansion of *IDH1* testing for cancers of unknown primary that occur in the liver or bile duct but agreed with applicant's pre-MSAC response arguing the risk that use of the test might expand beyond appropriate indications was small, as a diagnosis of CCA is required prior to genetic testing of the tumour tissue, due to the MBS item descriptor specifying 'histologically confirmed cholangiocarcinoma'.

MSAC agreed with the clinical management algorithm.

MSAC noted that the clinical evidence was derived primarily from the ClarIDHy trial, which compared ivosidenib with placebo in locally advanced or metastatic CCA patients with *IDH1* variants who had disease progression after at least one line of chemotherapy. MSAC noted that ivosidenib has inferior safety compared to standard treatment, but with manageable adverse events (AEs). MSAC noted that during ivosidenib therapy, there is a potential for prolongation of

the QT interval. Therefore, electrocardiogram (ECG) testing before and during treatment (an average of 7.7 ECG tests per patient) is required.

MSAC noted that the clinical claim was ivosidenib was superior in terms of efficacy compared to standard (palliative) care. Data from the ClarIDHy trial showed that, for patients with *IDH1* genetic variants, ivosidenib resulted in a small progression-free survival advantage (median ~1.3 months) and moderate overall survival (OS) advantage (median ~2.8 months) compared with standard treatment. However, MSAC noted the gain in OS was not statistically significant. Therefore, MSAC considered that gains were very modest, and survival remained poor. MSAC noted when adjustment was made for crossover from the placebo arm using a rank-preserving structural failure time model (RPSFT), it improved the OS survival gain with ivosidenib to a median of 5.2 months. Overall MSAC considered that testing would be comparatively effective if it provided access to ivosidenib.

MSAC noted that the submission presented a cost utility analysis with a 5-year time horizon, based on the ClarIDHy trial. The base case results demonstrated that ivosidenib was more costly but more effective than standard care in CCA patients with a *IDH1* genetic variant. The total cost associated with *IDH1* testing and ivosidenib treatment was \$redacted, compared with \$25,158.1 for no testing and standard of care (incremental cost of \$ redacted). MSAC noted the quality-adjusted life years (QALYs) associated with *IDH1* testing and ivosidenib were 1.009, compared with 0.481 for standard of care (incremental QALYs of 0.528). MSAC noted that this translated to a base case ICER of \$55,000 < \$75,000 per QALY. Sensitivity analyses demonstrated that the ICERs range from \$55,000 < \$75,000 to \$75,000 < \$95,000 per QALY for the companion test and treatment.

MSAC noted the financial impact and the applicant's updated estimated uptake of the test. MSAC noted assuming an 85% benefit, the financial impact to the MBS was \$0 < \$10 million in Year 1 increasing to \$0 < \$10 million in Year 6 and considered it to be a modest budget impact noting the rarity of the condition. MSAC noted that the financial impact to the total health budget was \$0 < \$10 million in Year 1 increasing to \$0 < \$10 million in Year 6.

Overall, MSAC considered *IDH1* genetic testing was comparatively safe and that if testing provided access to ivosidenib on the PBS it would improve health outcomes for the patients with CCA who harbour an *IDH1* variant. MSAC considered the financial cost to the MBS was acceptable. Therefore, MSAC supported listing of *IDH1* genetic variant testing for patients with cholangiocarcinoma (CCA). MSAC noted that the PBAC's positive recommendation for listing ivosidenib on the PBS depended on a further price reduction.

## 4. Background

MSAC had previously considered *IDH1* testing in patients with CCA to determine access to ivosidenib (Tibsovo®) for the treatment of locally advanced or metastatic cholangiocarcinoma in patients who have evidence of an *IDH1* variant and who have previously progressed on systemic therapy. The original application was considered by MSAC at its August 2024 meeting.

