

ADDENDUM

Product: Boceprevir, capsule, 200 mg, Victrelis®

Sponsor: Merck Sharp & Dohme (Australia) Pty Ltd

Date of PBAC Consideration: July 2012

Purpose of Application

Re-submission for a Section 100 (Highly Specialised Drugs Program) Private Hospital Authority Required and Public Hospital Authority Required (Streamlined) listing for treatment, managed by an accredited treatment centre, of chronic hepatitis C genotype 1 infection in combination with peginterferon alfa and ribavirin in patients 18 years or older who have compensated liver disease and who have received no prior or no more than one prior treatment with interferon alfa or peginterferon alfa for hepatitis C and who meet certain criteria.

Highly Specialised Drugs are medicines for the treatment of chronic conditions, which, because of their clinical use or other special features, are restricted to supply to public and private hospitals having access to appropriate specialist facilities.

Background

Refer to the Public Summary Document (PSD) from the March 2012 PBAC meeting above.

The Hepatitis C Stakeholder Meeting was held on 4 May 2012.

Listing Requested and PBAC's View

Changes to the March 2012 requested restriction are highlighted in bold.

Section 100 (Highly Specialised Drugs Program) Public*and Private Hospital Authority Required (Streamlined*)

Patients naïve to interferon based therapies (non-pegylated or pegylated)

Treatment, managed by an accredited treatment centre, of chronic hepatitis C in combination with peginterferon alfa and ribavirin in patients 18 years or older who have compensated liver disease and who have received no prior interferon alfa or peginterferon alfa treatment for hepatitis C and who satisfy all of the following criteria: (1) Documented chronic hepatitis C genotype 1 infection (repeatedly anti-HCV positive and HCV RNA positive);

(2) Female patients of child-bearing age are not pregnant, not breast-feeding, and both patient and their partner are using effective forms of contraception (one for each partner). Male patients and their partners are using effective forms of contraception (one for each partner). Female partners of male patients are not pregnant.

Patients may only continue treatment after the first 20 weeks of boceprevir treatment if plasma HCV RNA is not detectable by a HCV RNA qualitative assay at treatment week 24.

Note

Treatment centres are required to have access to the following appropriate specialist facilities for the provision of clinical support services for hepatitis C:

- (a) a nurse educator/counsellor for patients; and
- (b) 24 hour access by patients to medical advice; and
- (c) an established liver clinic; and
- (d) facilities for safe liver biopsy.

Authority Required (Streamlined*)

Patients who have failed one prior attempt at interferon based therapies (non-pegylated or pegylated)

Treatment, managed by an accredited treatment centre, of chronic hepatitis C in combination with peginterferon and ribavirin, in patients 18 years or older who have compensated liver disease and who have received no more

than one prior treatment with interferon alfa or peginterferon alfa for hepatitis C and who satisfy all of the following criteria:

- (1) Documented chronic hepatitis C genotype 1 infection (repeatedly anti-HCV positive and HCV RNA positive);
- (2) Female patients of child-bearing age are not pregnant, not breast-feeding, and both patient and their partner are using effective forms of contraception (one for each partner). Male patients and their partners are using effective forms of contraception (one for each partner). Female partners of male patients are not pregnant. Patients may only continue treatment after the first 8 weeks of boceprevir treatment if plasma HCV RNA is not detectable by an HCV RNA qualitative assay at treatment week 12. **Patients should also discontinue all therapy if plasma HCV-RNA is detectable by an HCV-RNA qualitative assay at treatment week 24.**

Note

Treatment centers are required to have access to the following appropriate specialist facilities for the provision of clinical support services for hepatitis C:

- (a) a nurse educator/counsellor for patients; and
- (b) 24 hour access by patients to medical advice; and
- (c) an established liver clinic; and
- (d) facilities for safe liver biopsy.

For PBAC's view, see Recommendation and Reasons.

Summary of Resubmission

The submission proposed a reduced ex-manufacturer price for boceprevir. As a result, the average cost of boceprevir per patient after 30 weeks of treatment was decreased to between \$15,000- \$45,000 (previously higher though in the same range).

The submission re-presented the revised model from the March 2012 submission with the reduced ICER for treatment naïve patients, at the 30 year time horizon and incorporating the updated drug cost, for treatment naïve patients between \$15,000- \$45,000/QALY and for treatment experienced patients between \$15,000- \$45,000/QALY.

For PBAC's view, see Recommendation and Reasons.

Estimated PBS Usage and Financial Implications

The submission's revised net financial estimates produced an Incremental Net cost to PBS within the range \$30 – \$60 million per year in Year 5, which was lower, though in the same range as the previous submission.

For PBAC's view, see Recommendation and Reasons.

Recommendation and Reasons

The PBAC recommended listing boceprevir as Section 100 Highly Specialised Drugs Program Private Hospital Authority Required and Public Hospital Authority Required (Streamlined) benefits only for treatment, managed by an accredited treatment centre, of chronic hepatitis C genotype 1 infection in combination with peginterferon alfa and ribavirin in patients 18 years or older who have compensated liver disease and who have received no prior treatment or no more than one prior treatment with interferon alfa or peginterferon alfa for hepatitis C and who meet certain criteria. Listing was recommended on the basis of acceptable cost effectiveness over peginterferon with ribavirin at the price proposed in the submission.

