4.01 OBETICHOLIC ACID
Tablet 5 mg
Tablet 10 mg
Ocaliva®
Chiesi Australia Pty Ltd

1 Purpose of Application

1.1 At its November 2020 meeting, the PBAC deferred making a recommendation for obeticholic acid (OCA) for the treatment of primary biliary cholangitis (PBC) in combination with ursodeoxycholic acid (UDCA) in UDCA inadequate responders and as monotherapy in patients intolerant to UDCA to seek a price reduction.

1.2 The purpose of this item was to consider the sponsor's revised:

- price;
- economic model; and
- financial impact estimates workbook that includes revised risk sharing arrangement (RSA) caps.

1.3 The PBAC noted that although the Sponsor had offered a further price reduction, the Sponsor again relied on the proposed RSA to achieve the ICER requested by the PBAC in November 2020.

2 Background

Registration status

2.1 OCA was registered by the TGA on 21 September 2018 for 'the treatment of primary biliary cholangitis (also known as primary biliary cirrhosis) in combination with ursodeoxycholic acid (UDCA) in adults with an inadequate response to UDCA or as monotherapy in adults unable to tolerate UDCA'.

Previous PBAC consideration

2.2 Submissions to list OCA had been rejected in November 2018 and March 2019.

2.3 In November 2020, the PBAC again acknowledged that there was a clinical need for effective PBC treatments, but considered that a price reduction would be required to address the uncertainties relating to the magnitude of the clinical benefit and the incremental cost-effectiveness ratio (ICER) (paragraph 7.1, obeticholic acid Public Summary Document (PSD), November 2020). The PBAC also considered that the calculated ICER should not be reliant on the proposed risk sharing arrangement (RSA)

to be achieved, particularly given the likely overestimated financial assumptions (paragraph 7.6, obeticholic acid PSD, November 2020).

2.4 In November 2020 (paragraph 7.6, obeticholic acid PSD), the PBAC considered that the ICER of $75,000 to <$95,000 per quality adjusted life year (QALY) remained too high and uncertain. This was particularly so given the uncertain magnitude of the clinical benefit and the unverified economic model inputs. In November 2020, the PBAC considered that an appropriate ICER, using the model presented, would be less than $55,000 to <$75,000 per QALY and would incorporate the following three changes only:

(i) a 0.015 disutility for pruritus applied yearly from Year 2 for the 30 year time horizon of the model (a disutility of 0.03 should be applied in Year 1);

(ii) the assumption that all patients received the full dose of OCA; and

(iii) a suitable price reduction for OCA.

2.5 In terms of the estimated financial impact, in November 2020 (paragraph 7.8, obeticholic acid PSD), the PBAC noted that the impact of listing OCA on the PBS/RPBS had increased to $200 million to < $300 million over the first six years (from $100 million to <$200 million in July 2019). The PBAC considered this to be an overestimate of the likely cost due to the resubmission:

- applying a compounding 10% annual growth rate to the number of UDCA treated patients from 2017 onwards. This resulted in the 5,000 to < 10,000 patients treated in 2017 increasing to 10,000 to < 20,000 patients in 2026. The PBAC noted the average growth rate over the period 2013-2017 was 8% and in 2017 it was 7%. The PBAC expected the diagnosis and incidence of PBC to be stable, and advised an annual growth rate of 7% should be applied in 2017 with it reducing by 0.5% each year such that the growth in 2026 is 2.5%;
- overestimating the number of continuing patients. The PBAC noted this was estimated in the resubmission to be 95% and considered it should be reduced to less than 90%;
- overestimating adherence to OCA. The PBAC noted this was estimated in the resubmission to be 93.55% and considered it should be 80%; and
- including grandfathered patients after Year 1. The PBAC considered the grandfathered patients should be accounted for in Year 1 only.

2.6 In November 2020 (paragraph 7.10, obeticholic acid PSD), the PBAC noted that the proposed RSA included a [redacted]% rebate for use above set financial caps. The PBAC considered such a RSA was appropriate to account for the uncertainties associated with the potential for continued use in non-responders and the uncertain uptake. The PBAC considered, due to the uncertain and overestimated financial impact, that the proposed reduction in the financial caps did not adequately address the financial risk

or cost effectiveness of OCA. The PBAC advised the financial caps should be based on the revised financial estimates, as outlined in paragraph 2.3.

3 Requested listing

3.1 The March 2021 proposal did not include an amended restriction. The proposed restrictions, with Secretariat amendments (additions in italics, deletions in strikethrough), are as per the November 2020 resubmission and evaluation.

