Hepatitis B: utilisation analysis

Drug utilisation sub-committee (DUSC)

February 2015

Abstract

Purpose

To examine the utilisation of medicines for the treatment of hepatitis B.

As the most recent new listing for hepatitis B occurred five years ago (December 2009) a predicted versus actual comparison is out of scope for this analysis.

This analysis focused on treatment of chronic hepatitis B. The vaccination program is out of scope for this analysis.

Background

The primary goal of treating hepatitis B patients is to improve patient survival by preventing or delaying the development of cirrhosis and liver cancer.[1]

Data Source / methodology

Data for the number of prescriptions for medicines used to treat hepatitis B were extracted from the Highly Specialised Drugs (HSD) database for the period January 2003 to June 2014 inclusive, based on the date that the prescription was supplied. These data were used to count the overall number of packs dispensed for medicines used to treat hepatitis B, and the annual cost to Government.

The number of patients was calculated by matching prescriptions from the Department of Human Services (DHS) Authority Approvals database with data from the DHS Medicare Pharmacy Claims database for the period July 2013 to June 2014, inclusive.

Key Findings

During the period July 2013 to June 2014:

- 12,953 patients received treatment for hepatitis B through the PBS.

[1] Gastroenterological Society of Australia. Chronic Hepatitis B (CHB) Recommendations – Australia and New Zealand (2010): Gastroenterological Society of Australia; 2009. Available from <http://www.gesa.org.au/professional.asp?cid=9&id=109>.

- 74,493 prescriptions were dispensed at a cost of $59,172,690.

Overall the market of hepatitis B medicines is growing. The DUSC noted this growth is largely attributable to entecavir and tenofovir use, which is consistent with the recommendation in clinical guidelines that most patients commence on these medicines.

Purpose of analysis

To examine the utilisation of medicines for the treatment of hepatitis B.

As the most recent new listing for hepatitis B occurred five years ago (December 2009) a predicted versus actual comparison is out of scope for this analysis.

This analysis focused on treatment of chronic hepatitis B. The vaccination program is out of scope for this analysis.

Background

Chronic Hepatitis B (CHB) Recommendations from the Gastroenterological Society of Australia (September 2009) was used as a main source of background information for this report. To view the guidelines visit the Gastroenterological Society of Australia.

Pharmacology

The primary goal of treating hepatitis B patients is to improve patient survival by preventing or delaying the development of cirrhosis and liver cancer.[1]

There are two groups of drugs used to treat hepatitis B; direct antiviral drugs (nucleoside/nucleotide analogues) and immunomodulatory drugs (interferons). Table 1 identifies the class of each PBS listed medicine. Nucleoside/nucleotide analogues reduce the amount of hepatitis B virus in the body by lowering the ability of the virus to multiply.[2]

Interferons are proteins that modify the response of the body's immune system to help fight infections and severe diseases.[3] In Australia, pegylated interferon has replaced standard interferon in chronic hepatitis B therapy.[1]

Therapeutic Goods Administration (TGA) approved indications

For details of the current TGA approved indications for medicines used in the treatment of hepatitis B refer to the Product Information (PI). The PIs for each product are available from the TGA (Product Information) page.

Dosage and administration

The table below summarises the dosage and frequency of administration for medicines used to treat hepatitis B.

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[2] Hepsera (adefovir). Consumer Medicine Information.. Melbourne: Gilead Sciences Pty Ltd. Prepared 5 September 2014. Available from <https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2010-CMI-03993-3>.
[3] Pegasys (peginterferon). Consumer Medicine Information. Sydney: Roche Products Pty Ltd. Prepared 28 July 2014. Available from <
https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2010-CMI-01159-3>.

