Australian Government

Department of Health

Application 1708

RNA PCR testing for access to PBS-subsidised bulevirtide for treatment of Hepatitis Delta Virus

This application form is to be completed for new and amended requests for public funding (including but not limited to the Medicare Benefits Schedule (MBS)). It describes the detailed information that the Australian Government Department of Health requires to determine whether a proposed medical service is suitable. Please use this template, along with the associated Application Form Instructions to prepare your application. Please complete all questions that are applicable to the proposed service, providing relevant information only. Applications not completed in full will not be accepted. The separate MSAC Guidelines should be used to guide health technology assessment (HTA) content of the Application Form

Should you require any further assistance, departmental staff are available through the Health Technology Assessment Team (HTA Team) on the email below to discuss the application form, or any other component of the Medical Services Advisory Committee process.

Email: hta@health.gov.au
Website: www.msac.gov.au

PART 1 – APPLICANT DETAILS

1. Applicant details (primary and alternative contacts)

Corporation / partnership details (where relevant):
Corporation name: Gilead Sciences Pty Limited
ABN: 71 072 611 708
Business trading name: Gilead Sciences Pty Limited

Primary contact name: REDACTED

Primary contact numbers
Business: REDACTED
Mobile: REDACTED
Email: REDACTED

Alternative contact name: REDACTED

Alternative contact numbers
Business: REDACTED
Mobile: REDACTED
Email: REDACTED

2. (a) Are you a consultant acting on behalf on an applicant?

☐ Yes
☒ No

(b) If yes what is the Applicant(s) name that you are acting on behalf of?

Not applicable

3. (a) Are you a lobbyist acting on behalf of an Applicant?

☐ Yes
☒ No

(b) If yes, are you listed on the Register of Lobbyists?

☐ Yes
☐ No

(c) Have you engaged a consultant on your behalf?

☐ Yes
☐ No

PART 2 – INFORMATION ABOUT THE PROPOSED MEDICAL SERVICE

4. Application title

RNA PCR testing for access to PBS-subsidised bulevirtide for treatment of Hepatitis Delta Virus

5. Provide a succinct description of the medical condition relevant to the proposed service (no more than 150 words – further information will be requested at Part F of the Application Form)

Hepatitis delta virus (HDV) is a rare and unique blood-borne virus that occurs in people infected with the hepatitis B virus (HBV) and is transmitted by exposure to contaminated blood or body fluids. HDV is reliant on HBV surface antigens (HBsAg) to infect human hepatocytes and to undergo viral assembly and transmission and therefore is only found either as a co-infection or as a super infection in patients with HBV infection. HDV infection causes hepatitis D, a form of viral hepatitis that is typically severe, rapidly progresses to cirrhosis, and is associated with increased risk of hepatocellular carcinoma (HCC) compared to HBV mono-infection. Liver cirrhosis and cancer occur on average earlier in HBV/HDV co-infection and the 5-year mortality of co-infected individuals is twice that of HBV mono-infection (Cornberg et al. 2020[1]). Chronic HDV infection has been described to cause cirrhosis and HCC with annual rates of 4% and 2.7%, respectively (Romeo et al. 2009[2]). There is currently no pharmacological standard of care for patients with HDV.

6. Provide a succinct description of the proposed medical service (no more than 150 words – further information will be requested at Part 6 of the Application Form)

Hepatitis D is a notifiable disease in Australia. Hepatitis D infection must be notified by medical practitioners and pathology services in writing within 5 days of diagnosis. The primary source of hepatitis D epidemiological data in Australia is the National Notifiable Disease Surveillance System (NNDSS).

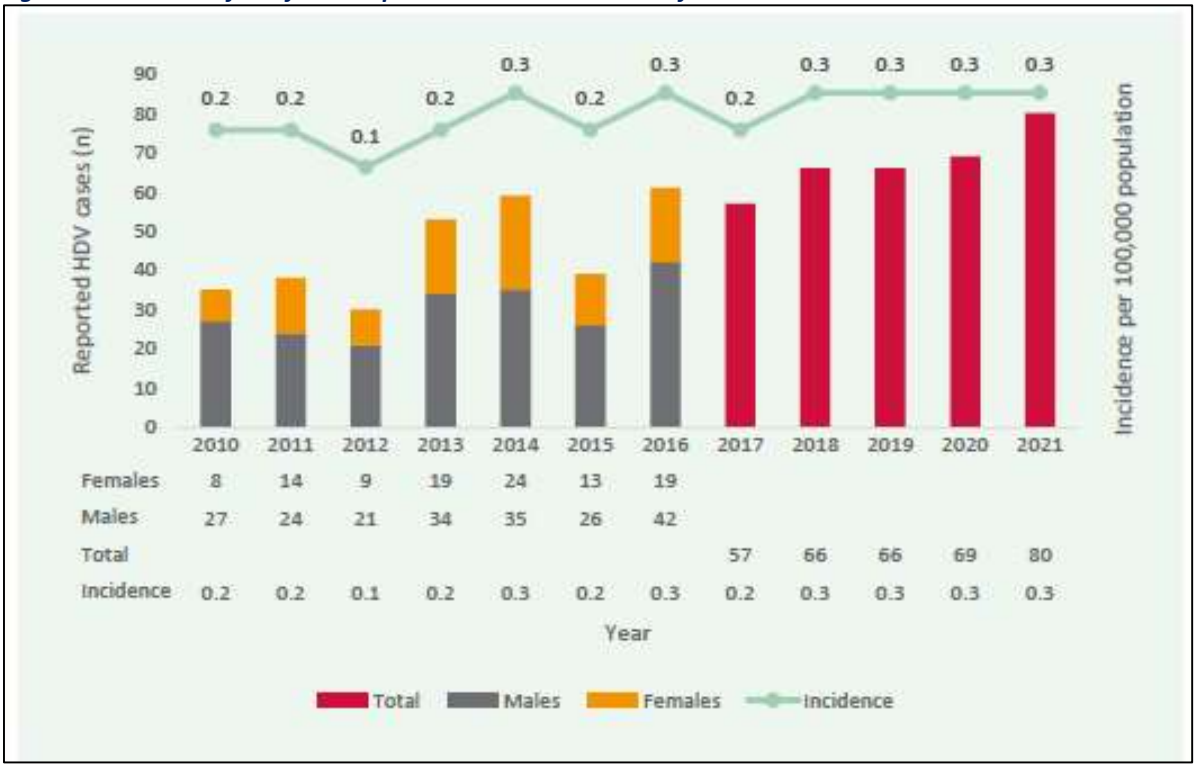
Based on annually reported data from the NNDSS, the diagnosed incidence of hepatitis D is low, with 69 cases notified nationwide in 2020 (**Figure 1**). The incidence of hepatitis D using notified cases is estimated at 0.3 per 100,000 population and has remained relatively stable over the past decade, ranging from 0.1–0.3 cases per 100,000 population from 2010–2020 (**Figure 1**).