MSAC deferred its decision and foreshadowed that it would reconsider if the PBAC recommended the PBS listing of ivosidenib for the treatment of adult patients with locally advanced or metastatic CCA with a confirmed *IDH1* variant and who have previously progressed on chemotherapy.

*IDH1* genetic testing is already funded for patients with glioma or glioblastoma (MSAC applications 1527<sup>1</sup> and 1709<sup>2</sup>) where patients can currently access *IDH1/2* testing under MBS item 73372, and gene panel testing under MBS item 73429. Other MBS items (73445, 73446, 73447 and 73448) are also available that provide gene panel testing for the diagnosis and classification of haematological malignancies, which must include genes described in clinical guidelines, and these currently include the *IDH1* gene.

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<sup>1</sup> MSAC Application 1527, available at: <http://www.msac.gov.au/internet/msac/publishing.nsf/Content/1527-public>

<sup>2</sup> MSAC Application 1709, available at: <http://www.msac.gov.au/internet/msac/publishing.nsf/Content/1709-public>

## 5. Prerequisites to implementation of any funding advice

The test is a Class 3 in-house *in vitro* diagnostic (IVD) and as such, is exempt from inclusion on the ARTG. However, laboratories providing the test and not using an ARTG listed product, must meet the requirements for in-house IVDs. Laboratories that manufacture class 1-3 in-house IVDs to perform this test must comply with the conformity assessment procedure in Part 6A, Schedule 3, of the *Therapeutic Goods (Medical Devices) Regulations 2002*<sup>3</sup>.

The ratified PICO confirmation stated that laboratories who offer the test will need to participate in the relevant Royal College of Pathologists of Australasia (RCPA) Quality Assurance Program or a similar external quality assurance program.

## 6. Proposal for public funding

The resubmission proposed a new MBS item descriptor for testing *IDH1* variant status in CCA patients and is presented in Table 2.

The proposed fee is identical to the current MBS item 73372 for *IDH1/2* variant testing.

**Table 2 Proposed MBS item descriptor**

|   |
|---|
| Category 6 – PATHOLOGY SERVICES   |
| XXXXX<br>Detection in tumour tissue of p.R132X tier 1 variant status, in a patient with histologically confirmed cholangiocarcinoma, to determine access to an isocitrate dehydrogenase 1 inhibitor under the Pharmaceutical Benefits Scheme (PBS). |
| Applicable only once per lifetime   |
| Fee: \$340  |

Source: Table 1-2, p19 of the resubmission

Due to unavailability of the MSAC PSD from the August 2024 meeting at the time of the resubmission lodgement, specific points relevant to MSAC’s consideration of the item descriptor were not addressed in the resubmission. The applicant confirmed in its pre-PBAC response for ivosidenib that it agreed to the MSAC supported item descriptor from the August 2024 meeting (Table 3).

**Table 3 MSAC’s revised MBS item descriptor**

|  |  |
|--|--|
|  | Category 6 – Pathology Services<br>Group P7 – Genetics |
| XXXXX<br>Detection in tumour tissue of <i>isocitrate dehydrogenase 1 (IDH1)</i> variant status, in a patient with histologically confirmed cholangiocarcinoma, to determine access to a relevant treatment under the Pharmaceutical Benefits Scheme. |  |
| Applicable only once per lifetime  |  |
| Fee: \$340 Benefit: 75% = \$255.00 85% = \$289.00  |  |

## 7. Summary of public consultation input

A summary of previous consultation feedback received for MSAC Application 1750 is available in the Public Summary Document. Please refer to application 1750 PSD August 2024<sup>4</sup> (pp 8-9).

<sup>3</sup> [Manufacturing or supplying in-house in-vitro diagnostic medical devices \(IVDs\) | Therapeutic Goods Administration \(TGA\)](#) Australian Department of Health, accessed 13 December 2024.

