# 4.03 RIBAVIRIN tablets, 400mg and 600mg, Ibavyr®, Clinect Pty Ltd

## 1 Purpose of Application

1.1 The reconsideration of the deferral of the July 2015 minor re-submission which sought General Schedule (Section 85) listings for ribavirin, in combination with sofosbuvir, for the treatment of adults with chronic hepatitis C (CHC) genotype 2 or 3.

## 2 Requested listing

2.1 The proposed wording of the restrictions are reproduced from July 2015 re-submission:

**Requested PBS listing: initiation of treatment for previously untreated patients (Chronic genotype 2 or 3 hepatitis C infection)**

| Name, Restriction, Manner of administration and form | Max. Qty | №.of Rpts | Dispensed Price for Max. Qty | Proprietary Name and Manufacturer |
|---|---|---|---|---|
| RIBAVIRIN | | | | Ibavyr® Clinect Pty Ltd |
| Tablets 400mg, 28 | 2 | 2 | $[redacted] | |
| Tablets 600mg, 28 | 2 | 2 | $[redacted] | |

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| **Category / Program** | GENERAL – General Schedule (Code GE) |
| **Prescriber type:** | ☐ Dental ☒ Medical Practitioners ☐ Nurse practitioners ☐ Optometrists ☐ Midwives |
| **Severity:** | – |
| **Condition:** | Chronic hepatitis C infection |
| **PBS Indication:** | Chronic hepatitis C infection |
| **Treatment phase:** | Initial treatment |
| **Restriction Level / Method:** | ☐ Restricted benefit<br>☒ Authority Required - In Writing<br>☒ Authority Required - Telephone<br>☐ Authority Required – Emergency<br>☐ Authority Required - Electronic<br>☒ Streamlined |
| **Treatment criteria:** | Must be treated in an accredited treatment centre. |
| **Clinical criteria:** | Patient must have compensated liver disease.<br>For patients with HCV genotype 2 infection:<br>The treatment must be in combination with sofosbuvir only.<br><br>For patients with HCV genotype 3 infection:<br>The treatment must be in combination with sofosbuvir only. |

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| **Population criteria:** | Patient must be 18 years or older.<br><br>Patient must not be pregnant or breastfeeding. Female partners of male patients must not be pregnant. Patients and their partners must each be using an effective form of contraception if of child-bearing age. |
| **Prescriber Instructions** | Evidence of chronic hepatitis C infection (repeatedly anti-HCV positive and HCV RNA positive) must be documented in the patient's medical records. |
| **Administrative Advice** | Note:<br>Increased repeats may be requested from the Department of Human Services for patients weighing equal to or greater than 75 kg<br><br>Treatment centres are required to have access to the following appropriate specialist facilities for the provision of clinical support services for hepatitis C:<br>a) a nurse educator/counsellor for patients; and<br>b) 24-hour access by patients to medical advice; and<br>c) an established liver clinic |

## Requested PBS listing: initiation of treatment for previously treated patients (Chronic genotype 2 or 3 hepatitis C infection)

| Name, Restriction, Manner of administration and form | Max. Qty | №.of Rpts | Dispensed Price for Max. Qty | Proprietary Name and Manufacturer |
|---|---|---|---|---|
| RIBAVIRIN | | | | Ibavyr® Clinect Pty Ltd |
| Tablets 400mg, 28 | 2 | 2 | $[redacted] | |
| Tablets 600mg, 28 | 2 | 2 | $[redacted] | |

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|---|---|
| **Category / Program** | GENERAL – General Schedule (Code GE) |
| **Prescriber type:** | ☐ Dental ☒ Medical Practitioners ☐ Nurse practitioners ☐ Optometrists ☐ Midwives |
| **Severity:** | – |
| **Condition:** | Chronic hepatitis C infection |
| **PBS Indication:** | Chronic hepatitis C infection |
| **Treatment phase:** | Initial treatment |
| **Restriction Level / Method:** | ☐ Restricted benefit<br>☒ Authority Required - In Writing<br>☒ Authority Required - Telephone<br>☐ Authority Required – Emergency<br>☐ Authority Required - Electronic<br>☒ Streamlined |
| **Treatment criteria:** | Must be treated in an accredited treatment centre. |