On average, 70 cases of HDV are reported each year to the Commonwealth Department of Health[3]. Yearly notifications are stable (rolling 5-year average between 2015 and 2020 is 66.8).

The definition of a notifiable HDV case is the detection of IgM or IgG to hepatitis D virus or detection of hepatitis D virus on liver biopsy in patients who are HBV surface antigen positive. Therefore, the detection of HDV should be based on positive anti-HDV antibody testing given it is faster and not invasive compared to a liver biopsy (MBS Items 69384, 69475, 69481). If HDV is detected, quantification of HDV viral load via HDV ribonucleic acid polymerase chain reaction (RNA PCR) should be undertaken to determine the extent of viral replication which informs clinical decision making. In Australia, the HDV RNA PCR test is only offered by VIDRL (Victorian Infectious Disease Reference Laboratory) and is not yet funded on the MBS. Any collections by other states/jurisdictions are sent to VIDRL for testing/processing.

[1] Cornberg M, et al. J Hepatol. 2020 Mar;72:539-57. doi: 10.1016/j.jhep.2019.11.003. Epub 2019 Nov 12.
[2] Romeo, R., et al., A 28-year study of the course of hepatitis delta infection: a risk factor for cirrhosis and hepatocellular carcinoma. Gastroenterology, 2009. 136(5): p. 1629-38.
[3] NNDSS fortnightly summary notes: https://www1.health.gov.au/internet/main/publishing.nsf/Content/cdnareport-fn26-20.htm

Figure 1: Incidence of notifiable hepatitis D cases in Australia from 2010-201



Source: Incident notified cases of hepatitis D per sex (2010–2016) and overall (2010–2020). Sex distribution is reported from 2010–2016 (NNDSS Annual Report data); from 2017–2020, only total case numbers have been released. Between 2010 and 2016, the number of males who reported hepatitis D consistently exceed that of females, with 42 cases versus 19 cases in 2016, respectively. From January 01 to August 15, 2021, 52 cases have been notified; assuming cases are notified at a consistent rate to 2019 and 2020, incident cases for 2021 is estimated at 80. Incidence per 100,000 population is provided in NNDSS Annual Reports from 2010–2016 and has been calculated for 2017–2021 based on Australian population estimates reported by the Australian Bureau of Statistics. HDV, hepatitis delta virus.

7. (a) Is this a request for MBS funding?

☒ Yes
☐ No

(b) If yes, is the medical service(s) proposed to be covered under an existing MBS item number(s) or is a new MBS item(s) being sought altogether?

☐ Amendment to existing MBS item(s)
☒ New MBS item(s)

(c) If an amendment to an existing item(s) is being sought, please list the relevant MBS item number(s) that are to be amended to include the proposed medical service/technology:

Not applicable

(d) If an amendment to an existing item(s) is being sought, what is the nature of the amendment(s)?

i. ☐ An amendment to the way the service is clinically delivered under the existing item(s)
ii. ☐ An amendment to the patient population under the existing item(s)
iii. ☐ An amendment to the schedule fee of the existing item(s)
iv. ☐ An amendment to the time and complexity of an existing item(s)
v. ☐ Access to an existing item(s) by a different health practitioner group
vi. ☐ Minor amendments to the item descriptor that does not affect how the service is delivered
vii. ☐ An amendment to an existing specific single consultation item
viii. ☐ An amendment to an existing global consultation item(s)
ix. ☐ Other (please describe below):

(e) If a new item(s) is being requested, what is the nature of the change to the MBS being sought?

i. ☐ A new item which also seeks to allow access to the MBS for a specific health practitioner group
ii. ☒ A new item that is proposing a way of clinically delivering a service that is new to the MBS (in terms of new technology and / or population)
iii. ☐ A new item for a specific single consultation item
iv. ☐ A new item for a global consultation item(s)

(f) Is the proposed service seeking public funding other than the MBS?