Name, Restriction, Manner of administration and form	**Max. Qty**	**№.of Rpts**	**DPMQ**	**Proprietary Name and Manufacturer**	
OBETICHOLIC ACID *obeticholic acid* tablet 5 mg, 30	1 pack	5	Published: $4,178.12 Effective: $[redacted]	OCALIVA®	Manufacturer: Intercept Pharma Australian Sponsor: Chiesi Australia Pty Ltd
Category/Program: ~~Section 85 (~~General Schedule~~)~~ *(Code GE)*					
Prescriber type: ☒Medical Practitioners					
Restriction type: ☒Authority Required - ~~In Writing~~ *non-immediate/full assessment by Services Australia*					
Condition: Primary biliary cholangitis *(previously known as Primary biliary cirrhosis)*					
~~**PBS**~~ **Indication:** Primary biliary cholangitis *(previously known as Primary biliary cirrhosis)*					
Treatment phase: Initial treatment					
Treatment criteria:					
Patient must be treated by a gastroenterologist or hepatologist or in consultation with a gastroenterologist or hepatologist.					
~~**Clinical**~~ ***Treatment*** **criteria: [group with other treatment criteria]**					
~~Treatment must be in combination~~ *Patient must be undergoing treatment* with ursodeoxycholic acid; or ~~(UDCA) in adults with an inadequate response to UDCA,~~					
~~Treatment~~ *Patient* must be *undergoing treatment with this drug* as monotherapy~~, in adults unable to tolerate UDCA, due to severe side effects~~ *if combination treatment with ursodeoxycholic acid is not tolerated*.					
Population criteria:					
Patient must have experienced an inadequate response to ursodeoxycholic acid					
Clinical criteria:					
Patient must not have severe liver disease, ~~OR~~					
AND					
Clinical criteria:					
Patient must not ~~have immunodeficiency diseases~~ *be immunocompromised*,					
AND					
Clinical criteria:					
The treatment must not be for sclerosing cholangitis					
AND					
Clinical criteria					
The treatment must not be for cholelithiasis					
AND					
Clinical criteria					
Patient must be aged 18 years or older					
AND					
Clinical criteria:					
~~The p~~*P*atient must have an alkaline phosphatase (ALP) ~~greater than or equal to~~ *of at least* 1.67 times the upper limit of normal (ULN) *having accounted for each of: (i) age (ii) gender (iii) laboratory to laboratory variances in the definition of 'normal', despite treatment with ursodeoxycholic acid for at least 12 months* ~~AND/OR~~ *or*					
Patient must have a total bilirubin ~~> 1x ULN but < 2x the ULN~~ between 1 to 2 times the ULN, *despite treatment with ursodeoxycholic acid for at least 12 months; or*					

Patient must have abnormal readings of at least one of: (i) alkaline phosphatase (ii) total bilirubin, if an intolerance of a severity requiring treatment discontinuation with ursodeoxycholic acid developed
Prescrib~~er~~*ing* ~~advice**~~*instructions*:** *Where an intolerance to ursodeoxycholic acid is claimed, state the intolerance.* ~~Severe side effects of UDCA therapy include diarrhoea, upper abdominal pain, decompensation of hepatic cirrhosis, calcification of gallstones, allergic reactions or urticaria~~ *Retain qualifying laboratory readings relating to either of alkaline phosphatase or total bilirubin in the patient's medical records. These figures are to be stated in this authority application and used for:* *(i) assessing whether an adequate response to treatment has been achieved under the Continuing treatment restriction;* *(ii) PBS compliance auditing purposes*
~~**Administrative Advice**: Not for use in the treatment of sclerosing cholangitis or cholelithiasis.~~
Administrative Advice: Special pricing arrangements apply
Caution: *Hepatic decompensation and failure, in some cases fatal, have been reported in post-marketing reports in patients with moderate to severe hepatic impairment when dosed incorrectly*

Name, Restriction, Manner of administration and form	Max. Qty	№.of Rpts	Proprietary Name and Manufacturer	
OBETICHOLIC ACID *Obeticholic acid* tablet 10 mg, 30 *Obeticholic acid tablet 5 mg, 30*	1 pack	5	OCALIVA®	Manufacturer: Intercept Pharma Australian Sponsor: Chiesi Australia Pty Ltd