Table 1: Dosage and administration of medicines used to treat hepatitis B

Brand name and sponsor	Drug	Type of drug	Dose and frequency of administration
Zeffix (Aspen Pharmacare Australia Pty Limited) Zetlam (Alphapharm Pty Ltd)	lamivudine	Nucleoside analogue	100 mg once daily in adults and children >12 years 3 mg/kg once daily to a maximum of 100 mg daily in children aged 2-11 years old Higher doses are recommended in patients with HIV coinfection
Hepsera (Gilead Sciences Pty Limited)	adefovir dipivoxil	Nucleotide analogue	10 mg once daily (adjusted in renally impaired patients)
Baraclude (Bristol-Myers Squibb Australia Pty Ltd)	entecavir	Nucleoside analogue	0.5 mg once daily in nucleoside naïve patients (adjusted in renally impaired patients) 1 mg once daily in patients with lamivudine resistance (adjusted in renally impaired patients)
Viread (Gilead Sciences Pty Limited)	tenofovir	Nucleotide analogue	300 mg once daily (adjusted in renally impaired patients) Dose is given as tenofovir disoproxil fumarate (300 mg tablet equivalent to 136 mg tenofovir)
Sebivo (Novartis Pharmaceuticals Australia Pty Limited)	telbivudine	Nucleoside analogue	600 mg once daily (adjusted in renally impaired patients)
Pegasys (Roche Products Pty Ltd)	peginterferon alfa-2a	Interferon	Subcutaneous injection 180 µg once a week for 48 weeks (adjusted in renally impaired patients)
Roferon-A (Roche Products Pty Ltd)	interferon alfa-2a	Interferon	Subcutaneous injection 4.5×10^6 units 3 times per week, increasing to a maximum of 18×10^6 units 3 times per week after one month if the lower dose is tolerated and there is no response
Intron A Redipen (Merck Sharp & Dohme (Australia) Pty Ltd)	interferon alfa-2b	Interferon	Subcutaneous injection 3×10^6 units 3 times per week, increasing to $5\text{-}10\times10^6$ units 3 times per week after one month if the lower dose is tolerated and there is no response

Source: Australian Medicines Handbook, 2013

The current Product Information (PI) and Consumer Medicine Information (CMI) are available from the TGA (Product Information) and the TGA (Consumer Medicines Information).

Clinical situation

It is estimated that only 55 per cent of people living with chronic hepatitis B are diagnosed. The Second National Hepatitis B Strategy 2014-2017 notes expert opinion that increasing

the proportion of those diagnosed to 80 per cent would significantly contribute to reducing hepatitis B associated morbidity and mortality, and reducing transmission.[4]

While estimates for the proportion of people living with chronic hepatitis B who are on treatment are uncertain, they are very low, ranging from 2.5–5 per cent. Similarly, there is limited information on the proportion of people living with chronic hepatitis B who are eligible for treatment; however, Australian and international estimates range from 10–25 per cent.[3]

The decision to treat a patient is based on whether they are at risk for the development of cirrhosis and its consequences, liver failure and liver cancer. Clinical factors which are considered are the level of hepatitis B virus (HBV DNA) in the blood, alanine aminotransferase (ALT) levels and whether there is inflammation or fibrosis in the liver, as seen in the results of a liver biopsy.[1] In general, a patient will require careful monitoring in the 'Immune Tolerance' and 'Immune Control' phases of the disease, and is likely to require treatment in the 'Immune Clearance' and 'Immune Escape' phases. To achieve continued clinical benefit, treatment may be required for years, decades or for the remainder of the patient's life. The decision to initiate treatment must balance the long-term benefits with the long-term risks, and consider anticipated compliance and any contraindications.[1]

Drug resistance is common with older direct antiviral agents, but newer agents such as tenofovir and entecavir have favourable resistance profiles.[5] According to clinical guidelines, tenofovir and entecavir are the preferred first-line therapies. Adefovir is also recommended as an appropriate first-line therapy, although the PBS listing for adefovir is restricted to second line use, after failure of antihepadnaviral therapy. In hepatitis B "e" antigen (HBeAg)-positive hepatitis B patients peginterferon is also an option for first line treatment. As lamivudine and telbivudine tend to have higher resistance rates they are generally not recommended in either HBeAg-positive or HBeAg-negative patients, although there are patient subgroups for whom lamivudine should be considered.[1] There are options for combination treatment, such as lamivudine plus adefovir, if the patient develops resistance to lamivudine.

PBS listing details

Details of the PBS listing including listing date, indication, list price, maximum quantities and number of repeats, presentation, dose forms, brand name, manufacturer can be found in Appendix A.

Restriction

The PBS restrictions of medicines used to treat hepatitis B are summarised in the table below.

[4] Australian Government Department of Health. Second National Hepatitis B Strategy 2014–2017. Canberra: Department of Health; 2014. Available from <http://www.health.gov.au/internet/main/publishing.nsf/Content/ohp-bbvs-hepb>.
[5] Australian Medicines Handbook. Adelaide: Australian Medicines Handbook Pty Ltd; 2013.