<sup>4</sup> <http://www.msac.gov.au/internet/msac/publishing.nsf/Content/1750-public>

## 8. Comparative effectiveness

No new clinical evidence was presented in this resubmission. The clinical evidence in the original submission was primarily based on the ClariDHy trial, a multicentre, randomised, double-blinded, placebo-controlled phase 3 study. At its August 2024 meeting, MSAC had considered the evidence demonstrated that treating patients who have an *IDH1* variant with ivosidenib resulted in a modest improvement to survival, and so advised the testing would be comparatively effective if it provided access to ivosidenib.

## 9. Comparative safety

No additional safety data were presented in the resubmission. MSAC had considered there to be no additional adverse events expected from this testing because testing for *IDH1* variants would be performed on the same tumour tissue used to histologically diagnose CCA.

## 10. Economic evaluation

The PBAC resubmission presented a revised cost-effectiveness analysis, based on inputs recommended by the PBAC in its July 2024 consideration of ivosidenib. The respecified base case results demonstrated that ivosidenib was more costly but more effective than standard of care in patients with CCA who harboured an *IDH1* variant. In patients with *IDH1* variants, the cost associated with *IDH1* testing and ivosidenib treatment was \$redacted compared to \$25,158 with no testing and SoC (incremental cost \$redacted). The quality adjusted life years (QALYs) associated with ivosidenib treatment, for patients with *IDH1* variant who underwent treatment with ivosidenib were 1.009 compared to 0.481 for no testing and standard of care (SOC) (incremental QALYs 0.528). The respecified base case ICER was \$55,000 < \$75,000 per QALY (Table 4).

Table 4 Results of the respecified base case analysis

|                               | Cost                    | Incremental cost        | Effectiveness | Incremental effectiveness | ICER                           |
|-------------------------------|-------------------------|-------------------------|---------------|---------------------------|--------------------------------|
| <i>IDH1</i> test + ivosidenib | \$redacted <sup>1</sup> | \$redacted <sup>1</sup> | 1.009         | 0.528                     | redacted <sup>1</sup> per QALY |
| No test + SOC                 | \$25,158.11             |                         | 0.481         |                           |                                |

Source: Table ES 1 of resubmission Executive summary

Abbreviations: ICER= incremental cost-effectiveness ratio; *IDH1* = isocitrate dehydrogenase 1 gene; SOC = standard of care.

The redact values correspond to the following ranges:

<sup>1</sup>\$55,000 < \$75,000

The resubmission presented univariable and multivariable sensitivity analyses based on input from PBAC ESC from the July 2024 PBAC meeting.

## 11. Financial/budgetary impacts

The resubmission presented updated utilisation and financial estimates based on advice provided by the PBAC and Drug Utilisation Sub Committee (DUSC) on the July 2024 submission. The budget impact model was updated with the following changes:

- The uptake rate of the *IDH1* test was increased to redacted% (from redacted% in the previous submission).
- A rate of progression to 2L treatment was incorporated into the model, assumed to be 70% per DUSC feedback (assumed 100% in previous submission).
- The uptake rate of ivosidenib was increased to redacted % (previously redacted % to redacted %), as the rate of progression to 2L treatment already incorporated uptake.

Similar to the previous submission, the financial analysis included MBS costs associated with electrocardiogram (ECG) monitoring in patients receiving ivosidenib treatment. As ivosidenib therapy is associated with an increased risk of prolongation of QTc interval, the ivosidenib product information recommends performing an ECG prior to treatment initiation, at least weekly

during the first 3 weeks of therapy and at least monthly thereafter. Based on the average duration of treatment of 25.1 weeks as modelled in the economic evaluation, the submission assumed an average of 7.77 ECGs per patient treated with ivosidenib.