Category/Program: ~~Section 85 (~~General Schedule~~)~~ *(Code GE)*
Prescriber type: ☒Medical Practitioners ☒Nurse practitioners
Condition: Primary biliary cholangitis *(previously known as Primary biliary cirrhosis)*
~~PBS~~ Indication: Primary biliary cholangitis *(previously known as Primary biliary cirrhosis)*
Treatment phase: Continuing treatment
Restriction type: ☒Authority Required - immediate/real time assessment by Services Australia (telephone/online)
~~**Treatment criteria**:~~
Patient must be treated by a gastroenterologist or hepatologist or in consultation with a gastroenterologist or hepatologist.
Clinical criteria:
~~Patient must have previously been issued with an authority prescription for this drug for this condition,~~ *Patient must have previously received PBS-subsidised treatment with this drug for this condition*
~~**AND**~~
~~**Clinical criteria:**~~
~~Patient must have adequately tolerated 5 mg dose at 6 months assessment, OR~~
AND
Clinical criteria:
Patient must have achieved an adequate response to ~~5 mg~~ *this drug* as defined *as at least one of: (i)* ~~an~~ *current (within the past 4 weeks)* ALP measurement ~~<~~*less than* 1.67 x ULN, *(ii)* ~~≥~~ *a reduction in the current (within the past 4 weeks) ALP reading of at least a* 15% ~~decrease from~~*compared to the* baseline ~~in ALP~~, *measurement stated in the Initial treatment Authority application, (iii)* ~~and~~ *a current (within the past 4 weeks)* total bilirubin ~~<~~ *~~less than~~* ~~1x ULN~~ *measurement within the normal reference range*
~~**AND**~~
~~**Clinical criteria:**~~
~~Patient must continue to achieve an adequate response at yearly assessments, OR~~
~~***AND***~~
~~***Clinical criteria:***~~
~~*Patient must* Nnot have *(i)* compensated cirrhosis, *(ii)* decompensated cirrhosis or *(iii)* hepatocellular carcinoma.~~
Administrative Advice: Not for use in the treatment of sclerosing cholangitis or cholelithiasis.
Administrative Advice: Special pricing arrangements apply
Administrative Advice: **Note** For prescribing by nurse practitioners as continuing therapy only, where the treatment of, and prescribing of medicine for, a patient has been initiated by a ~~gastroenterologist or a hepatologist or in consultation with a gastroenterologist or hepatologist~~ *medical practitioner*. Further information can be found in the Explanatory Notes for Nurse Practitioners.
Caution: *Hepatic decompensation and failure, in some cases fatal, have been reported in post-marketing reports in patients with moderate to severe hepatic impairment when dosed incorrectly*

3.2 In the March 2021 meeting pre-PBAC response, the sponsor accepted the addition of the Caution note alerting prescribers to the need for dosage adjustment in patients who experience severe pruritus or moderate or severe hepatic impairment. The pre-PBAC response also stated that a grandfathering restriction would be required; the PBAC agreed.

3.3 The sponsor and Secretariat had proposed a written-only Authority for initial treatment, but reconsideration of whether there is: (i) a high risk of non-compliance with a particular criterion or Prescriber instruction, and, (ii) a high ability for Services Australia to independently verify a particular response given by the PBS prescriber

applied, resulted in the view that not one criterion had both a high risk of non-compliance and high verifiability. Based on a patient prevalence of approximately 5,000 to < 10,000 patients over the first six years of listing, and noting the presence of a proposed RSA, the PBAC considered that an immediate type assessment (telephone/online) authority for the initial supply and a Streamlined authority for the continuing supply of OCA would be appropriate.

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

4 Comparator

4.1 The previous submissions nominated UDCA monotherapy as the main comparator for UDCA inadequate responders and placebo as the main comparator for UDCA intolerant patients. The PBAC has previously considered these to be the appropriate comparators (paragraph 7.4, obeticholic acid PSD, November 2018).

4.2 In addition, in November 2020 the PBAC considered OCA monotherapy would likely be acceptably cost-effective in UDCA intolerant patients at the same reduced price as for the UDCA-inadequate responders (paragraph 7.7, obeticholic acid PSD, November 2020). Accordingly, the revised economic model is a cost-utility analysis versus UDCA.

5 Consideration of the evidence

Sponsor hearing

5.1 There was no hearing for this item as it was a minor submission.

Consumer comments

5.2 The PBAC noted that no consumer comments were received for this item.

Economic analysis

5.3 Table 1 outlines the changes to the economic model which were recommended by the PBAC in November 2020 (paragraph 2.2) and how and/or if the recommendations have been addressed in the March 2021 revised economic model.

Table 1: PBAC recommended changes to the November 2020 economic model

	November 2020	PBAC recommendation	Changed in model?
Disutility value for pruritus	0.03, applied in Year 1 only	0.03 in Year 1, 0.015 in Years 2 to 30	Yes, as requested
Dose of OCA	21% would receive half-dose, with no change in efficacy	100% of patients should receive full-dose	Yes, as requested
Effective DPMQ of OCA	$ [redacted] in submission ($ [redacted] in pre-PBAC response)	Should be reduced to give ICER of < $ [redacted][1]/QALY	Yes, to $ [redacted] which was 10% lower than pre-PBAC response.
ICER	$ [redacted][2]/QALY in submission $ [redacted][3]/QALY in pre-PBAC (which incorporated the RSA)	ICER should be < $ [redacted][1]/QALY with the three changes outlined above only	ICER = $ [redacted][1]/QALY The reduced effective DPMQ, in combination with the other 2 changes outlined in the rows above, did not result in an ICER of < $ [redacted][1].