☐ Yes
☒ No

(g) If yes, please advise:

Not applicable

8. What is the type of medical service/technology?

☐ Therapeutic medical service
☐ Investigative medical service
☐ Single consultation medical service
☐ Global consultation medical service
☐ Allied health service
☒ Co-dependent technology
☐ Hybrid health technology

9. For investigative services, advise the specific purpose of performing the service *(which could be one or more of the following)*:

i. ☒ To be used as a screening tool in asymptomatic populations
ii. ☒ Assists in establishing a diagnosis in symptomatic patients
iii. ☐ Provides information about prognosis
iv. ☒ Identifies a patient as suitable for therapy by predicting a variation in the effect of the therapy
v. ☒ Monitors a patient over time to assess treatment response and guide subsequent treatment decisions

10. Does your service rely on another medical product to achieve or to enhance its intended effect?

☒ Pharmaceutical / Biological
☐ Prosthesis or device
☐ No

The proposed test will determine eligibility for treatment and response to treatment with bulevirtide (**REDACTED**) through the PBS.

11. (a) If the proposed service has a pharmaceutical component to it, is it already covered under an existing Pharmaceutical Benefits Scheme (PBS) listing?

☐ Yes
☒ No

(b) If yes, please list the relevant PBS item code(s):

Not applicable

(c) If no, is an application (submission) in the process of being considered by the Pharmaceutical Benefits Advisory Committee (PBAC)?

☐ Yes (please provide PBAC submission item number below)
☒ No

Gilead plans to submit the Co-dependent MSAC/PBAC Application in latter half of 2022 for bulevirtide (**REDACTED**), an antiviral medicine used to treat chronic (long-term) hepatitis delta virus (HDV) infection in adults with compensated liver disease.

(d) If you are seeking both MBS and PBS listing, what is the trade name and generic name of the pharmaceutical?

Trade name: (**REDACTED)**
Generic name: bulevirtide

12. (a) If the proposed service is dependent on the use of a prosthesis, is it already included on the Prostheses List?

☐ Yes
☒ No

(b) If yes, please provide the following information (where relevant):

Not applicable

(c) If no, is an application in the process of being considered by a Clinical Advisory Group or the Prostheses List Advisory Committee (PLAC)?

Not applicable

(d) Are there any other sponsor(s) and/or manufacturer(s) that have a similar prosthesis or device component in the Australian marketplace which this application is relevant to?

Not applicable

(e) If yes, please provide the name(s) of the sponsor(s) and / or manufacturer(s):

Not applicable

13. Please identify any single and / or multi-use consumables delivered as part of the service?

Single use consumables: None
Multi-use consumables: None

PART 3 – INFORMATION ABOUT REGULATORY REQUIREMENTS

14. (a) If the proposed medical service involves use of a medical device, in-vitro diagnostic test, pharmaceutical product, radioactive tracer, or any other type of therapeutic good, please provide details

Type of therapeutic good: In-house conventional PT-PCR; positive sample qunaitifed by real-time PCR
Manufacturer's name: VIDRL (Victorian Infectious Disease Reference Laboratory)
Sponsor's name: VIDRL (Victorian Infectious Disease Reference Laboratory)

HDV Quantification (viral load) Assay

This test measures the amount of HDV RNA present in the blood and is used to determine current infection and monitor response to therapy. VIDRL uses an in-house assay that detects all known genotypes.

VIDRL (Victorian Infectious Disease Reference Laboratory[4]) is a leading Australian infectious diseases reference laboratory located in Melbourne, Victoria and is now part of the Peter Doherty Institute for Infection and Immunity (the Doherty).

VIDRL provides laboratory services for the Department of Health Victoria, Victorian hospitals and clinics, the Commonwealth Department of Health, and the World Health Organisation.

REDACTED

(b) Has it been listed on the Australian Register of Therapeutic Goods (ARTG) by the Therapeutic Goods Administration (TGA)? If the therapeutic good has been listed on the ARTG, please state the ARTG identification numbers, TGA-approved indication(s), and TGA-approved purpose(s).

Not listed on the ARTG

(c) If a medical device is involved, has the medical device been classified by TGA as a Class III OR Active Implantable Medical Device (AIMD) under the TGA regulatory scheme for devices?

Not applicable

(d) Is the therapeutic good classified by TGA for Research Use Only (RUO)?

15. (a) <u>If not listed on the ARTG</u>, is the therapeutic good to be used in the service exempt from the regulatory requirements of the *Therapeutic Goods Act 1989*?

☐ Yes
☒ No

Further details will be provided during the PICO development and submission.

(b) If the therapeutic good is <u>not ARTG listed</u>, is the therapeutic good in the process of being considered by TGA?

☐ **Yes**
☒ **No**

(c) If **the therapeutic good is NOT in the process of being considered by TGA, is an application to TGA being prepared?**

☐ Yes (please provide details below)
☒ No

[4] VIDRL - https://www.vidrl.org.au/about/

PART 4 – SUMMARY OF EVIDENCE

16. Provide one or more recent (published) high quality clinical studies that support use of the proposed health service/technology. At 'Application Form lodgement', please do not attach full text articles; just provide a summary.