Table 2: PBS restrictions of medicines used to treat hepatitis B

	LAM	ADV	ETV	TDF	LdT	IFN alfa-2a	IFN alfa-2b	pegIFN
Patients without cirrhosis:								
nucleoside analogue naïve with elevated HBV DNA levels and evidence of chronic liver injury				✓	✓			
elevated HBV DNA levels and evidence of chronic liver injury	✓		✓			✓	✓	✓
after antihepadnaviral therapy failure with or without combination treatment with lamivudine		✓		✓				
after failure of lamivudine		✓	✓					
Patients with cirrhosis:								
nucleoside analogue naïve with detectable HBV DNA				✓	✓			
detectable HBV DNA	✓		✓			✓	✓	✓
after antihepadnaviral therapy failure with or without combination treatment with lamivudine		✓		✓				
after failure of lamivudine		✓	✓					

Abbreviations: LAM: lamivudine; ADV: adefovir; ETV: entecavir; TDF:tenofovir; LdT:telbivudine; IFN alfa-2a: interferon alfa-2a; IFN alfa-2b: interferon alfa-2b; pegIFN: peginterferon alfa-2a

Full wording of the restrictions are available from the PBS website.

Date of listing on PBS

The date of first PBS listing of medicines used to treat hepatitis B are summarised in the table below.

Table 3: Date of first PBS listing of medicines used to treat hepatitis B

Drug	Date of first PBS listing for hepatitis B
interferon alfa-2a	1 November 2001
interferon alfa-2b	1 November 2001
lamivudine	1 November 2001
adefovir	1 December 2004
peginterferon alfa-2a	1 October 2006
entecavir	1 December 2006
telbivudine	1 August 2008
tenofovir	1 December 2009

Changes to listing

Historical changes to the listings of medicines used to treat hepatitis B are tabulated in the appendices.

Current PBS listing details are available from the PBS website.

Relevant aspects of the PBAC considerations

Entecavir July 2006 meeting

Entecavir was recommended on a cost effectiveness basis compared to lamivudine for the treatment of hepatitis B patients in nucleos(t)ide naïve patients.

Entecavir was recommended on a cost minimisation basis compared to adefovir for the treatment of hepatitis B patients in lamivudine resistant patients.

The PBAC noted the overall market for chronic hepatitis B was not expected to grow or to grow more rapidly as a result of listing entecavir.

For further details refer to the Public Summary Document from the July 2006 PBAC meeting.

Tenofovir November 2008 meeting

The PBAC recommended the listing of tenofovir on the S100 Highly Specialised Drugs Program of the PBS for the treatment patients with HBeAg-positive chronic hepatitis B who are nucleoside analogue naïve on a cost minimisation basis to entecavir 0.5 mg tablets.

The PBAC did not accept the claim that tenofovir is equally effective as entecavir in nucleoside naïve HBeAg negative patients because this conclusion relied on the assumption that tenofovir is equally effective in nucleoside naïve HBeAg negative and HBeAg positive patients.

The PBAC rejected the application for listing of tenofovir for the treatment of hepatitis in nucleoside experienced patients.

For further details refer to the Public Summary Document from the November 2008 PBAC meeting.

Tenofovir July 2009 meeting

The PBAC recommended extending the listing of tenofovir on a cost-minimisation basis compared with entecavir 0.5 mg for treatment of chronic hepatitis B in nucleoside analogue naïve patients and on a cost-minimisation basis compared with adefovir 10 mg for patients who have failed previous antihepadnaviral therapy.

The submission estimated the likely number of patients/year to be less than 10,000 in Year 5 of listing.

For further details refer to the Public Summary Document from the July 2009 PBAC meeting.

Previous reviews by the DUSC

A 12 month predicted versus actual review was completed for adefovir for the June 2006 DUSC meeting. The review found the actual utilisation of adefovir was slightly more than half of that predicted in the submission for the first year of listing.

The DUSC concluded that the lower than expected use may have been due to differences in interpretation of the requirement to have failed lamivudine therapy prior to being prescribed adefovir; as the treatment duration of lamivudine was not clinically well defined. Therefore the time between a patient being considered to have failed lamivudine and requiring transition to adefovir may be different in practice to that proposed in the submission.

Methods

Data for the number of prescriptions for medicines used to treat hepatitis B were extracted from the Highly Specialised Drugs (HSD) database for the period January 2003 to June 2014 inclusive, based on the date that the prescription was supplied. These data were used to count the overall number of packs dispensed for medicines used to treat hepatitis B, and the annual cost to Government.

The number of patients was calculated by matching prescriptions from the Department of Human Services (DHS) Authority Approvals database with data from the DHS Medicare Pharmacy Claims database for the period July 2013 to June 2014, inclusive. The number of patients treated overall and for each drug was determined by counting the number of individual de-identified personal identification numbers in this period. Data manipulation was undertaken using SAS.