Source: Complied during the evaluation using Ocaliva Economic Evaluation PBAC Jan 2021 Excel workbook
DPMQ = dispensed price for maximum quantity; ICER = incremental cost-effectiveness ratio; OCA = obeticholic acid; PBAC = Pharmaceutical Benefits Advisory Committee; QALY = quality-adjusted life year; RSA = risk sharing arrangement
The redacted values correspond to the following ranges:
[1]*$55,000 to <$75,000/QALY gained*
[2]*$75,000 to <$95,000/QALY gained*
[3]*$35,000 to <$45,000/QALY gained*

5.4 The revised economic model incorporated the changes in the disutility value for pruritus and the dose of OCA as requested by the PBAC in November 2020. The proposed effective dispensed price for maximum quantity (DPMQ) of $ [redacted] (or approved ex-manufacturer price (AEMP) of $ [redacted]) resulted in an ICER of $55,000 to < $75,000 per quality-adjusted life year (QALY). The Sponsor indicated that it was unable to reduce the ICER to less than $55,000 to <$75,000 per QALY through a reduction in the DPMQ of OCA only.

5.5 In order to achieve an ICER of less than $55,000 to <$75,000 per QALY, the effective DPMQ of OCA would have to be less than $ [redacted] (i.e. the AEMP would have to be less than $ [redacted]).

5.6 Although the PBAC stated in November 2020 that it considered that the calculated ICER should not be reliant on the RSA to be achieved (paragraph 7.6, obeticholic acid PSD, November 2020), the Sponsor relied on the revised financial estimates and the revised RSA, which consisted of caps that were on average 29% below the revised financial estimates (over the first five years of listing) beyond which [redacted]% rebates would be applied, to achieve an ICER of less than $55,000 to <$75,000 per QALY.

5.7 If the caps were exceeded by an average of 29% over the first five years of listing, and this reduction was applied to the effective DPMQ, the resulting average price would be $ [redacted] (DPMQ level; $ [redacted] AEMP level) and the resulting ICER would be $45,000 to < $55,000 per QALY.

Estimated PBS usage & financial implications

5.8 Table 2 outlines the changes to the financial impact estimates which were recommended by the PBAC in November 2020 (paragraph 2.3) and how and/or if the recommendations have been addressed in the March 2021 revised financial impact estimates.

Table 2: PBAC recommended changes to the November 2020 financial impact estimates

	November 2020	PBAC recommendation	Changed in workbook?
Growth rate of UDCA treated patients	10% annual rate from 2017 onwards	7% in 2017, and reducing by 0.5% per year so that growth in 2026 is 2.5%	Yes, as requested
Number of continuing patients	95%	Less than 90%	Changed to 90%
Adherence to OCA	93.55%	80%	Yes, as requested
Grandfathered patients	Included after Year 1	Include only in Year 1	Yes, as requested
Effective DPMQ of OCA	$[redacted]	-	$[redacted]

Source: Compiled during evaluation using Ocalvia_UCM-Release-3-Workbook-v106 Jan 2021 Excel workbook
DPMQ = dispensed price for maximum quantity; OCA = obeticholic acid; PBAC = Pharmaceutical Benefits Advisory Committee; UDCA = ursodeoxycholic acid

5.9 The changes to the financial impact estimates outlined above resulted in the revised patient, prescription and financial impact estimates in Table 3.

Table 3: A comparison of the November 2020 and March 2021 patient, prescription and financial impact estimates

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
OCA patients						
March 2021	[redacted]1	[redacted]1	[redacted]1	[redacted]1	[redacted]1	[redacted]1
November 2020	[redacted]1	[redacted]1	[redacted]1	[redacted]1	[redacted]1	[redacted]1
OCA prescriptions						
March 2021	[redacted]2	[redacted]2	[redacted]2	[redacted]2	[redacted]2	[redacted]2
November 2020	[redacted]2	[redacted]2	[redacted]2	[redacted]2	[redacted]2	[redacted]3
Cost of OCA to PBS/RPBS						
November 2020	$[redacted]4	$[redacted]4	$[redacted]4	$[redacted]4	$[redacted]4	$[redacted]5
March 2021	$[redacted]6	$[redacted]6	$[redacted]6	$[redacted]6	$[redacted]6	$[redacted]6
If DPMQ of OCA = $[redacted]*	$[redacted]6	$[redacted]6	$[redacted]6	$[redacted]6	$[redacted]6	$[redacted]6
Net costs – March 2021						
Net cost to PBS/RPBS#	$[redacted]6	$[redacted]6	$[redacted]6	$[redacted]6	$[redacted]6	$[redacted]6
Net cost to MBS	$[redacted]7	$[redacted]7	$[redacted]7	$[redacted]7	$[redacted]7	$[redacted]7
Net cost to Government	$[redacted]6	$[redacted]6	$[redacted]6	$[redacted]6	$[redacted]6	$[redacted]6