	Type of study design	Title of journal article or research project	Short description of research	Website link to journal article or research	Date of publication
1.	Retrospective cohort study	Epidemiology and clinical outcomes of hepatitis delta (D) virus infection in Queensland, Australia	To investigate the epidemiology, clinical characteristics and outcomes of those with hepatitis delta virus (HDV) infection in Queensland, Australia.	https://www.ijidonline.com/article/S1201-9712(18)34463-1/fulltext	2018
2.	Retrospective cohort study	Epidemiology and phylogenetic analysis of hepatitis D virus infection in Australia	Notifiable disease surveillance and laboratory testing data were analysed to assess demographics, risk factors and trends. HDV serology and RNA testing were performed on requested samples from 2010 to 2016. Sequencing of a 500-nucleotide amplicon of the delta antigen and phylogenetic analysis of the strains from 2009 to 2016 were also conducted.	https://doi.org/10.1111/imj.13967	2018
3.	Retrospective cohort study	Hepatitis D virus in Victoria 2000–2009	To determine the number of reported cases of HDV in Victoria, Australia between 2000–2009 and to explore screening practices in patients at risk of HDV infection over the same time period.	https://onlinelibrary.wiley.com/doi/10.1111/imj.12247	2013
4.	Study of diagnostic accuracy	Development and performance of prototype serologic and molecular tests for hepatitis delta infection	Development of prototype serologic (anti-HDV IgG) and molecular (quantitative reverse-transcription polymerase chain reaction, qRT-PCR) assays to detect HDV infection, adapted for high-throughput screening on the Abbott ARCHITECT (serology) and m2000 (molecular) platforms, respectively.	https://www.nature.com/articles/s41598-018-20455-5 Presented as poster 2017 (see study 5 below, Rodgers 2017)	2018

	Type of study design	Title of journal article or research project	Short description of research	Website link to journal article or research	Date of publication
5.	Study of diagnostic accuracy	High prevalence of Hepatitis delta virus amongst Cameroonian HBsAg positive specimens	Plasma specimens were received from consenting subjects participating in surveillance studies in Cameroon collected over 8 years from 2007 – 2015. Samples were initially screened for antibodies (IgG) to HDV using a prototype HDV serology assay developed on the Abbott ARCHITECT	https://www.croiconference.org/wp-content/uploads/sites/2/posters/2017/577_Rodgers.pdf Poster presentation of study 4 publication (Coller 2018)	2017

17. Identify yet-to-be-published research that may have results available in the near future (that could be relevant to your application). Do not attach full text articles; this is just a summary.

REDACTED

PART 5 – CLINICAL ENDORSEMENT AND CONSUMER INFORMATION

18. **List all appropriate professional bodies/organisations representing the health professionals who provide the service. For MBS-related applications ONLY, please attach a brief 'Statement of Clinical Relevance' from the most relevant college/society.**

    Victorian Infectious Diseases Reference Laboratory, https://www.vidrl.org.au/
    Gastroenterological Society of Australia, https://www.gesa.org.au/
    Australasian Hepatology Association, https://www.hepatologyassociation.com.au/
    Australasian Society for HIV, Viral Hepatitis & Sexual Health Medicines, https://www.ashm.org.au/about/
    The Royal College of Pathologists of Australasia (RCPA), https://www.rcpa.edu.au/
    Australia Society of Infectious Diseases, https://www.asid.net.au/,

19. **List any professional bodies / organisations that may be impacted by this medical service (i.e. those who provide the comparator service):**

    None

20. **List the consumer organisations relevant to the proposed medical service (noting there is NO NEED to attach a support letter at the 'Application Lodgement' stage of the MSAC process):**

    Hepatitis Australia, https://www.hepatitisaustralia.com/
    The Liver Foundation, https://www.liver.org.au/

21. **List the relevant sponsor(s) and / or manufacturer(s) who produce similar products relevant to the proposed medical service**

    None

22. **Nominate two experts that can be contacted about the proposed medical service, and current clinical management of the condition**

    REDACTED

PART 6 – POPULATION (AND PRIOR TESTS), INTERVENTION, COMPARATOR, OUTCOME (PICO)

PART 6a – INFORMATION ABOUT THE PROPOSED POPULATION

23. Define the medical condition, including providing information on the natural history of the condition and a high level summary of associated burden of disease (in terms of both morbidity and mortality):

What is Hepatitis Delta Virus

Hepatitis delta virus (HDV) is a rare and unique blood-borne virus that occurs in people infected with the hepatitis B virus (HBV) and is transmitted by exposure to contaminated blood or body fluids. HDV is reliant on HBV surface antigens (HBsAg) to infect human hepatocytes and to undergo viral assembly and transmission and therefore is only found either as a co-infection or as a super infection in people with HBV infection. The liver disease associated with HDV runs a more progressive course than chronic hepatitis B (CHB) and may lead to cirrhosis within 2 years in 10–15% of patients (Yurdaydin et al. 2010[5]). Chronic HDV infection is associated with faster progression to fibrosis and cirrhosis, earlier onset of hepatic complications and likelihood of liver transplantation (Niro et al. 2010, Buti et al. 2011, Heidrich et al. 2013). Liver cirrhosis and cancer occur on average earlier in HBV/HDV co-infection and the 5-year mortality of co-infected individuals is twice that of HBV mono-infection (Cornberg et al. 2020[6]). Chronic HDV infection has been described to cause cirrhosis and HCC with annual rates of 4% and 2.7%, respectively (Romeo et al. 2009[7]).

The liver disease associated with HDV runs a more progressive course than chronic hepatitis B (CHB) and may lead to cirrhosis within 2 years in 10–15% of patients (Yurdaydin et al. 2010). Chronic HDV infection is associated with faster progression to fibrosis and cirrhosis, earlier onset of hepatic complications and likelihood of liver transplantation (Niro et al. 2010, Buti et al. 2011, Heidrich et al. 2013). Liver cirrhosis and cancer occur on average earlier in HBV/HDV co-infection and the 5-year mortality of co-infected individuals is twice that of HBV mono-infection (Cornberg et al. 2007). Chronic HDV infection causes cirrhosis and HCC with annual rates of 4% and 2.7%, respectively (Romeo et al. 2009).

