# MSAC Application 1827

## Testing for hepatitis B virus (HBV) and hepatitis B virus surface antigen (HBsAg) to support the use of PBS subsidised bepirovisen in people with chronic hepatitis B (CHB)

## PICO Set

# Context

This application seeks preliminary clarification from the Medical Services Advisory Committee (MSAC) regarding the suitability and proposed amendment of a number of existing Medical Benefits Schedule (MBS) pathology services items to align with the evolving treatment landscape for chronic hepatitis B (CHB) infection with the availability of multiple novel curative pharmacological treatment options, including bepirovirsen, over the next few years. In particular, the application seeks to clarify:

- Whether current MBS Items 69482 and/or 69483 are adequately specified to permit ongoing quantitative assessment of hepatitis B virus deoxyribonucleic acid (HBV DNA) in patients with a previous diagnosis of CHB who have subsequently been functionally cured of the condition[1]

Should these current MBS Items ultimately be deemed insufficient for or inapplicable to the emerging treatment context of CHB, subsequent advice along with the appropriate HTA pathway is sought regarding relevant additions or amendments to the schedule to accommodate this imminent change to current clinical practice of CHB diagnosis and treatment monitoring.

For the purposes of the application, the proposed intervention has been specified as a the laboratory testing algorithm required to identify a subset of CHB patients who would be eligible to receive a prospectively curative regimen of bepirovirsen (fixed duration of 24 weeks), evaluate response to treatment, assess functional cure status and suitability for discontinuation of standard antiviral therapy, and then monitor maintenance of these outcomes over long-term follow-up.

A subsequent submission to the Pharmaceutical Benefits Advisory Committee (PBAC) seeking reimbursement is planned for the bepirovirsen regimen itself. The applicant does not believe an integrated co-dependent technology application is either appropriate or required in this scenario, as the tests themselves are well established and already funded through the MBS, no new technology is being introduced, and any changes to the schedule would be limited. Changes in utilisation are also likely marginal and probably overall cost saving due to reduced downstream MBS testings, which can be adequately captured within cost-effectiveness and financial implications modelling in the planned PBAC submission.

# Population

**Describe the population in which the proposed health technology is intended to be used:**

There are two proposed target populations for testings:

1. Target population patients for treatment initiation and response monitoring
2. Target population for ongoing monitoring (post-treatment) for functionally cured patients

**Population 1** – CHB patients for treatment initiation and response monitoring

The initial target population for the proposed intervention is patients with CHB receiving stable therapy with a nucleos(t)ide analogue (NA) who are being assessed for eligibility to receive a prospectively curative treatment regimen of bepirovirsen. However, this narrows over the time to patients who are deemed eligible for and receive treatment with bepirovirsen. Those receiving the finite treatment course require monitoring for response as part of the proposed intervention.

[1] Functional cure defined as sustained HBsAg loss and HBV DNA less than the lower limit of quantitation (LLOQ) following 24 weeks off-treatment (Ghanny et al, 2023).

Current MBS items for qualitative and/or quantitative assessment of hepatitis B surface antigen (HBsAg) testing (MBS item 69481) and HBV DNA testing (69483) adequately support the proposed intervention relating to Population 1.

**Population 2** – CHB patients (subset of Population 1) achieving functional cure requiring ongoing monitoring

The target population is those CHB patients who achieve a functionally curative outcome as a result of treatment with bepirovirsen (or any another agent) and have ceased NA therapy[2].

Population 2 is where clarification is being sought in this application with respect to the adequacy of current MBS items for the HBV DNA testing component of the intervention.