Source: Ocaliva UCM-Release-3-Workbook-v102 Excel workbook from November 2020 resubmission and Ocaliva_UCM-Release-3-Workbook-v106 Jan 2021 Excel workbook supplied for March 2021
DPMQ = dispensed price for maximum quantity; ICER = incremental cost-effectiveness ratio; OCA = obeticholic acid; PBS = Pharmaceutical Benefits Scheme; RPBS = Repatriation Pharmaceutical Benefits Scheme
* $[redacted] = DPMQ below which is required to obtain an ICER of < $55,000 to < $75,000
# Net cost to PBS/RPBS minus cost offsets
The redacted values correspond to the following ranges:
[1] 500 to < 5,000
[2] $5,000 to < $15,000
[3] $15,000 to < $25,000
[4] $30 million to < $40 million
[5] $40 million to < $50 million
[6] $10 million to < $20 million
[7] $0 to < $10 million

5.10 In November 2020 the resubmission estimated that there would be 5,000 to < 10,000 patients treated with OCA for a total cost of $200 million to < $300 million over the first six years of listing. The changes made in the March 2021 proposal resulted in 5,000 to < 10,000 patients treated with OCA for a total cost of $100 million to < $200 million over the first six years of listing.

Financial Management – Risk Sharing Arrangements

5.11 The Sponsor has proposed revised caps, beyond which [redacted]% rebates would be applied, based on the revised financial impact estimates presented in Table 3.

5.12 The revised caps were, on average, 29% below the revised estimated financial impact from Year 1 to Year 5.

Table 4: A comparison of the November 2020 and March 2021 proposed caps, beyond which [redacted]% rebates would be applied

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
March 2021						
Net cost to PBS/RPBS	$[redacted][1]	$[redacted][1]	$[redacted][1]	$[redacted][1]	$[redacted][1]	$[redacted][1]
Cap level	$[redacted][1]	$[redacted][1]	$[redacted][1]	$[redacted][1]	$[redacted][1]	-
% cap is below net cost	47%	33%	22%	22%	22%	-
November 2020						
Cap level	$[redacted][1]	$[redacted][1]	$[redacted][1]	$[redacted][1]	-	-

Source: Ocaliva UCM-Release-3-Workbook-v102 Excel workbook from November 2020 resubmission and Ocalvia_UCM-Release-3-Workbook-v106 Jan 2021 Excel workbook supplied for March 2021

The redacted values correspond to the following ranges:

[1] $10 million to < $20 million

5.13 In November 2020 the proposed total spend on OCA was $70 million to < $80 million over the first four years of listing. In March 2021, the proposed maximum spend on OCA was $60 million to < $70 million over the first five years of listing.

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

6 PBAC Outcome

6.1 The PBAC recommended the listing of obeticholic acid (OCA) for the treatment of primary biliary cholangitis (PBC) in combination with ursodeoxycholic acid (UDCA) in UDCA inadequate responders and as monotherapy in patients intolerant to UDCA. The PBAC was satisfied that OCA provides, for some patients, an improvement in efficacy compared to UDCA monotherapy in UDCA inadequate responders and placebo in UDCA intolerant patients. The PBAC considered that the estimated incremental cost effectiveness ratio (ICER) was acceptable when considered in conjunction with the estimated financial impact and proposed risk-sharing arrangement (RSA).

6.2 The PBAC recalled that it had previously considered:

(i) OCA + UDCA to be superior in terms of effectiveness compared to UDCA monotherapy in patients who were UDCA inadequate responders; however, the magnitude of the clinical benefit was uncertain given the relatively small sample size in the key clinical trial (PIOSE, n = 200) and as over 50% of patients failed to meet the primary end point at 12 months;

(ii) that the claim that OCA monotherapy was superior in terms of effectiveness compared to placebo in UDCA intolerant patients was uncertain due to the small sample size (n = 16); however, likely reasonable in the context of the small number of patients expected to be treated with monotherapy; and

(iii) that OCA + UDCA and OCA monotherapy were inferior in terms of safety compared to UDCA and placebo respectively.

6.3 The PBAC noted that an updated economic model was presented for the UDCA inadequate responders (i.e. those receiving OCA + UDCA) that included:

- changes to the disutility value of pruritus (0.03 in Year 1 and 0.015 in Years 2 to 30 compared to 0.03 in Year 1 only in November 2020). The PBAC considered that this change was appropriate;
- 100% of patients receiving a full dose of OCA (in November 2020 21% of patients received a half dose, with no change in efficacy). The PBAC considered that this change was appropriate; and
- a 10% price reduction to the effective dispensed price for maximum quantity (DPMQ) of OCA.