How is Hepatitis Delta Virus Diagnosed

Hepatitis D is a notifiable disease in Australia. Hepatitis D infection must be notified by medical practitioners and pathology services in writing within 5 days of diagnosis based on the detection of HDV antibodies in patients who are HBV positive. The primary source of hepatitis D epidemiological data is the National Notifiable Disease Surveillance System (NNDSS).

Based on annually reported data from the NNDSS, the diagnosed incidence of hepatitis D is very low, with 69 cases notified nationwide in 2020 (**Figure 1**). The incidence of hepatitis D is estimated at 0.3 per 100,000 population and has remained relatively stable over the past decade, ranging from 0.1–0.3 cases per 100,000 population from 2010–2020 (**Figure 1**).

On average, 70 cases of HDV are reported each year to the department of health[8]. Yearly notifications are stable (rolling 5year average between 2015 and 2020 is 66.8).

In terms of diagnosis, positive anti-HDV antibody testing (MBS Items 69384, 69475, 69481) should always be followed by a HDV RNA PCR test given the extent of viral replication informs clinical decision making. In Australia, the HDV RNA PCR test is only offered by VIDRL (Victorian Infectious Disease Reference Laboratory) and potentially Westmead Hospital (to be confirmed). Any collections by other states/jurisdictions are sent to VIDRL for testing/processing.

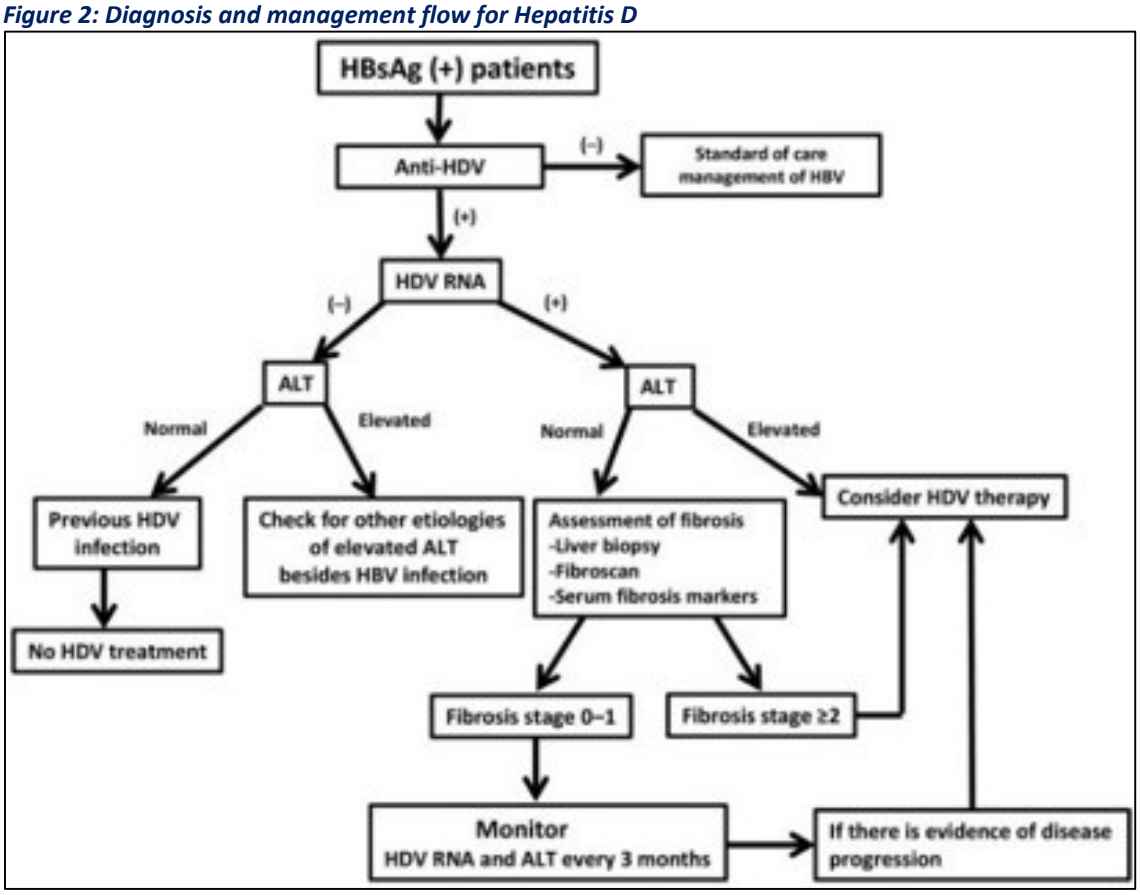
[5] Yurdaydın C, Idilman R, Bozkaya H, Bozdayi AM. Natural history and treatment of chronic delta hepatitis. J Viral Hepat. 2010 Nov;17(11):749-56. doi: 10.1111/j.1365-2893.2010.01353.x. Epub 2010 Aug 15. PMID: 20723036.
[6] Cornberg M, et al. J Hepatol. 2020 Mar;72:539-57. doi: 10.1016/j.jhep.2019.11.003. Epub 2019 Nov 12.
[7] Romeo, R., et al., A 28-year study of the course of hepatitis delta infection: a risk factor for cirrhosis and hepatocellular carcinoma. Gastroenterology, 2009. 136(5): p. 1629-38.
[8] NNDSS fortnightly summary notes: https://www1.health.gov.au/internet/main/publishing.nsf/Content/cdnareport-fn26-20.htm

24. Specify the characteristics of patients with (or suspected of having) the medical condition, who would be eligible for the proposed medical service/technology (including details on how a patient would be investigated, managed and referred within the Australian health care system, in the lead up to being eligible for the service):

Proactive diagnosis and management of hepatitis D in people with hepatitis B is essential to mitigate or delay the elevated risk of cirrhosis, end-stage liver disease (ESLD), and hepatocellular carcinoma (HCC). Australian guidelines recommend that people with hepatitis D be referred to specialist care, due to the increased risk of poor outcomes and need for specialised treatment decisions compared to hepatitis B alone.

