

4.04 SIMEPREVIR, capsule, 150mg, OLYSIO®, Janssen-Cilag Pty Ltd.

1 Purpose of Application

- 1.1 The submission requested a Section 100 (Highly Specialised Drugs Program) Authority Required (Streamlined) listing for simeprevir in combination with sofosbuvir (SMV+SOF) for the treatment of patients with genotype 1 chronic hepatitis C (CHC) infection who have compensated liver disease, irrespective of previous treatment history.

2 Background

- 2.1 The submission was originally made under the TGA/PBAC Parallel Process. Simeprevir was listed on the Australian Register of Therapeutic Goods on the 17th July 2014 for the following indication:

For the treatment of chronic hepatitis C (CHC) genotype 1 (GT1) or genotype 4 (GT4) infection, in combination with other medicinal products for the treatment of CHC infection.

- 2.2 However, the Dosage and Administration section of the current TGA-approved Product Information of simeprevir stipulates that it must be administered in combination with PR. An application had been lodged with the TGA to request changes to the Dosage and Administration section of the current Product Information. These changes related to recommendations on the use of simeprevir in combination with sofosbuvir.
- 2.3 Simeprevir was recommended for Section 100 (Highly Specialised Drugs Program) listing on the PBS for treatment of chronic genotype 1 hepatitis C infection in combination with PR at the July 2014 PBAC meeting.
- 2.4 Sofosbuvir was recommended for Section 85 Authority Required listing at the March 2015 PBAC meeting for the treatment of CHC.
- 2.5 At its July 2015 meeting, the PBAC deferred their recommendation as a positive TGA Delegate's Overview was not available at the time of consideration. The PBAC was of a mind to recommend listing of simeprevir, in combination with sofosbuvir, but decided to wait for finalisation of the TGA registration process to determine the circumstances of listing. The TGA registration process is now sufficiently progressed to allow PBAC reconsideration.

3 PBAC consideration of the evidence

- 3.1 The PBAC noted the availability of a positive TGA Delegate's Overview for the 12 week treatment course of simeprevir in combination with sofosbuvir for the treatment of GT1 [REDACTED]. No evidence in addition to July 2015 consideration was provided by the sponsor.

- 3.2 The PBAC noted the recent publication of Backus LI et al. Effectiveness of sofosbuvir-based regimens in genotype 1 and 2 hepatitis C virus infection in 4026 U.S. Veterans. *Alimentary Pharmacology and Therapeutics* 2015. The conclusion in this real-world patient population was that SVR rates were lower than in clinical trials.

4 PBAC Outcome

- 4.1 The PBAC recommended the Authority Required listing of simeprevir in combination with sofosbuvir (SMV+SOF) for the treatment of patients with genotype 1 chronic hepatitis C (CHC) infection on the basis of non-inferior efficacy and safety with ledipasvir/sofosbuvir (LDV/SOF), and with daclatasvir in combination with sofosbuvir (DCV+SOF) as recommended in March 2015, and with paritaprevir/ritonavir/ombitasvir + dasabuvir ± ribavirin (Viekira PAK/Viekira PAK-RBV), as recommended in July 2015.
- 4.2 The PBAC recommended the price of a course of treatment for SMV+SOF should be the same as the price of a course of treatment with LDV/SOF.
- 4.3 The PBAC reiterated that the Committee recognised that the new treatments for HCV resulted in high rates of sustained virological response, where the HCV virus could not be detected in the blood of patients 12 weeks after treatment commenced. The PBAC noted the large number of comments and presentations from patients, health care professionals and organisations that have previously been received, highlighting the benefits of the availability of new treatments, particularly IFN-free regimens.
- 4.4 The PBAC reiterated that it was appropriate that the new all oral treatment regimens be listed in the General Schedule, to facilitate the longer term objectives for access to treatment, increase treatment rates and outcomes with a view to treating all patients with CHC over time.
- 4.5 The PBAC noted that although the original submission proposed simeprevir in combination with peginterferon and ribavirin; and 'no treatment' as comparators, the sponsor in its Pre-Sub-Committee Response (PSCR) proposed other IFN-free treatments (LDV/SOF, DAC+SOF and Viekira PAK +/- RBV) as the main comparators. The PBAC agreed that these treatments were the most appropriate comparators for the consideration of all other oral HCV treatments, following the recommendations to list the sofosbuvir-containing regimens and Viekira PAK +/- RBV.
- 4.6 The PBAC recalled that on the basis of the available evidence, it had previously considered it reasonable to accept that a course of SMV+SOF was non-inferior in terms of comparative efficacy with a course of LDV/SOF or DCV+SOF or Viekira PAK/Viekira PAK-RBV for treatment of Genotype 1 CHC; and that it was reasonable to consider that a course of SMV+SOF had a similar safety profile as the ribavirin-free courses of LDV/SOF, DCV+SOF and Viekira PAK.
- 4.7 The PBAC further recalled that in its consideration of the submission at the July 2015 meeting, it considered that a cost-minimisation approach was appropriate, as the clinical evidence presented in the submission suggested that there is no basis on which to consider that one course of SMV+ SOF was more effective than a course of treatment with one of the other high efficacy/ low toxicity IFN-free regimens. .
- 4.8 The PBAC noted that no additional financial impact is expected from the listing of