6.4 The PBAC noted that the ICER was $55,000 to < $75,000 per quality adjusted life year (QALY). The PBAC noted that although the above three changes resulted in an ICER that was less than that presented in the November 2020 resubmission of $75,000 to < $95,000 per QALY, the ICER was not less than $55,000 to < $75,000 per QALY as requested by the PBAC in November 2020.

6.5 The PBAC noted that revised utilisation and financial impact estimates were presented that included:

- a growth rate of UDCA treated patients which was 7% in 2017 and which reduced by 0.5% per year so that it was 2.5% in Year 6. The PBAC considered that this change was appropriate;
- a change to the proportion of continuing patients (reduced from 95% to 90%). The PBAC considered that this change was appropriate; and
- a change to the adherence to OCA (reduced from 93.55% to 80%). The PBAC considered that this change was appropriate.

6.6 The PBAC considered that the changes resulted in a more reasonable estimate of utilisation (5,000 to < 10,000 patients treated with OCA over the first six years of

listing compared to 5,000 to < 10,000 in November 2020) and, when combined with the proposed effective DPMQ of OCA, a more reasonable financial impact estimation ($100 million to < $200 million over the first six years of listing compared to $200 million to < $300 million in November 2020).

6.7 The PBAC noted that a revised RSA was presented which proposed caps beyond which [redacted]% rebates would be applied. The PBAC noted that the caps were, on average, 29% below the revised financial impact estimates for Years 1 to 5. This will be managed through a Special Revenue Arrangement (SRA) rather than a traditional RSA. The PBAC noted that the proposed maximum spend on OCA was $60 million to < $70 million over the first five years of listing.

6.8 The PBAC recalled that it had previously stated that the calculated ICER should not be reliant on the RSA/SRA to be achieved, particularly given the likely overestimated financial assumptions. However, the PBAC noted that the sponsor had applied the changes recommended by the PBAC in November 2020 and considered that the revised financial impact estimates were now more reasonable. The PBAC noted that if the actual estimates were realised and the caps were exceeded as estimated over the first five years of listing, and this reduction was applied to the effective DPMQ, the resulting ICER would be $45,000 to < $55,000 per QALY, which was less than the ICER requested in November 2020 of $55,000 to < $75,000 per QALY.

6.9 The PBAC considered that the proposed SRA mitigated the outstanding uncertainty surrounding the patient number and financial impact estimates. The PBAC also considered that the combination of the price reduction, the changes to the economic model and the proposed SRA reduced the inherent uncertainty in the model and the ICER.

6.10 The PBAC considered that initial treatment of OCA should be an Authority Required (immediate assessment – telephone/online) listing and continuing treatment should be an Authority Required (Streamlined) listing. Conditions warranting a written-only authority required type listing were not present in relation to the recommended listing. Concurrent use with UDCA would be required, except where an intolerance exists, despite a prior inadequate response to UDCA. This was to align with the TGA registered indication.

6.11 The PBAC advised that continuing treatment of OCA is suitable for prescribing by nurse practitioners.

6.12 The PBAC advised that OCA should not be exempt from the Early Supply Rule.

6.13 The PBAC advised that under Section 101(3BA) of the *National Health Act 1953* OCA should not be treated as interchangeable on an individual patient basis with any other drug.

6.14 The PBAC found that the criteria prescribed by the National Health (Pharmaceuticals and Vaccines – Cost Recovery) Regulations 2009 for Pricing Pathway A were not met.

Specifically the PBAC found that in the circumstances of its recommendation for OCA:

a) The treatment is not expected to provide a substantial and clinically relevant improvement in efficacy over standard of care. The PBAC considered this criterion was not met as the available evidence was of variable quality and the magnitude of the benefit was uncertain;

b) The treatment is not expected to address a high and urgent unmet clinical need;

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.

6.15 The PBAC noted that this submission was not eligible for an Independent Review, as it received a positive recommendation.

Outcome:
Recommended

7 Recommended listing

7.1 Add new medicinal product (obeticholic acid) as follows:

MEDICINAL PRODUCT medicinal product pack	**PBS item code**	**Max. Qty packs**	**Max. Qty units**	**№.of Rpts**	**Available brands**
OBETICHOLIC ACID					
obeticholic acid tablet 5 mg, 30	NEW	1	30	5	Ocaliva
		Max.Qty multiplier = 1; Repeat Increases: nil			
Restriction Summary Number: [New] / Treatment of Concept: [New]					
	Category/Program: General Schedule (Code GE)				
	Prescriber type: ☒ Medical Practitioners				
	Restriction type: ☒ Authority Required (immediate/real-time assessment by Services Australia)				
	Condition: Primary biliary cholangitis (previously known as Primary biliary cirrhosis)				
	Indication: Primary biliary cholangitis (previously known as Primary biliary cirrhosis)				
	Treatment phase: Initial treatment				
	Population criteria				
	Patient must be aged 18 years or over				
	AND				
	Treatment criteria:				
	Patient must be treated by one of: (i) a gastroenterologist, (ii) a hepatologist; or				
	Patient must be treated by a medical practitioner who has consulted at least one of the above mentioned specialist types, with agreement reached that the patient should be treated with this pharmaceutical benefit on this occasion				
	AND				
	Treatment criteria:				
	Patient must be undergoing concurrent treatment with ursodeoxycholic acid, following this authority application; or				
	Patient must be undergoing treatment with this drug as monotherapy following this authority application, because combination treatment with ursodeoxycholic acid is not tolerated.				
	Clinical criteria:				