The resubmission estimated a net cost to the MBS (assuming 80% rebate for both *IDH1* testing and electrocardiogram [ECG] monitoring) of \$0 < \$10 million in Year 1 to \$0 < \$10 million in Year 6. The revised net cost to the MBS calculated by the department assuming 85% rebate increased this cost to more than \$0 < \$10 million in Year 1 and \$0 < \$10 million in Year 6. Including the cost of revised *IDH1* testing (85% benefit), the listing of ivosidenib is expected to result in a net cost to the health budget of \$0 < \$10 million in Year 1 growing to almost \$0 < \$10 million in Year 6 (Table 5).

**Table 5: Estimated use and financial implications**

|  | Year 1                      | Year 2                      | Year 3                      | Year 4                      | Year 5                      | Year 6                      |
|--|-----------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|
| <b>Estimated extent of use</b>   |                             |                             |                             |                             |                             |                             |
| Number of patients tested  | redacted <sup>2</sup>       | redacted <sup>2</sup>       | redacted <sup>2</sup>       | redacted <sup>2</sup>       | redacted <sup>2</sup>       | redacted <sup>2</sup>       |
| Patients treated <sup>a</sup>  | redacted <sup>1</sup>       | redacted <sup>1</sup>       | redacted <sup>1</sup>       | redacted <sup>1</sup>       | redacted <sup>1</sup>       | redacted <sup>1</sup>       |
| Number of scripts dispensed <sup>b</sup>   | redacted                    | redacted                    | redacted                    | redacted                    | redacted                    | redacted                    |
| <b>Estimated financial implications</b>  |                             |                             |                             |                             |                             |                             |
| Cost to PBS/RPBS \$  | redacted <sup>3</sup>       | redacted <sup>3</sup>       | redacted <sup>3</sup>       | redacted <sup>3</sup>       | redacted <sup>3</sup>       | redacted <sup>3</sup>       |
| Cost to MBS for testing \$ (assuming 80% benefit)  | redacted <sup>3</sup>       | redacted <sup>3</sup>       | redacted <sup>3</sup>       | redacted <sup>3</sup>       | redacted <sup>3</sup>       | redacted <sup>3</sup>       |
| <i>Cost to MBS for testing \$ (assuming 85% benefit fee of \$289)</i>                          | <i>redacted<sup>3</sup></i> | <i>redacted<sup>3</sup></i> | <i>redacted<sup>3</sup></i> | <i>redacted<sup>3</sup></i> | <i>redacted<sup>3</sup></i> | <i>redacted<sup>3</sup></i> |
| Cost to MBS for increased ECG monitoring \$ (assuming 80% benefit)                             | redacted <sup>3</sup>       | redacted <sup>3</sup>       | redacted <sup>3</sup>       | redacted <sup>3</sup>       | redacted <sup>3</sup>       | redacted <sup>3</sup>       |
| <i>Cost to MBS for increased ECG monitoring \$ (85% benefit fee of \$30.30 for item 11704)</i> | <i>redacted<sup>3</sup></i> | <i>redacted<sup>3</sup></i> | <i>redacted<sup>3</sup></i> | <i>redacted<sup>3</sup></i> | <i>redacted<sup>3</sup></i> | <i>redacted<sup>3</sup></i> |
| Net cost to MBS \$ (assuming 80% benefit)  | redacted <sup>3</sup>       | redacted <sup>3</sup>       | redacted <sup>3</sup>       | redacted <sup>3</sup>       | redacted <sup>3</sup>       | redacted <sup>3</sup>       |
| <i>Net cost to MBS \$ (assuming 85% benefit)</i>   | <i>redacted<sup>3</sup></i> | <i>redacted<sup>3</sup></i> | <i>redacted<sup>3</sup></i> | <i>redacted<sup>3</sup></i> | <i>redacted<sup>3</sup></i> | <i>redacted<sup>3</sup></i> |
| <b>Net cost to health budget (PBS/RPBS/MBS) \$</b>   | <b>redacted<sup>3</sup></b> | <b>redacted<sup>3</sup></b> | <b>redacted<sup>3</sup></b> | <b>redacted<sup>3</sup></b> | <b>redacted<sup>3</sup></b> | <b>redacted<sup>3</sup></b> |
| <i>Net cost to health budget \$ (PBS/RPBS/MBS adjusted for 85% benefit)</i>                    | <i>redacted<sup>3</sup></i> | <i>redacted<sup>3</sup></i> | <i>redacted<sup>3</sup></i> | <i>redacted<sup>3</sup></i> | <i>redacted<sup>3</sup></i> | <i>redacted<sup>3</sup></i> |
| <b>Previous submission (August 2024)</b>   |                             |                             |                             |                             |                             |                             |
| Number of patients tested  | redacted <sup>2</sup>       | redacted <sup>2</sup>       | redacted <sup>2</sup>       | redacted <sup>2</sup>       | redacted <sup>2</sup>       | redacted <sup>2</sup>       |
| Patients treated   | redacted <sup>1</sup>       | redacted <sup>1</sup>       | redacted <sup>1</sup>       | redacted <sup>1</sup>       | redacted <sup>1</sup>       | redacted <sup>1</sup>       |
| Number of scripts dispensed <sup>b</sup>   | redacted <sup>1</sup>       | redacted <sup>2</sup>       | redacted <sup>2</sup>       | redacted <sup>2</sup>       | redacted <sup>2</sup>       | redacted <sup>2</sup>       |
| Cost to PBS/RPBS \$  | redacted <sup>3</sup>       | redacted <sup>3</sup>       | redacted <sup>3</sup>       | redacted <sup>3</sup>       | redacted <sup>3</sup>       | redacted <sup>3</sup>       |
| Net cost to MBS \$ (assuming 85% benefit)  | redacted <sup>3</sup>       | redacted <sup>3</sup>       | redacted <sup>3</sup>       | redacted <sup>3</sup>       | redacted <sup>3</sup>       | redacted <sup>3</sup>       |
| <b>Net cost to health budget (PBS/RPBS/MBS)</b>  | <b>redacted<sup>3</sup></b> | <b>redacted<sup>3</sup></b> | <b>redacted<sup>3</sup></b> | <b>redacted<sup>3</sup></b> | <b>redacted<sup>3</sup></b> | <b>redacted<sup>3</sup></b> |