Per the Gastroenterological Society of Australia (GESA) 2009–10 chronic hepatitis B (CHB) guidelines, the principal goal of chronic hepatitis D (CHD) treatment is to prevent or delay development of the complications of cirrhosis and HCC by achieving undetectable HDV RNA per PCR, and normalisation of alanine aminotransferase (ALT; elevated ALT levels indicate liver injury).

Figure 2: Diagnosis and management flow for Hepatitis D



Source: Best international practice flow chart for diagnosis and treatment of hepatitis D. Sourced from Shah et al. 2019. ALT, alanine aminotransferase; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; HDV, hepatitis delta virus; RNA, ribonucleic acid.

How/who tests for HDV (RNA) in Australia

VIDRL (Victorian Infectious Disease Reference Laboratory) is the leading Australian infectious diseases reference laboratory located in Melbourne, Victoria for HDV RNA PCR testing, and we believe the only laboratory to offer HDV RNA PCR testing.

REDACTED

HDV RNA is not a commercially available assay and is currently not reimbursed in Australia.

PART 6b – INFORMATION ABOUT THE INTERVENTION

25. Describe the key components and clinical steps involved in delivering the proposed medical service/technology:

CURRENT VIDRL TEST
Turn around time is 2 weeks

The specimen required:	Serum (clotted blood), Blook (ACD or EDTA)
Specimen type minimum:	500mcL
Testing frequency:	VIDRL performs the test weekly
Reference ranges:	375-10,000,000 IU/mL
Lower cut-off:	375 IU/mL
Units of measure:	IU/mL

REDACTED

26. Does the proposed medical service include a registered trademark component with characteristics that distinguishes it from other similar health components?

None

27. If the proposed medical service has a prosthesis or device component to it, does it involve a new approach towards managing a particular sub-group of the population with the specific medical condition?

Not applicable

28. If applicable, are there any limitations on the provision of the proposed medical service delivered to the patient (i.e. accessibility, dosage, quantity, duration or frequency)?

In Australia, only VIDRL is currently providing the proposed medical service, thus all samples collected nationally will need to be forwarded to VIDRL, Victoria for processing.

29. If applicable, identify any healthcare resources or other medical services that would need to be delivered <u>at the same time</u> as the proposed medical service:

None

30. If applicable, advise which health professionals will primarily deliver the proposed service:

Pathologists, in particular VIRDL

31. If applicable, advise whether the proposed medical service could be delegated or referred to another professional for delivery:

Not applicable and the proposed medical service could not be delegated or referred to another professional for delivery.

32. If applicable, specify any proposed limitations on who might deliver the proposed medical service, or who might provide a referral for it:

In Australia, only VIRDL is currently providing the proposed medical service, thus all samples collected nationally will need to be forwarded to VIDRL, Victoria for processing.

33. If applicable, advise what type of training or qualifications would be required to perform the proposed service, as well as any accreditation requirements to support service delivery:

VIDRL perform annual quality assurance checks and have NATA accreditation.

34. (a) Indicate the proposed setting(s) in which the proposed medical service will be delivered (select <u>ALL</u> relevant settings):

- ☐ Inpatient private hospital (admitted patient)
- ☐ Inpatient public hospital (admitted patient)
- ☐ Private outpatient clinic
- ☐ Public outpatient clinic
- ☐ Emergency Department
- ☐ Private consulting rooms - GP

☐ Private consulting rooms – specialist
☐ Private consulting rooms – other health practitioner (nurse or allied health)
☐ Private day surgery clinic (admitted patient)
☐ Private day surgery clinic (non-admitted patient)
☐ Public day surgery clinic (admitted patient)
☐ Public day surgery clinic (non-admitted patient)
☐ Residential aged care facility
☐ Patient's home
☒ Laboratory

(b) Where the proposed medical service is provided in more than one setting, please describe the rationale related to each:

Not applicable

35. Is the proposed medical service intended to be entirely rendered in Australia?

☒ Yes
☐ No

PART 6c – INFORMATION ABOUT THE COMPARATOR(S)

36. Nominate the appropriate comparator(s) for the proposed medical service (i.e. how is the proposed population currently managed in the absence of the proposed medical service being available in the Australian health care system). This includes identifying health care resources that are needed to be delivered at the same time as the comparator service):

Test: No HDV RNA testing, i.e., no Medicare Benefits Schedule (MBS) item **REDACTED**
Drug: There is currently no pharmacological standard of care for patients with HDV.

37. Does the medical service (that has been nominated as the comparator) have an existing MBS item number(s)?

☐ Yes (please list all relevant MBS item numbers below)
☒ No

38. (a) Will the proposed medical service/technology be used in addition to, or instead of, the nominated comparator(s)?