The DUSC noted that as there were only 12 months of complete patient level data available, it was not possible to complete a length of treatment analysis.

Limitations of the data

Until July 2013 some HSD prescriptions were processed through the DHS Offline processing system, and these prescriptions do not have attached patient information. Therefore a patient level analysis has not been performed prior to July 2013 as the data are likely to be incomplete.

Some medicines used to treat hepatitis B are also listed for other indications, such as hepatitis C, HIV, myelogenous leukaemia in the chronic phase and malignant melanoma. Where a drug is listed for more than one indication under the same PBS item code it was not possible to separate these in the HSD data prior to July 2013.

The item codes for tenofovir include use for HIV. Figure 1 shows the use of tenofovir in the HSD database. All use of tenofovir prior to 1 December 2009 was for HIV treatment. The decrease in the use of tenofovir from the first quarter of 2006 is likely because a combination item of tenofovir with emtricitabine was listed for the treatment of HIV effective 1 February 2006.

Tenofovir was PBS listed for hepatitis B on 1 December 2009. In Figure 1, Hepatitis B (actual) represents the use of tenofovir for hepatitis B in the data set which matched the authority approvals and pharmacy claims data from July 2013 to June 2014. A trend function was used to estimate the amount of use of hepatitis B treatment before July 2013. This use was subtracted from the total use of tenofovir to estimate the use of tenofovir for HIV.

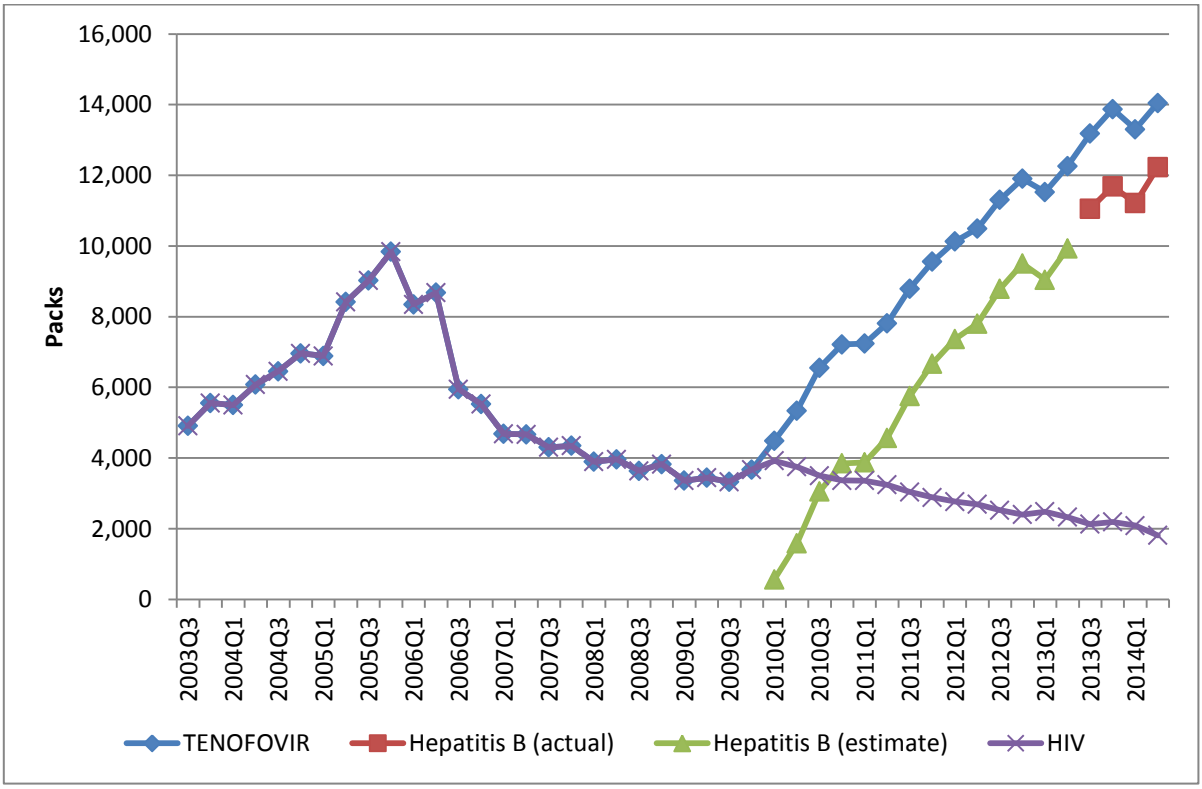

Figure 1: Estimated proportion of use of tenofovir over time

Lamivudine is also PBS listed for HIV but under separate PBS item codes which were excluded from this analysis. Use of interferon alfa-2a and interferon alfa-2b includes use for Philadelphia chromosome positive myelogenous leukaemia in the chronic phase. Use of peginterferon alfa-2a includes use for hepatitis C. As the use of interferons is quite low compared to direct antiviral drugs, the use of the interferons has not been adjusted.