The PBAC considered that the restriction for boceprevir in combination with peginterferon and ribavirin should limit the duration of treatment with boceprevir to 24 weeks in treatment naive patients and to 32 weeks in treatment experienced patients, consistent with the duration of treatment recommended in the TGA approved Product Information. The PBAC also recommended that treatment with boceprevir be limited to a maximum of 44 weeks for treatment experienced patients with prior null response and for patients with cirrhosis. The PBAC recommended that patients who have failed to respond to treatment with another NS3 protease inhibitor not be permitted to be treated with boceprevir and that this should also be specified in the restriction for boceprevir/PR. The PBAC recommended that there should be separate restrictions for treatment naive and treatment experienced patients.

The PBAC noted that the only update to the economic model in this minor submission from the March 2012 submission was a reduction in price. The price reduction resulted in revised base case ICERs at a 50 year time horizon of \$15,000- \$45,000 per QALY for treatment naive patients and \$15,000- \$45,000 per QALY for treatment experienced patients (both reduced though in the same range from the March 2012 submission) The PBAC considered that the uncertainties with the economic model identified in March 2012 remained and therefore the resulting cost effectiveness of boceprevir/PR was uncertain. However, as noted in March 2012, the PBAC acknowledged that a number of the uncertainties in the economic modelling were difficult to resolve in the absence of new and current data to use in the model. The PBAC remained concerned about the 50 year time horizon of the model and noted that when the time horizon was reduced to 30 years the revised ICERs in this submission were higher though in the same range (\$15,000- \$45,000) per QALY for treatment naive patients and higher though in the same range (\$15,000- \$45,000) per QALY for treatment experienced patients. The PBAC considered that although the appropriate time horizon for the model was not clear, 50 years was probably excessive and 30 years would be more reasonable.

The PBAC considered that boceprevir or telaprevir/PR will replace PR as the existing standard of care for almost all patients treated for chronic hepatitis C genotype 1 infection. The PBAC noted in the DUSC review that less than 10,000 patients are treated annually, and that a recent decline in use is probably due to patients waiting for new treatments, including boceprevir and telaprevir, to become available before commencing treatment, and patients participating in clinical trials. The PBAC agreed with advice from clinicians, that utilisation may increase back to levels seen 1-2 years ago, but that there will not be a new group of patients seeking treatment as a result of the listing of boceprevir or telaprevir.

The PBAC considered the proportion of patients with chronic hepatitis C virus genotype 1 remained uncertain and in particular that the proportion of treatment naive and treatment experienced patients remained uncertain. The PBAC recommended that boceprevir/PR be listed with separate restrictions for treatment naive and treatment experienced patients, so that the proportion of PBS utilisation of boceprevir/PR for treatment experienced and treatment naive patient could be determined.

The PBAC considered that a Risk Share Agreement (RSA) between the sponsors of boceprevir and telaprevir and the Government would be required and that the RSA must include both boceprevir and telaprevir. The PBAC recommended that the sponsors of boceprevir and telaprevir rebate to the Government 100 % of the cost of telaprevir and boceprevir above the estimates accepted by the PBAC.

The PBAC acknowledged and noted the consumer comments on this item.

In accordance with subsection 101(3BA) of the *National Health Act 1953* ('the Act'), the PBAC advised that the Committee is of the opinion that, on the basis of the material available to its July 2012 meeting, that boceprevir should be treated as interchangeable on an individual patient basis with telaprevir.

Recommendation:

BOCEPREVIR, capsule, 200 mg

Restriction:

To be finalised:

- Add treatment duration as noted below.
- Limit to 44 weeks for null responders
- Add switching after failing to respond to another NS3 protease inhibitor not permitted.
- Definition of failure to be finalised.

“The treatment course is limited to 24 weeks” and “The treatment course is limited to 32 weeks” in the treatment naïve and treatment experienced restrictions respectively; and

Replacement of the additional statement in the treatment experienced restriction with “Patients-must discontinue all therapy if plasma HCV-RNA is detectable by an HCV-RNA qualitative assay at treatment week 24.”

Section 100 (Highly Specialised Drugs Program)

Private Hospital/Private Clinic Authority Required

Public Hospital Authority Required (STREAMLINED)

Patients naïve to interferon based therapies (non-pegylated or pegylated)

Treatment, managed by an accredited treatment centre, of chronic hepatitis C in combination with peginterferon alfa and ribavirin in patients 18 years or older who have compensated liver disease and who have received no prior interferon alfa or peginterferon alfa treatment for hepatitis C and who satisfy all of the following criteria: (1) Documented chronic hepatitis C genotype 1 infection (repeatedly anti-HCV positive and HCV RNA positive); (2) Female patients of child-bearing age are not pregnant, not breast-feeding, and both patient and their partner are using effective forms of contraception (one for each partner). Male patients and their partners are using effective forms of contraception (one for each partner). Female partners of male patients are not pregnant. Patients may only continue treatment after the first 20 weeks of boceprevir treatment if plasma HCV RNA is not detectable by a HCV RNA qualitative assay at treatment week 24.

Note

Treatment centres are required to have access to the following appropriate specialist facilities for the provision of clinical support services for hepatitis C:

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- (b) 24 hour access by patients to medical advice; and
- (c) an established liver clinic; and
- (d) facilities for safe liver biopsy.

Maximum quantity: 672

Repeats: 2

Section 100 (Highly Specialised Drugs Program)

Private Hospital/Private Clinic Authority Required

Public Hospital Authority Required (STREAMLINED)

Patients who have failed one prior attempt at interferon based therapies (non-pegylated or pegylated)

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- (d) facilities for safe liver biopsy.

Maximum quantity: 672

Repeats: 3

13. 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.

14. Sponsor's Comment

MSD looks forward to working with the PBAC to get boceprevir listed on the PBS as soon as possible.