Direct-acting Antivirals for Hepatitis C Stakeholder Meeting Outcome Statement

12 – 1 pm Thursday 13 December 2018 (teleconference)

Attendees

Members of the Pharmaceutical Benefits Advisory Committee (PBAC), representatives from the Australasian Society of HIV, Viral Hepatitis and Sexual Health Medicine (ASHM), the Gastroenterological Society of Australia (GESA), Hepatitis Australia, The Kirby Institute, Burnet Institute, the Department of Human Services (DHS) and the Department of Health along with health practitioners with expertise in the management of hepatitis C were in attendance.

Non-departmental attendees undertook confidentiality declarations and provided conflict of interest statements.

Purpose of the meeting

The PBAC Chair outlined that the objective of the stakeholder meeting was to receive advice and clinical perspectives on potential changes to the prescribing requirements for PBS-subsidised access to direct-acting antiviral (DAA) regimens for treatment of chronic hepatitis C (CHC) infection. The PBAC Chair noted that the meeting provided the opportunity to build upon earlier written consultation with key stakeholders undertaken in May/June 2018.

Background

DAA regimens (not requiring co-administration of interferon) were first listed on the PBS in March 2016 for the treatment of CHC infection. The regimens listed included ledipasvir with sofosbuvir (Harvoni®, Gilead Sciences Pty Ltd) for genotype 1 (GT 1), sofosbuvir (Sovaldi®, Gilead Sciences Pty Ltd) for genotypes 2 (GT 2) and 3 (GT 3) (in combination with ribavirin(RBV)), and daclatasvir (Daklinza®, Bristol Myers Squibb Australia Pty Ltd) for GT 1 and GT 3 (in combination with sofosbuvir). Initially, treatment for genotypes 4-6 (GT 4, GT5 and GT6) continued to require interferon as part of the treatment regimen.

In May 2016, paritaprevir with ritonavir with ombitasvir and dasabuvir (+/-RBV) (Viekira Pak®, AbbVie Pty Ltd) was listed on the PBS for GT 1. Elbasvir with grazoprevir (Zepatier®, Merck, Sharp and Dohme Australia Pty Ltd) was listed on the PBS in January 2017 for GT 1 and GT 4.

The first 'pan-genotypic' regimen, sofosbuvir with velpatasvir (Epclusa®, Gilead Sciences Pty Ltd) was listed on the PBS in August 2017. This regimen covers all genotypes in a single 12-week course regardless of prior treatment or cirrhotic status. A second pan-genotypic regimen, glecaprevir with pibrentasvir (Maviret®, AbbVie Pty Ltd) was PBS listed in August 2018. Patients with hepatitis C virus (HCV) GT1 who were previously treated with an NS5A inhibitor or NS3/4A protease inhibitor are included in the TGA indication for glecaprevir with pibrentasvir. The PBAC also recommended the pan-genotypic regimen, sofosbuvir with

velpatasvir and voxilaprevir (Vosevi®, Gilead Sciences Pty Ltd) following its consideration at the PBAC's March 2018 meeting. The listing process is not yet finalised for sofosbuvir with velpatasvir and voxilaprevir. The TGA indication for this regimen includes patients who have previously been treated with an NS5A inhibitor.

The current prescribing requirements for PBS-subsidised access to DAA regimens are outlined in the *General Statement for Drugs for the Treatment of Hepatitis C*. All treatments are currently Authority Required (In Writing or Telephone) listings and require patients to be aged 18 years or older, and the prescriber must provide the patient's HCV genotype and cirrhotic status at time of seeking authority approval. Treatment matrix are provided to inform prescribers of the PBS subsidised treatment regimens that are available. The treatment matrix is organised by genotype, cirrhotic status and whether the patient has received prior treatment. At the time the matrix was written the available prior treatments were protease inhibitor (such as boceprevir, simeprevir or telaprevir) and/or interferon based.

At its March 2018 meeting, the PBAC considered a submission to amend the current listing of grazoprevir with elbasvir from Authority Required (In Writing or Telephone) to Authority Required (STREAMLINED). The PBAC deferred the submission, pending further consultation with stakeholders on the CHC treatment matrix given the introduction of new DAA treatments since the General Statement was developed.

The PBAC asked the Secretariat to initiate consultation with relevant stakeholders regarding the current structure of the PBS listing for CHC and to review the components of the restriction. The PBAC sought the advice of the: Australian college of Rural and Remote Medicine; Australian HCV Treatment Guidelines Steering Committee; ASHM; GESA; Hepatitis Australia; Viral Hepatitis Clinical Research Program, Kirby Institute; and the Royal Australian College of General Practitioners. Stakeholder input from the written consultation conducted in May/June 2018 provided feedback on the current authority level of DAA regimens and age restrictions, the mandatory requirement for pre-treatment HCV genotype and cirrhotic status and barriers associated with Section 100 Highly Specialised Drugs Program prescribing of these medicines.