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| **Clinical criteria:** | Patient must have compensated liver disease.<br>The patient must have received prior therapy with an interferon-based regimen.<br><br>For patients with HCV genotype 2 infection:<br>The treatment must be in combination with sofosbuvir only,<br><br>For patients with HCV genotype 3 infection:<br>The treatment must be in combination with sofosbuvir only, |
| **Population criteria:** | Patient must be 18 years or older.<br><br>Patient must not be pregnant or breastfeeding. Female partners of male patients must not be pregnant. Patients and their partners must each be using an effective form of contraception if of child-bearing age. |
| **Prescriber Instructions** | Evidence of chronic hepatitis C infection (repeatedly anti-HCV positive and HCV RNA positive) must be documented in the patient's medical records. |
| **Administrative Advice** | Note:<br>Increased repeats may be requested from the Department of Human Services for patients weighing equal to or greater than 75 kg<br><br>Treatment centres are required to have access to the following appropriate specialist facilities for the provision of clinical support services for hepatitis C:<br>a) a nurse educator/counsellor for patients; and<br>b) 24-hour access by patients to medical advice; and<br>c) an established liver clinic |

## Requested PBS listing: continuation of treatment (Chronic genotype 3 hepatitis C infection, patients electing 24 week regimen)

| Name, Restriction, Manner of administration and form | Max. Qty | №.of Rpts | Dispensed Price for Max. Qty | Proprietary Name and Manufacturer |
|---|---|---|---|---|
| RIBAVIRIN | | | | Ibavyr® Clinect Pty Ltd |
| Tablets 400mg, 28 | 2 | 2 | $[redacted] | |
| Tablets 600mg, 28 | 2 | 2 | $[redacted] | |

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|---|---|
| **Category / Program** | GENERAL – General Schedule (Code GE) |
| **Prescriber type:** | ☐ Dental ☒ Medical Practitioners ☐ Nurse practitioners ☐ Optometrists ☐ Midwives |
| **Severity:** | – |
| **Condition:** | Chronic hepatitis C infection |
| **PBS Indication:** | Chronic hepatitis C infection |
| **Treatment phase:** | Continuing treatment |
| **Restriction Level / Method:** | ☐ Restricted benefit<br>☒ Authority Required - In Writing<br>☒ Authority Required - Telephone<br>☐ Authority Required – Emergency<br>☐ Authority Required - Electronic<br>☒ Streamlined |

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| **Treatment criteria:** | Must be treated in an accredited treatment centre. |
| **Clinical criteria:** | Patient must have initiated ribavirin treatment under PBS Item number [TBC for initiation listing] for the first 12 weeks of the same course of treatment,<br><br>The treatment must be in combination with sofosbuvir only. |
| **Population criteria:** | Patient must be 18 years or older.<br><br>Patient must not be pregnant or breastfeeding. Female partners of male patients must not be pregnant. Patients and their partners must each be using an effective form of contraception if of child-bearing age. |
| **Prescriber Instructions** | Evidence of chronic hepatitis C infection (repeatedly anti-HCV positive and HCV RNA positive) must be documented in the patient's medical records. |
| **Administrative Advice** | Note:<br>Increased repeats may be requested from the Department of Human Services for patients weighing equal to or greater than 75 kg<br><br>Treatment centres are required to have access to the following appropriate specialist facilities for the provision of clinical support services for hepatitis C:<br>a) a nurse educator/counsellor for patients; and<br>b) 24-hour access by patients to medical advice; and<br>c) an established liver clinic |

## 3 Background

3.1 TGA status at time of PBAC consideration: Ribavirin was registered with the TGA in February 2015 for the treatment of CHC in adults, in combination with other oral agents.

3.2 A major submission for ribavirin for the treatment of genotypes 2 and 3 CHC (Section 100 (Highly Specialised Drugs Program) Authority Required (Streamlined) listing) was rejected by the PBAC at the March 2015 meeting, on the basis that the submission had not justified the incremental cost-effectiveness of ribavirin compared to the currently listed ribavirin-based items.

3.3 A minor resubmission was made in July 2015 with a revised listing in Section 85, and a reduced price based on shadow pricing of the ribavirin component of the Pegasys RBV® from 2004/2005. The PBAC noted that the stand-alone ribavirin, at its requested price, was not considered to be cost-minimised to the product most likely to be substituted (the ribavirin component in the co-packaged Pegasys RBV® and Pegatron®, at their current prices) Therefore, the PBAC deferred its decision for the listing of ribavirin for the treatment of chronic hepatitis C (CHC).

## 4 PBAC consideration of the evidence

4.1 The PBAC noted that the pre-PBAC response restated the evidence provided in the March 2015 and July 2015 submissions.