For the period July 2013 to June 2014, prescriptions for HIV, hepatitis C and leukaemia were excluded from the data before counting the number of patients.

Results

Analysis of drug utilisation

Overall utilisation

The figure below shows the use of medicines used to treat hepatitis B since 2003.

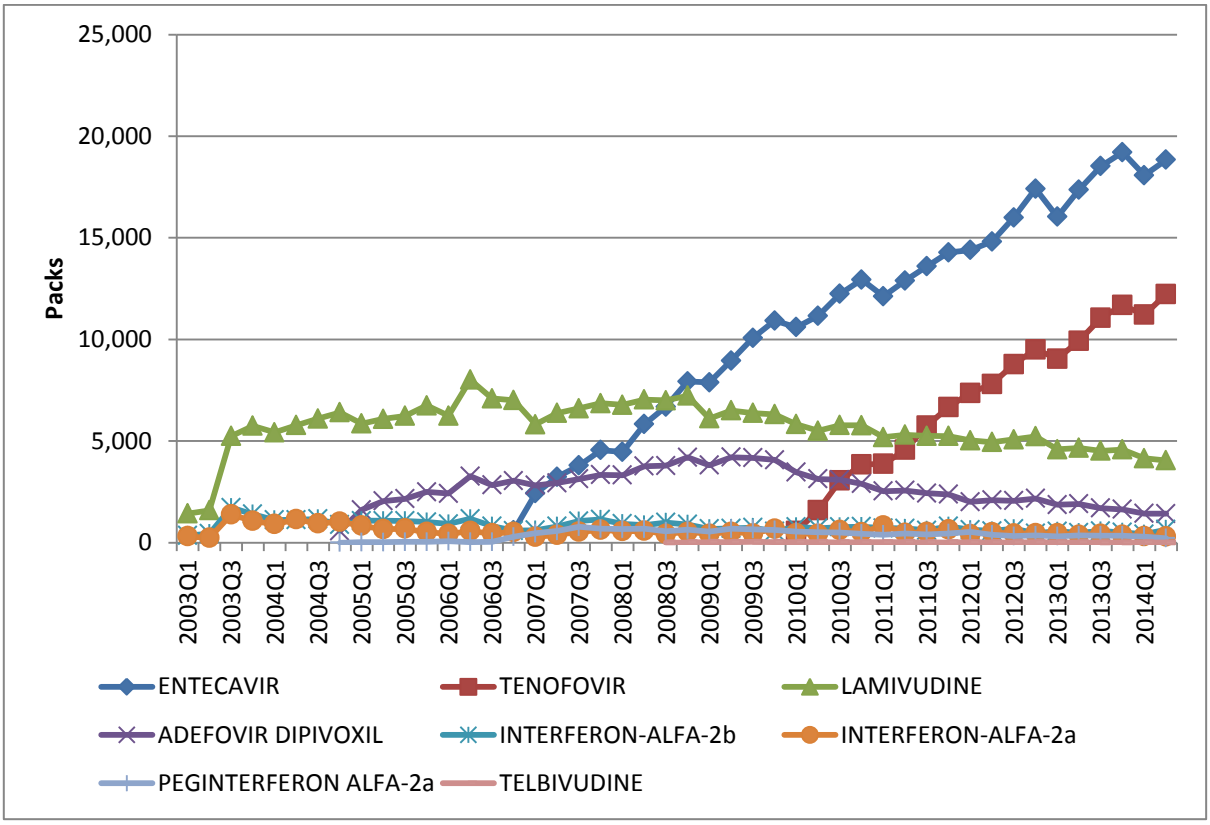

Figure 2: Use of medicines used to treat hepatitis B over time

Note that the use of tenofovir has been adjusted to exclude use for HIV, please see Figure 1 for more information.

The table below summarises the packs supplied by quarter and calendar year since 2003.