Summary and Outcomes of the Discussion

Current utilisation of DAAs

- The PBAC Chair noted the findings of the Drug utilisation sub-committee (DUSC) utilisation review of DAA medicines listed on the PBS for the treatment of CHC.
- Stakeholders noted that utilisation and uptake of the DAA therapies in 2016 was higher than anticipated. This was despite the extensive consultation undertaken before the listing of DAAs to estimate the number of patients awaiting these therapies.
- Stakeholders noted that the number of initiations on DAA therapy had declined from 4,400 incident patients per month during the first four months of listing to an average of 1,280 patients per month by December 2017. Based on current trends, stakeholders considered approximately 15,000–16,000 patients would initiate DAA

therapy in 2018. Stakeholders considered that at this level of DAA initiation Australia may achieve WHO HCV elimination targets by 2030, however higher initiation rates (approximately 19,000 patients per year) would likely be required to meet National Hepatitis C Strategy targets for 2022.

- Stakeholders noted that the vast majority of patients (~95%) were dispensed the full number of original and repeat prescriptions for their allocated DAA regimen that the prescriber had applied for when seeking an Authority approval. Stakeholders considered this an encouraging sign that the duration of treatment with DAAs in practice was consistent with guidelines.
- Stakeholders agreed that the DUSC utilisation review of DAA medicines highlighted that the data collection component of the current prescribing requirements for PBS-subsidised access to DAA regimens provided a very useful mechanism to monitor use of these medicines.
- Stakeholders noted that some populations, such as people who inject drugs, those in corrective services settings and new migrant communities are often more difficult to track and engage with treatment. Stakeholders suggested that new/additional models of care might be required to eliminate HCV from specific populations not currently engaged with the existing arrangements.
- The PBAC Chair noted the treatment landscape had changed substantially since the listing of the first DAAs in March 2016, and stated that the PBAC had tried to be responsive to changes in the treatment landscape.
- The PBAC Chair considered the DUSC utilisation review of DAA medicines revealed positive trends, such as the increasing proportion of DAA prescribing by general practitioners and the high uptake of pan-genotypic regimens since first listing in late 2017.
- However, the PBAC Chair also noted there were outstanding and important issues raised in previous written correspondence on these listings and highlighted the value of the roundtable discussion to explore these matters.

Mandatory requirement for pre-treatment HCV genotype

- Stakeholders generally agreed that the mandatory requirement for pre-treatment HCV genotype when obtaining authorisation to prescribe DAA therapy was a barrier to initiating treatment for some patients.
- Stakeholders considered that without the mandatory requirement most patients would still have genotyping done. However, for some patients, awaiting the results of genotype testing may delay initiation of therapy and increase the risk of loss to follow up. Stakeholders highlighted that this was of particular concern in the corrective services setting where any delay to treatment may be a barrier as patients often move between settings at frequent and unexpected intervals. Stakeholders indicated that in this setting there may also be barriers to undertaking genotyping at the same time as HCV RNA testing due to cost constraints.
- Stakeholders considered that, while it was informative for monitoring purposes to have data on genotype recorded as part of the current Authority Required (In Writing or Telephone) listing, it may be counterproductive if it limits treatment use.

- Stakeholders noted that no Point of Care (PoC) tests for HCV are approved in Australia, however trials involving these tests were complete and an application for the TGA was anticipated in the near future. Stakeholders considered that the potential availability of PoC tests in the future did not reduce the argument for removal of the mandatory requirement for pre-treatment HCV genotype for all DAA regimens to simplify patient care.
- Stakeholders considered that for prescribing pan-genotypic therapies, the need to wait for confirmation of genotype was reduced for many patients. However, stakeholders noted that genotype specific DAA therapy still required knowledge of genotype before treatment initiation and considered that such regimens were used more commonly in the community setting. It was also noted that in some instances, general practitioners are referring patients to specialists with a positive HCV RNA test, but with no genotype result, which can result in a delay in initiating therapy under current prescribing arrangements.

Mandatory requirement for obtaining cirrhotic status prior to DAA initiation

- Stakeholders agreed an assessment of a patient's cirrhotic status prior to commencing therapy was an important part of assessment and should continue as part of standard practice. Stakeholders noted that DAA dose duration differs for some regimens depending on cirrhotic status. It was also noted that people with cirrhosis continue to have long-term risks and complications of cirrhosis even after cure. Hence, stakeholders considered that knowledge of cirrhotic status remained important in decision making regarding treatment and post-treatment follow up.
- Stakeholders noted that there are various ways to assess cirrhotic status and agreed the manner of assessment should be a clinical consideration.
- Stakeholders supported maintaining the requirement to confirm a patient's cirrhotic status as part of the pre-treatment assessment.