simeprevir in combination with sofosbuvir over the financial impact of the listing of the previously recommended IFN-free treatments for CHC. This is because simeprevir in combination with sofosbuvir is expected to directly substitute for other CHC treatment regimens.

- 4.9 The PBAC recommended a risk-sharing arrangement between sponsors of all IFN-free oral treatments 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. The Committee recommended that the Department negotiate RSAs based on DUSC estimates of the patient population (from the March 2015 considerations) and treatment course per patient for each medicine, in a manner that can be implemented and managed by the Department. 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.
- 4.10 The PBAC recalled that at its March 2015 meeting it had advised the Minister that the current listing of simeprevir in combination with peginterferon alfa and ribavirin is no longer cost-effective. In this context, the PBAC noted that the SVR of patients treated with SMV in combination with peginterferon and ribavirin was approximately 80% (in trials QUEST 1, QUEST 2 and PILLAR). This SVR is lower than observed in trials of SMV+SOF.
- 4.11 The PBAC noted that the Department had advised Janssen, the sponsor of simeprevir, of the PBAC's March 2015 advice to the Minister in relation to its drug and that no response had been received from Janssen. The PBAC advised the Minister that the current listing of simeprevir should be removed, or if retained, the price of simeprevir should be adjusted so that the General Schedule cost of the simeprevir with peginterferon and ribavirin treatment regimen is no more than ■% of the cost of the new treatments for CHC recommended at the March and July 2015 meetings of PBAC. The PBAC further advised the Minister that it is appropriate for its recommendations in respect of the current simeprevir listing to be implemented at the same time as any new interferon-free CHC treatments are listed.
- 4.12 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, SMV+SOF should not be treated as interchangeable with other recommended treatments for CHC on an individual patient basis.
- 4.13 The PBAC noted that suitability of prescribing SMV+SOF by nurse practitioners would depend on the final listing conditions of SMV+SOF. 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.
- 4.14 The PBAC recommended that the Safety Net 20 Day Rule should apply to all the interferon-free DAA regimens.
- 4.15 The submission is not eligible for an Independent Review, because the PBAC made a positive recommendation.

- 4.16 The PBAC acknowledged that there was a high clinical need for more effective and tolerable treatment for HCV. The PBAC noted that there is a large number (around 230,000) of patients with the chronic HCV who are untreated and that the utilisation of existing listings was low as patients were contraindicated or unwilling to take interferon. Based on the prevalence of HCV and the financial estimate presented in the submission for all oral treatments, the PBAC considered that there would be a significant opportunity cost to the Commonwealth of listing oral treatments as their uptake would be substantially higher than currently subsidised medicines. The PBAC reiterated its view that the clinical management of individuals with HCV is moving so rapidly that a broader Government and community approach is needed to maximise the clinical outcomes and patient access to treatment. As well as subsidising new treatment on the PBS, other factors that increase the capacity to treat patients need to be explored.

Outcome:

Recommended.

5 Recommended listing

- 5.1 Modify existing listing:
Restriction to be finalised

6 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.

7 Sponsor's Comment

The sponsor had no comment.