Table 4: Packs per quarter and year for all hepatitis B medicines

	Q1	Q2	Q3	Q4	Total by Calendar Year
2003	2,095	2,273	8,357	8,218	20,944
2004	7,464	8,054	8,212	8,904	32,634
2005	9,410	9,905	10,199	10,818	40,333
2006	10,097	13,057	11,249	12,068	46,471
2007	12,434	14,306	15,911	17,209	59,860
2008	16,743	18,777	19,471	21,443	76,435
2009	19,495	21,620	22,519	26,880	90,514
2010	26,215	26,814	29,587	30,594	113,210
2011	29,059	30,235	31,631	33,393	124,317
2012	33,183	33,856	35,910	38,038	140,987
2013	35,355	37,450	39,292	40,542	152,639
2014	38,015	39,529			77,544

*Note: the figure reported for 2014 is for January to June 2014 (inclusive). These figures include some use for indications other than hepatitis B, however use of tenofovir prior to its hepatitis B listing on 1 December 2009 has been excluded (see 'Limitations of the data' p9-10 and Figure 1 for more information).

Use of hepatitis B medicines is increasing. The population rate of diagnosis of hepatitis B infection in Australia declined slightly from 33.8 per 100,000 population in 2009 to 30.9 in 2013[6], which suggests the diagnosed prevalence may be fairly stable. The graph of overall utilisation by drug suggests the market is growing, largely due to the use of entecavir and tenofovir.

Utilisation by relevant sub-populations/regions or patient level analysis

In the 12 month period from July 2013 to June 2014, 12,953 patients accessed PBS listed medicine for hepatitis B.

The number of patients who accessed each drug is below. Note that a patient is counted once for each drug they received in this time period, and as patients may receive more than one medicine in the period, the sum of these patients is higher than the count of patients when they are not split by drug.

[6] The Kirby Institute. HIV, viral hepatitis and sexually transmissible infections in Australia Annual Surveillance Report 2014. Sydney; The Kirby Institute; 2014. Available from < https://kirby.unsw.edu.au/surveillance/2014-annual-surveillance-report-hiv-viral-hepatitis-stis>.

Table 5: Count of patients who received hepatitis B medicine during the period July 2013 to June 2014, by drug

Drug name	Number of patients
ADEFOVIR DIPIVOXIL	623
ENTECAVIR	7,175
INTERFERON ALFA-2A	1
LAMIVUDINE	1,696
PEGINTERFERON ALFA-2A	168
TELBIVUDINE	5
TENOFOVIR	4,641

Note that during this period interferon alfa-2b was PBS listed for hepatitis B but no prescriptions were recorded as being for hepatitis B.

The clinical guidelines recommend pegylated interferon be used rather than the older interferons. Only one patient used interferon alfa-2a for hepatitis B in the period July 2013 to June 2014, and there were no patients who used interferon alfa-2b for hepatitis B in this period.

Analysis of expenditure

Table 6: Cost to Government of medicines used to treat hepatitis B since 2003

Year	Cost to Government
2003	$3,291,262
2004	$4,914,580
2005	$9,818,377
2006	$12,215,030
2007	$21,980,871
2008	$28,889,980
2009	$36,395,481
2010	$46,507,626
2011	$51,100,477
2012	$58,120,201
2013	$62,710,354
2014*	$31,805,409

These figures are based on the date of supply.
*Note: the figure reported for 2014 is for the first six months of the year. These figures include some use for indications other than hepatitis B, however use of tenofovir prior to its listing on 1 December 2009 has been excluded (see Figure 1Figure 1 for more information).

Analysis of actual versus predicted utilisation

As the most recent new listing for hepatitis B occurred five years ago (December 2009) a predicted versus actual comparison is out of scope for this analysis.

Discussion

The use of hepatitis B medicines is increasing with time. The population rate of diagnosis of hepatitis B infection in Australia declined slightly from 33.8 per 100,000 population in 2009 to 30.9 in 2013[5], which suggests the diagnosed prevalence may be fairly stable. The DUSC agreed that the growth in the use of hepatitis B medicines is likely being driven by the introduction of newer drugs with lower rates of resistance, the use of combination treatment and patients being able to be treated with these drugs for a longer duration. The DUSC also considered that increased testing, in accordance with national guidelines, could increase detection, diagnosis and treatment in the future. DUSC noted that an estimated 45 per cent of prevalent patients are undiagnosed and that it is likely these patients have not shown any symptoms and may be diagnosed in the future.

To estimate future patterns of use, the DUSC considered it would be informative to know more about the history of the epidemiology of hepatitis B and whether the diagnosis rate has changed over time. However, future treated prevalence of hepatitis B in Australia will be influenced by a number of factors, including the patterns of immigration from endemic countries, levels of testing and access to accredited prescribers.