☒ In addition to (i.e. it is an add-on service)
☐ Instead of (i.e. it is a replacement or alternative)

(b) If yes, please outline the extent to which the current service/comparator is expected to be substituted

Not applicable

PART 6c CONTINUED – INFORMATION ABOUT ALGORITHMS (CLINICAL MANAGEMENT PATHWAYS)s

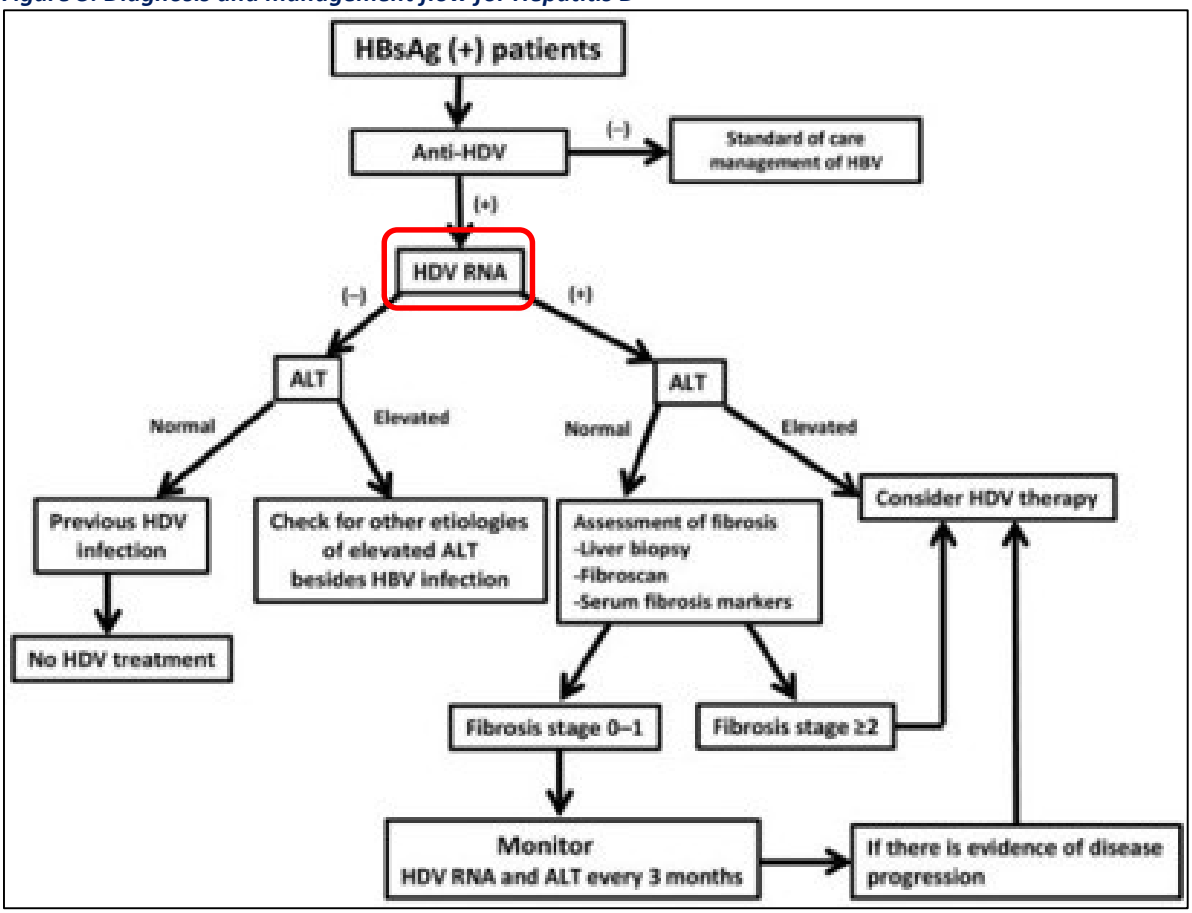
39. Define and summarise the CURRENT clinical management pathway (algorithm) that patients follow when they receive the COMPARATOR service (i.e. the landscape before the proposed service is introduced). An easy-to-follow flowchart is preferred, depicting the current clinical management pathway), but dot-points would be acceptable. Please include health care resources used in the current landscape (e.g. pharmaceuticals, diagnostics and investigative services, etc.).

Current Hepatitis Delta Clinical Management

Proactive diagnosis and management of hepatitis D in people with hepatitis B is essential to mitigate or delay the elevated risk of cirrhosis, end-stage liver disease (ESLD), and hepatocellular carcinoma (HCC). Australian guidelines recommend that people with hepatitis D be referred to specialist care, due to the increased risk of poor outcomes and need for specialised treatment decisions compared to hepatitis B alone.

Per the Gastroenterological Society of Australia (GESA) 2009–10 chronic hepatitis B (CHB) guidelines, the principal goal of chronic hepatitis D (CHD) treatment is to prevent or delay development of the complications of cirrhosis and HCC by achieving undetectable HDV RNA per PCR, and normalisation of ALT.

Figure 3: Diagnosis and management flow for Hepatitis D



Source: Best international practice flow chart for diagnosis and treatment of hepatitis D. Sourced from Shah et al. 2019 [86]. ALT, alanine aminotransferase; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; HDV, hepatitis delta virus; RNA, ribonucleic acid.

40. Define and summarise the PROPOSED clinical management pathway (algorithm) that patients would follow <u>after</u> the proposed service/technology is introduced, including variation in health care resources.

The proposed clinical management pathway (algorithm) would follow the same pathway. The difference is that the HDV RNA test (see red box, Figure 2) would be reimbursed through the MBS, rather than not reimbursed and at a "private" cost to patients.