	Patient must have experienced an inadequate response to ursodeoxycholic acid, despite treatment with ursodeoxycholic acid for at least 52 weeks at a therapeutic dose, prior to initiating treatment with this drug
	AND
	Clinical criteria:
	Patient must not have/be each of: (i) severe liver disease, (ii) immunocompromised
	AND
	Clinical criteria:
	Patient must have an alkaline phosphatase (ALP) level of at least 1.67 times the upper limit of normal (ULN) having accounted for each of: (i) age, (ii) gender, (iii) laboratory to laboratory variances in the definition of 'normal', despite treatment with ursodeoxycholic acid for at least 52 cumulative weeks; or
	Patient must have a total bilirubin level between 1 to 2 times the ULN, despite treatment with ursodeoxycholic acid for at least 52 cumulative weeks; or
	Patient must have abnormal readings of at least one of: (i) alkaline phosphatase (ii) total bilirubin, in the presence of an intolerance of a severity requiring treatment discontinuation with ursodeoxycholic acid
	Prescribing instructions: Document and retain in the patient's medical records the qualifying baseline laboratory reading for the purpose of assessing response to treatment under the 'Continuing treatment' restriction.
	Administrative Advice: Not for use in the treatment of sclerosing cholangitis or cholelithiasis.
	Administrative Advice: Laboratory readings requested in this authority application must be no older than 52 weeks
	Administrative Advice: In accordance with the dosing directions in the approved Product Information, the 10 mg presentation is not PBS listed for initiation of treatment.
	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.
	Caution: Hepatic decompensation and failure, in some cases fatal, have been reported in post-marketing reports in patients with moderate to severe hepatic impairment when dosed incorrectly

MEDICINAL PRODUCT **medicinal product pack**	**PBS item code**	**Max. Qty packs**	**Max. Qty units**	**№.of Rpts**	**Available brands**
OBETICHOLIC ACID					
obeticholic acid tablet 5 mg, 30	NEW	1	30	5	Ocaliva
obeticholic acid tablet 10 mg, 30	NEW	1	30	5	Ocaliva
		Max.Qty multiplier = 1; Repeat Increases: nil			

Restriction Summary Number: [New] / Treatment of Concept: [New code 2]	
	Category/Program: General Schedule (Code GE)
	Prescriber type: ☒ Medical Practitioners ☒ Nurse practitioners (CTO)
	Restriction type: ☒ Authority Required (STREAMLINED) [new code 2]
	Indication: Primary biliary cholangitis (previously known as Primary biliary cirrhosis)
	Treatment phase: Continuing treatment
	Treatment criteria:
	Patient must be treated by one of: (i) a gastroenterologist, (ii) a hepatologist; or
	Patient must be treated by an eligible practitioner type who has consulted at least one of the above mentioned specialist types, with agreement reached that the patient should be treated with this pharmaceutical benefit on this occasion
	AND
	Treatment criteria:
	Patient must be undergoing current treatment with this drug through the PBS, with treatment having occurred through one of: (i) the 'Initial treatment' listing, (ii) 'Grandfather' arrangements, at least once
	AND
	Treatment criteria:
	Patient must be undergoing concurrent treatment with ursodeoxycholic acid, following this authority application; or
	Patient must be undergoing treatment with this drug as monotherapy following this authority application, because combination treatment with ursodeoxycholic acid is not tolerated.