The DUSC considered the PBS restrictions provide flexibility for prescribers to choose the best treatment for their patient.

DUSC actions

- The DUSC referred the report to the PBAC for information.

Context for analysis

The DUSC is a Sub Committee of the Pharmaceutical Benefits Advisory Committee (PBAC). The DUSC assesses estimates on projected usage and financial cost of medicines.

The DUSC also analyses data on actual use of medicines, including the utilisation of PBS listed medicines, and provides advice to the PBAC on these matters. This may include outlining how the current utilisation of PBS medicines compares with the use as recommended by the PBAC.

The DUSC operates in accordance with the quality use of medicines objective of the National Medicines Policy and considers that the DUSC utilisation analyses will assist consumers and health professionals to better understand the costs, benefits and risks of medicines.

The utilisation analysis report was provided to the pharmaceutical sponsors of each drug and comments on the report were provided to DUSC prior to its consideration of the analysis.

Sponsors' comments

Alphapharm Pty Ltd
Aspen Pharma Pty Ltd
Apotex Pty Ltd
Bristol-Myers Squibb Australia Pty Ltd
Merck Sharp & Dohme (Australia) Pty Ltd
Novartis Pharmaceuticals Australia Pty Limited
Roche Products Pty Ltd

The sponsors have no comment.

Appendix A

PBS listing details (as at 1 November 2014)

Table 7: PBS listing of medicines to treat hepatitis B

Item	Name, form & strength, pack size	Max. quant.	Rpts	DPMQ	Brand name and manufacturer
5770Q	LAMIVUDINE 100 mg tablet, 28	2	5	$162.44	Zeffix (Aspen Pharmacare Australia Pty Limited)
6257H	LAMIVUDINE 100 mg tablet, 28	2	5	$175.70	Zetlam (Alphapharm Pty Ltd)
5771R	LAMIVUDINE 5 mg/mL oral liquid, 240 mL	2	5	$226.25	Zeffix (Aspen Pharmacare Australia Pty Limited)
6271C	LAMIVUDINE 5 mg/mL oral liquid, 240 mL	2	5	$242.06	
5606C	ADEFOVIR DIPIVOXIL 10 mg tablet, 30	2	5	$1,250.00	Hepsera (Gilead Sciences Pty Limited)
6450L	ADEFOVIR DIPIVOXIL 10 mg tablet, 30	2	5	$1,296.76	
5711N	ENTECAVIR 500 microgram tablet, 30	2	5	$768.60	Baraclude (Bristol-Myers Squibb Australia Pty Ltd)
5712P	ENTECAVIR 1 mg tablet, 30	2	5	$1,250.00	
9602J	ENTECAVIR 500 microgram tablet, 30	2	5	$806.10	
9603K	ENTECAVIR 1 mg tablet, 30	2	5	$1,296.76	
6358P	TENOFOVIR 300 mg tablet, 30	2	5	$1,011.60	Viread (Gilead Sciences Pty Limited)
9563H	TENOFOVIR 300 mg tablet, 30	2	5	$966.20	
9562G	TELBIVUDINE 600 mg tablet, 28	2	5	$501.76	Sebivo (Novartis Pharmaceuticals Australia Pty Limited)
9630W	TELBIVUDINE 600 mg tablet, 28	2	5	$528.60	
6439X	PEGINTERFERON ALFA-2A 135 microgram/0.5 mL injection, 4 x 0.5 mL syringes	2	5	$2,378.56	Pegasys (Roche Products Pty Ltd)