PART 6d – INFORMATION ABOUT CLINICAL OUTCOMES

41. Summarise the clinical claims for the proposed medical service against the appropriate comparator(s), in terms of consequences for health outcomes (comparative benefits and harms):

42. Please state what the overall clinical claim is:

HDV RNA testing to inform use of bulevirtide and that the use of bulevirtide is superior to no pharmacological treatment

43. List the key health outcomes (major and minor – prioritising major key health outcomes first) that will need to be measured in assessing the clinical claim for the proposed medical service/technology (versus the comparator):

Clinical Effectiveness Outcomes:
Biochemical and virologic response

Safety Outcomes:
Incidence of adverse events
Adverse events in non-cirrhotic and cirrhotic patients with compensated liver disease
Impact on patients of false positive and false negative test resultss

Test related
Diagnostic accuracy
Prognostic accuracy
Change in clinical management
Test turn-around time

PART 7 – INFORMATION ABOUT ESTIMATED UTILISATION

44. Estimate the prevalence and/or incidence of the condition in the proposed population:

As previously noted, hepatitis D is a notifiable disease in Australia and must be notified by medical practitioners and pathology services in writing within 5 days of diagnosis. The primary source of hepatitis D epidemiological data is the National Notifiable Disease Surveillance System (NNDSS).

Based on annually reported data from the NNDSS, the diagnosed incidence of hepatitis D is very low, with 69 cases notified nationwide in 2020 (Figure 1). The incidence of hepatitis D is estimated at 0.3 per 100,000 population and has remained relatively stable over the past decade, ranging from 0.1–0.3 cases per 100,000 population from 2010–2020 (Figure 1).

On average, 70 cases of HDV are reported each year to the department of health. Yearly notifications are stable (rolling 5-year average between 2015 and 2020 is 66.8). It should be noted that the majority of HDV cases are born overseas. For example, in a Victorian study, 64% of those diagnosed between 2010-2016 were born overseas, most commonly in Sudan, Pakistan and Vietnam (Jackson et al 2018[9]).

The 11-year prevalent diagnosed HDV cases in Australia is 658 (2010-2021)[10].

However, with the availability of HDV RNA test reimbursed on the MBS and the availability of a therapy to treat HDV on the PBS, the number of notifiable HDV cases will mostly increase and patients may be diagnosed earlier and with appropriate management may result in a reduction in longer-term sequalae of disease.

45. Estimate the number of times the proposed medical service/technology would be delivered to a patient per year:

REDACTED

46. How many years would the proposed medical service/technology be required for the patient?

REDACTED

47. Estimate the projected number of patients who will utilise the proposed medical service(s) for the first full year:

As noted, on average 70 cases of HDV are reported each year to the department of health and yearly notifications are stable (rolling 5-year average between 2015 and 2020 is 66.8). The 11-year prevalent diagnosed HDV cases in Australia is 658 (2010-2021). It is likely that diagnosis of disease is delayed due to the lack of a publicly funded diagnostic test and the availability of the test at a cost to patients at only 1 or 2 sites. With the availability of HDV RNA test reimbursed on the MBS and the availability of a new therapy on the PBS, the number of notifiable HDV cases will mostly increase as diagnostic testing becomes more common.

In the first full year, our initial estimation is that potentially up to a maximum of 658 patients will be tested with a diagnostic HDV RNA test.

REDACTED

48. Estimate the anticipated uptake of the proposed medical service/technology over the next three years, factoring in any constraints in the health system in meeting the needs of the proposed population (such as supply and demand factors), as well as provide commentary on risk of 'leakage' to populations not targeted by the service.

REDACTED

[9] Jackson, K., et al., (2018), Epidemiology and phylogenetic analysis of hepatitis D virus infection in Australia. Intern Med J, 48: 1308-1317. https://doi.org/10.1111/imj.13967

[10] NNDSS, Australia's notifiable disease status: annual report of the National Notifiable Diseases Surveillance System. Commun Dis Intell Q Rep, 2010, 2011, 2012, 2013, 2014, 2015, 2016, 2017, 2018, 2019, 2020, 2021.

PART 8 – COST INFORMATION

49. Indicate the likely cost of providing the proposed medical service. Where possible, please provide overall cost and breakdown:

The indicative cost for the test is approximately $100

50. Specify how long the proposed medical service/technology typically takes to perform:

CURRENT VIDRL TEST
Turnaround time is 2 weeks

The specimen required:	Serum (clotted blood), Blood (ACD or EDTA)
Specimen type minimum:	500mcL
Testing frequency:	VIDRL performs the test weekly
Reference ranges:	375-10,000,000 IU/mL
Lower cut-off:	375 IU/mL
Units of measure:	IU/mL

REDACTED

51. If public funding is sought through the MBS, please draft a proposed MBS item descriptor to define the population and usage characteristics that defines eligibility for the medical service/technology.

MBS item description for HDV Diagnosis

Category PATHOLOGY SERVICES – P3 - Microbiology
Proposed item descriptor: Quantitation of Hepatitis D viral RNA in patients who are Hepatitis D surface antigen positive - 1 test Fee: $100

MBS item description for continuation of therapy with bulevirtide for HDV treatment

Category PATHOLOGY SERVICES – P3 - Microbiology
Proposed item descriptor: Quantitation of Hepatitis D viral RNA in patients who are Hepatitis D surface antigen positive and who have chronic hepatitis D and are receiving bulevirtude therapy. To a maximum of 2 of this item in a 12 month period. Fee: $100

52. If public funding is sought through an alternative (non-MBS) funding arrangement, please draft a service description to define the population and usage characteristics that defines eligibility for the service/technology.

Not applicable.