4.2 The PBAC recalled that in March 2015, it was of a mind to recommend listing, if stand-alone ribavirin was cost-minimised to the ribavirin in the co-pack with peg-interferon most likely to be replaced. The PBAC noted that highest number of PBS services in the period of 2013-2014 was for the co-pack of Pegasys RBV® (PBS item9527K/6396P, containing 168 tablets of ribavirin (RBV)) and that in this case the ex-manufacturer price of 200 mg ribavirin was $[redacted]. The PBAC considered that this was an appropriate basis for the on-going pricing of ribavirin.

## 5 PBAC Outcome

5.1 The PBAC recommended the Authority Required listing of ribavirin in combination with direct acting antivirals (DAAs) for the treatment of chronic hepatitis C (CHC).

5.2 While the submission requested treatment of patients infected with Genotype 2 and 3 HCV, the PBAC noted that in clinical practice, some other patient groups may derive benefit from the additional of ribavirin to a course of an interferon-free regimen. Ribavirin may be added to a 12-week regimen daclatasvir and sofosbuvir for the treatment of Genotype 1 HCV-infected cirrhotic patients who are treatment naïve or have failed prior peginterferon alfa/ribavirin treatment. The PBAC considered that access to ribavirin should not be restricted to patients infected with specific genotypes of the virus.

5.3 The PBAC noted that no new clinical data were presented in the July 2015 re-submission and recalled that the submission lodged for the March 2015 consideration did not provide any clinical evidence in support of the combination treatment of SOF+R for treatment of genotypes 2 and 3 HCV infection, but referred to the sofosbuvir submission considered at the July 2014 PBAC meeting for relevant data on the effectiveness and safety of SOF+R in the proposed PBS population. The PBAC has accepted the clinical benefit of this treatment regimen for treating genotypes 2 and 3 HCV infections.

5.4 The PBAC recalled in the context of the consideration of the sofosbuvir submission at the March 2015 meeting, that most appropriate scenario to determine the cost of a treatment would be based on the largest groups of the total prevalent population, in this case treatment naïve non-cirrhotic Genotype 3 patients (weighing less than 75kg) treated with SOF+ RBV 24 weeks as a proxy for all Genotype 3, 2, 4, 5 and 6 patients.

5.5 The PBAC considered that with the clinical evidence available for IFN-free regimens, there was no basis on which to recommend that any one treatment (including those that are in combination with ribavirin) be more expensive than another.

5.6 The PBAC noted that no additional financial impact is expected from the listing of ribavirin over the financial impact of the listing of the previously recommended IFN-free treatments for CHC. This is because ribavirin containing regimens are expected to directly substitute for other CHC treatment regimens..

5.7 The PBAC recommended a risk-sharing arrangement between sponsors of all IFN-free oral treatments (including this sponsor) and the Department to give budget certainty to the Commonwealth, while not constraining prescribing and patient access to treatment. The PBAC confirmed their view from the March 2015 meeting, and recommended that a RSA should consist of a cap on expenditure, with a 100% rebate for budget certainty. In the context of recent considerations of IFN-free treatment regiments, the PBAC emphasised the importance of ensuring that these arrangements can be implemented in a way that would manage the overall cost to the Commonwealth for these medicines.

5.8 In accordance with subsection 101(3BA) of the *National Health Act 1953*, the PBAC advised that the Committee is of the opinion that, on the basis of the material available at the July 2015 meeting ribavirin should not be treated as interchangeable with other recommended treatments of CHC on an individual patient basis.

5.9 The PBAC noted that suitability of prescribing ribavirin by nurse practitioners would depend on the final listing conditions of ribavirin. The PBAC were of a mind that in principle nurse practitioners prescribing was likely to be suitable in the context of a shared care model.

5.10 The PBAC recommended that the Safety Net 20 Day Rule should apply to all the interferon-free DAA regimens.

5.11 The submission is not eligible for an Independent Review, because the PBAC made a positive recommendation.

**Outcome:**
Recommended.

## 6 Recommended listing

6.1 Add new item:
Restriction to be finalised

## 7 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised in Australia. It considers submissions in this context. A PBAC decision not to recommend listing or not to recommend changing a listing does not represent a final PBAC view about the merits of the medicine. A company can resubmit to the PBAC or seek independent review of the PBAC decision.

## 8 Sponsor's Comment

The sponsor had no comment.