	Clinical criteria:
	Patient must have achieved an adequate response to this drug, defined as having at least one of: (i) an alkaline phosphate (ALP) level less than 1.67 time the upper limit of normal (ULN), (ii) a reduction in the ALP reading of at least a 15% compared to the baseline level provided with the initial authority application, (iii) a total bilirubin level within the normal reference range
	Prescribing Instructions: The improvement in the qualifying laboratory reading(s) has/have been documented in the patient's medical records.
	Administrative Advice: Not for use in the treatment of sclerosing cholangitis or cholelithiasis.
	Administrative Advice: Laboratory readings requested in this authority application must be no older than 52 weeks
	Administrative Advice: Special pricing arrangements apply
	Administrative Advice: **Note** **Continuing Therapy Only:** For prescribing by nurse practitioners as continuing therapy only, where the treatment of, and prescribing of medicine for, a patient has been initiated by a medical practitioner. Further information can be found in the Explanatory Notes for Nurse Practitioners.
	Caution: Hepatic decompensation and failure, in some cases fatal, have been reported in post-marketing reports in patients with moderate to severe hepatic impairment when dosed incorrectly
Restriction Summary Number: [New] / Treatment of Concept: [New]	
	Category/Program: General Schedule (Code GE)
	Prescriber type: ☒ Medical Practitioners ☒ Nurse practitioners (CTO)
	Restriction type: ☒ Authority Required (immediate/real-time assessment by Services Australia)
	Indication: Primary biliary cholangitis (previously known as Primary biliary cirrhosis)
	Treatment phase: Transitioning from non-PBS to PBS subsidised supply – 'Grandfather' arrangements
	Population criteria
	Patient must be aged 18 years or over
	Treatment criteria:
	Patient must be treated by one of: (i) a gastroenterologist, (ii) a hepatologist; or
	Patient must be treated by an eligible practitioner type who has consulted at least one of the above mentioned specialist types, with agreement reached that the patient should be treated with this pharmaceutical benefit on this occasion
	AND
	Treatment criteria:
	Patient must be undergoing concurrent treatment with ursodeoxycholic acid, following this authority application; or
	Patient must be undergoing treatment with this drug as monotherapy following this authority application, because combination treatment with ursodeoxycholic acid is not tolerated.
	Clinical criteria:
	Patient must have received treatment with this drug for this PBS indication prior to [insert listing date here]
	AND
	Clinical criteria:
	Patient must have experienced an inadequate response to ursodeoxycholic acid, despite treatment with ursodeoxycholic acid for at least 52 weeks at a therapeutic dose, prior to initiating treatment with this drug
	AND
	Clinical criteria:
	Patient must not have/be each of: (i) severe liver disease, (ii) immunocompromised
	AND
	Clinical criteria:
	Patient must have had, prior to initiating treatment with this drug, an alkaline phosphatase (ALP) level of at least 1.67 times the upper limit of normal (ULN) having accounted for each of: (i) age, (ii) gender, (iii) laboratory to laboratory variances in the definition of 'normal', despite treatment with ursodeoxycholic acid for at least 52 cumulative weeks or
	Patient must have had, prior to initiating treatment with this drug, a total bilirubin level between 1 to 2 times the ULN, despite treatment with ursodeoxycholic acid for at least 52 cumulative weeks or
	Patient must have had, prior to initiating treatment with this drug, abnormal readings of at least one of: (i) alkaline phosphatase (ii) total bilirubin, in the presence of an intolerance of a severity requiring treatment discontinuation with ursodeoxycholic acid
	Prescribing instructions: Document and retain in the patient's medical records the qualifying baseline laboratory reading for the purpose of assessing response to treatment under the 'Continuing treatment' restriction.

	Administrative Advice: Not for use in the treatment of sclerosing cholangitis or cholelithiasis.
	Administrative Advice: Patients may qualify for PBS-subsidised treatment under this restriction once only. For continuing PBS-subsidised treatment, a 'Grandfathered' patient must qualify under the 'Continuing treatment' criteria.
	Administrative Advice: This grandfather restriction will cease to operate from 12 months after the date specified in the clinical criteria.
	Administrative Advice: Special pricing arrangements apply
	Administrative Advice: **Note** **Continuing Therapy Only:** For prescribing by nurse practitioners as continuing therapy only, where the treatment of, and prescribing of medicine for, a patient has been initiated by a medical practitioner. Further information can be found in the Explanatory Notes for Nurse Practitioners.
	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.
	Caution: Hepatic decompensation and failure, in some cases fatal, have been reported in post-marketing reports in patients with moderate to severe hepatic impairment when dosed incorrectly

This restriction may be subject to further review. Should there be any changes made to the restriction the Sponsor will be informed.

8 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised through the Pharmaceutical Benefits Scheme (PBS) in Australia. It considers applications regarding the listing of medicines on the PBS and provides advice about other matters relating to the operation of the PBS in this context. A PBAC decision in relation to PBS listings does not necessarily represent a final PBAC view about the merits of the medicine or the circumstances in which it should be made available through the PBS. The PBAC welcomes applications containing new information at any time.

9 Sponsor's Comment

Chiesi Australia welcomes the PBAC's decision to recommend Ocaliva for the treatment of primary biliary cholangitis (PBC) in combination with ursodeoxycholic acid (UDCA) in adults with an inadequate response to UDCA or as monotherapy in adults unable to tolerate UDCA. The availability of Ocaliva on the PBS is an important step forward for the management of PBC, and will lead to improved access for those living with PBC, providing them with greater treatment options in an area where there are limited therapeutic opportunities.