6449K	PEGINTERFERON ALFA-2A 180 microgram/0.5 mL injection, 4 x 0.5 mL syringes	2	5	$2,747.22	
9515T	PEGINTERFERON ALFA-2A 135 microgram/0.5 mL injection, 4 x 0.5 mL syringes	2	5	$2,331.80	
9516W	PEGINTERFERON ALFA-2A 180 microgram/0.5 mL injection, 4 x 0.5 mL syringes	2	5	$2,700.46	
5759D	INTERFERON ALFA-2A 3 million international units/0.5 mL injection, 1 x 0.5 mL syringe	30	5	$894.00	Roferon-A (Roche Products Pty Ltd)
5760E	INTERFERON ALFA-2A 4.5 million international units/0.5 mL injection, 1 x 0.5 mL syringe	30	5	$1,341.00	
5761F	INTERFERON ALFA-2A 6 million international units/0.5 mL injection, 1 x 0.5 mL syringe	30	5	$1,787.40	
5762G	INTERFERON ALFA-2A 9 million international units/0.5 mL injection, 1 x 0.5 mL syringe	30	5	$2,681.40	
6210W	INTERFERON ALFA-2A 3 million international units/0.5 mL injection, 1 x 0.5 mL syringe	30	5	$936.46	
6211X	INTERFERON ALFA-2A 4.5 million international units/0.5 mL injection, 1 x 0.5 mL syringe	30	5	$1,387.66	
6212Y	INTERFERON ALFA-2A 6 million international units/0.5 mL injection, 1 x 0.5 mL syringe	30	5	$1,834.06	
6213B	INTERFERON ALFA-2A 9 million international units/0.5 mL injection, 1 x 0.5 mL syringe	30	5	$2,728.06	
5763H	INTERFERON ALFA-2B 18 million international units/1.2 mL injection, 1 x 1.2 mL cartridge	2	5	$357.48	Intron A Redipen (Merck Sharp & Dohme (Australia) Pty Ltd)
5764J	INTERFERON ALFA-2B 30 million international units/1.2 mL injection, 1 x 1.2 mL cartridge	2	5	$595.80	
5765K	INTERFERON ALFA-2B 60 million international units/1.2 mL injection, 1 x 1.2 mL cartridge	2	5	$1,191.60	

6253D	INTERFERON ALFA-2B 18 million international units/1.2 mL injection, 1 x 1.2 mL cartridge	2	5	$378.54	
6254E	INTERFERON ALFA-2B 30 million international units/1.2 mL injection, 1 x 1.2 mL cartridge	2	5	$626.40	
6255F	INTERFERON ALFA-2B 60 million international units/1.2 mL injection, 1 x 1.2 mL cartridge	2	5	$1,238.36	
5766L	INTERFERON ALFA-2B 18 million international units/3 mL injection, 1 x 3 mL vial	15	5	$2,681.10	Intron A (Merck Sharp & Dohme (Australia) Pty Ltd)
5767M	INTERFERON ALFA-2B 25 million international units/2.5 mL injection, 1 x 2.5 mL vial	15	5	$3,723.75	
5768N	INTERFERON ALFA-2B 10 million international units/mL injection, 5 x 1 mL vials	3	5	$1,489.50	
6218G	INTERFERON ALFA-2B 18 million international units/3 mL injection, 1 x 3 mL vial	15	5	$2,727.91	
6219H	INTERFERON ALFA-2B 25 million international units/2.5 mL injection, 1 x 2.5 mL vial	15	5	$3,770.56	
6246R	INTERFERON ALFA-2B 10 million international units/mL injection, 5 x 1 mL vials	3	5	$1,536.25	

Source: pbs.gov.au

Changes to listing

Table 8: Changes to the PBS listing of medicines to treat hepatitis B

Drug	Comment	Date
interferon alfa-2a	First PBS listed	1 November 2001
interferon alfa-2b	First PBS listed	1 November 2001
lamivudine	First PBS listed	1 November 2001
adefovir	First PBS listed	1 December 2004
peginterferon alfa-2a	First PBS listed	1 October 2006
entecavir	First PBS listed	1 December 2006

adefovir	The original restriction included a note which stated patients may receive treatment in combination with lamivudine for three months and immunocompromised patients may receive combination therapy for 12 months. The note was changed to "Patients may receive treatment in combination with lamivudine but not with other PBS-subsidised antihepadnaviral therapy."	1 March 2008
entecavir	Requirement removed that patients must be 16 years or older	1 July 2008
telbivudine	First PBS listed	1 August 2008
tenofovir	First PBS listed	1 December 2009
interferon alfa-2a	Current specified levels of HBV elevation are included in the restriction	1 November 2011
interferon alfa-2b		
lamivudine		
entecavir		
telbivudine		
peginterferon alfa-2a		
tenofovir	Current specified levels of HBV elevation are included in the restriction for patients who are nucleoside analogue naive	1 November 2011
adefovir	Requirement removed that "women of child bearing age are not pregnant, not breast-feeding, and are using an effective form of contraception"	1 November 2011
peginterferon alfa-2a	Requirement removed for the patient to have chronic hepatitis B and compensated liver disease	1 March 2012
interferon alfa-2a	Restrictions split into patients with and without cirrhosis	1 March 2012
interferon alfa-2b		
lamivudine		
adefovir		
entecavir		
telbivudine		
peginterferon alfa-2a		
tenofovir		

Current PBS listing details are available from pbs.gov.au

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