<sup>a</sup> Assumes 9.15% prevalence of *IDH1*m, 80% with advanced/metastatic disease and 70% progressing to second line treatment.

<sup>b</sup> Includes 14 scripts for 5 grandfathered patients in year 1. Assuming 5.62 scripts per incident patients treated with ivosidenib. The number of scripts was estimated based on a treatment duration of 25.11 weeks and a compliance rate of 95.9%. The number of scripts per grandfathered patients was estimated to be 2.81 (=5.62/2).

Abbreviations: ECG = electrocardiogram; MBS= Medicare Benefits Schedule; PBS = Pharmaceutical Benefits Scheme; RPBS= Repatriation Pharmaceutical Benefits Scheme

Source: Table 6 Commentary Executive Summary, Table MSAC 9 1750 August 2024 MSAC PSD, Financial excel spreadsheet "4.1\_Budget impact model\_Aug2024\_FINAL"

Texts in italics calculated by the department

The redacted values correspond to the following ranges:

<sup>1</sup>< 500

<sup>2</sup>500 to < 5,000

<sup>3</sup>\$0 to < \$10 million

## **12. Applicant comments on MSAC's Public Summary Document**

Servier welcomes the positive recommendation made by MSAC and looks forward to working with the Department of Health and Aged Care to help facilitate access to IDH1 testing on the MBS for patients with cholangiocarcinoma at the earliest opportunity. Servier wishes to thank the Committees for working constructively throughout the process, and the cholangiocarcinoma clinical and patient community for providing valuable input to inform the Committees' deliberations.

## **13. Further information on MSAC**

MSAC Terms of Reference and other information are available on the MSAC Website:  
[visit the MSAC website](#)