Consideration of an Authority Required (STREAMLINED) listing

- Stakeholders generally supported the implementation of an Authority Required (STREAMLINED) listing for DAA regimens to simplify patient care.
- Stakeholders considered it important to incorporate cirrhotic status into any Authority Required (STREAMLINED) listing for DAA regimens. Stakeholders suggested that any such amendments could be modelled on the current Authority Required (STREAMLINED) listings for medicines for the treatment of chronic hepatitis B infection. It was noted that the accuracy of cirrhotic status in utilisation data may be reduced by such an approach due to the potential for inaccurate code selection at the point of prescribing or dispensing.
- The PBAC Chair noted the discussion and indicated that further investigation would be required to ascertain whether an Authority Required (STREAMLINED) approach would be feasible in this context.

Other matters relating to the PBS listings of DAAs for the treatment of CHC

Prescribing DAAs under the Section 100 Highly Specialised Drugs Program

- Stakeholders raised concerns regarding the Section 100 Highly Specialised Drugs Program prescribing of DAAs, which is required for patients treated in hospital care or in corrective services. Concerns raised related to the inability of nurse practitioners to prescribe in these settings under current Section 100 arrangements with stakeholders considering this a barrier to treatment.
- The Department noted the issues raised were embedded within the legislation underpinning the Section 100 Highly Specialised Drugs Program. The PBAC Chair indicated that the concerns raised would be taken into consideration in work currently being undertaken in this area.

Restriction of DAA use to patients aged 18 years and older

- Stakeholders noted that data were available which may support the use of some DAA regimens in children and adolescents, and that treatment in these populations is available in some countries.
- The PBAC Chair advised the DAA listings were initially restricted to patients aged 18 years and older based on the clinical evidence available at the time of listing. The PBAC Chair advised the age restriction was also influenced by the fact that these were new medicines (hence limited adverse event information was available at the time of listing) and there were specific concerns around their use in practice. The PBAC Chair advised that the Department would consult with the TGA to obtain any information regarding applications to remove or alter age restrictions on any DAA regimens' Australian registration.

Restriction of DAA use to patients with 'chronic' hepatitis C infection

- The use of the term 'chronic' in the PBS indication for use and the requirement for evidence of CHC infection as stated in the *General Statement for Drugs for the Treatment of Hepatitis C* were raised as potential barriers to use. Some stakeholders suggested that there was increasing evidence that treating HCV early (i.e. patients with acute hepatitis C infection) decreased infection transmission rates in patients who are engaging in high-risk behaviour.
- Stakeholders noted that spontaneous resolution of HCV can occur during the acute phase for some patients.
- The PBAC Chair noted the PBAC would want to see evidence of efficacy and cost-effectiveness of use in the acute hepatitis C infection population prior to recommending such amendments to the PBS listings.

Removal of regimens from the General Statement for Drugs for the Treatment of Hepatitis C

- Stakeholders agreed that interferon-based regimen options should be removed from the General Statement as interferon-free options were now available for all genotypes.
- Stakeholders considered that the regimens listed under the General Statement should be reviewed to ensure that those listed are consistent with current guidelines and have not been withdrawn from the Australian market.

Use of salvage regimens in CHC

- Stakeholders noted that only one salvage regimen was currently available on the PBS and an additional PBAC recommendation was yet to be listed. Stakeholders considered that it would be useful to be able to use combinations of drugs in this context as evidence emerges and suggested that any revision of the *General Statement for the Treatment of Hepatitis C* should take this into account. Stakeholders suggested that this approach was not appropriate in the treatment naïve setting.

Summary and next steps

The PBAC Chair thanked stakeholders for participating in the teleconference and considered the advice provided on potential changes to the prescribing requirements for PBS subsidised access to DAA regimens to be valuable.

Stakeholders generally agreed:

- the mandatory requirement for pre-treatment HCV genotype was a barrier to initiating DAA therapy for some patients;
- the requirement to confirm a patients cirrhotic status as part of the pre-treatment assessment should remain;
- the implementation of an Authority Required (STREAMLINED) listing for DAA regimens would simplify patient care;
- consideration should be given to removing the restriction of DAA use to patients aged 18 years and older;
- interferon-based regimen options should be removed from the *General Statement for the Treatment of Hepatitis C*.

The PBAC Chair indicated a willingness of the PBAC to reassess the current structure of the *General Statement for the Treatment of Hepatitis C* with a view to making it simpler for prescribers. The PBAC Chair stated that the outcomes of the stakeholder meeting would be used to inform future PBAC considerations on this issue.