**Specify any characteristics of patients with, or suspected of having, the medical condition, who are proposed to be eligible for the proposed health technology, describing how a patient would be investigated, managed and referred within the Australian healthcare system in the lead up to being considered eligible for the technology:**

Diagnosis of CHB is complex, requiring multiple and sometimes repeated laboratory assessments, that are usually carried out in a mixed general practice and specialist treatment setting. Definitive diagnosis of a current hepatitis B virus (HBV) infection can be based on a confirmed positive qualitative enzyme immunoassay result for hepatitis B surface antigen (HBsAG). This is usually accompanied by further confirmatory chemiluminescent immunoassay outcomes for anti-HB core and surface antibodies: anti-HBc and anti-HBs. Differentiation between acute and chronic HBV infections technically requires positive HBsAG results ≥6 months apart but can in practice usually be established immediately with reference to detailed patient history and careful interpretation of further immunoglobulin (IgM) assay outcomes for anti-HBc (Towell & Cowie 2012); (GESA 2022).

Once a definitive diagnosis of CHB has been established, clinical management continues within a mixed general practice and specialist (hepatology, gastroenterology, infectious diseases) setting. Recommended regular laboratory assessments conducted in this setting include HBV viral load, which is measured using a quantitative real time polymerase chain reaction (PCR) DNA assay, qualitative hepatitis B e-antigen (HBeAg) status, qualitative/quantitative HBsAG status/levels, standard liver function tests (ALT/AST), full blood examination (FBE), hepatocellular carcinoma (HCC) surveillance, and periodic (non-invasive) assessment of fibrosis/cirrhosis (GESA 2022).

Antiviral treatment is recommended for a subset of patients with CHB, especially but not exclusively for those with evidence of cirrhosis. The main contemporary pharmacological management options are NAs, including entecavir and tenofovir disoproxil or alafenamide (preferred) as well as lamivudine, adefovir and telbivudine (alternative). Pegylated interferon is another option in some cases but has been largely superseded as a frontline treatment in most developed country settings and is no longer reliably available in Australia. Treatment is typically initiated by a specialist and maintained throughout life, in a mixed care model (GESA 2022).

As discussed further below, all elements of the current diagnostic, monitoring and management algorithms for CHB are understood to be adequately (if imperfectly) covered by existing Medical Benefits Scheme (MBS) and Pharmaceutical Benefits Scheme (PBS) subsidy arrangements. However, the definition of optimal CHB management is rapidly evolving, with recently published international guidelines recommending more regular and intensive laboratory monitoring, and

[2] Rates of functional cure with bepirovirsen treatment are subject to pending B-Well 1/2 trial results (NCT05630807/ NCT05630820)

earlier initiation of antiviral therapy, than either previous iterations or the most recent Australian consensus statement (AASLD/IDSA 2025); (EASL 2025); (GESA 2022). Furthermore, multiple new typically curative CHB therapies are in advanced clinical development and/or progressing through registration activities globally, which will almost certainly require a much more nuanced approach to patient selection, monitoring and management, than currently available alternatives.

In the specific scenario considered in this application, the lead indication for bepirovirsen is likely to require that patients have a confirmed diagnosis of CHB, are receiving stable NA therapy, and have a recent quantitative HBsAg test result ≤3,000 IU/mL. They would also typically and ideally be under the care of an appropriate specialist, have a recent quantitative HBV DNA viral load test result <90 IU/mL and alanine aminotransferase (ALT) ≤2 x ULN.

**Provide a rationale for the specifics of the eligible population:**

The rationale for this target population is based on the eligibility criteria for the pivotal phase III trials of bepirovirsen (B-Well 1&2) which were themselves informed by previous phase I/II studies.

**Are there any prerequisite tests?**

Yes. Prerequisite tests for the proposed population include those required to establish a definitive diagnosis of CHB: always qualitative HBsAg and usually anti-HBc and anti-HBs.

**Are the prerequisite tests MBS funded?**

Yes. HBsAg testing is clearly covered and frequently claimed under current MBS Items 69475, 69478, 69481 and 69484. HBV DNA (quantitative) testing is covered under 69482 and 69483.

# Intervention

**Name of the proposed health technology:**

The proposed health technology is a new CHB testing algorithm comprised of established laboratory tests for HBsAG (quantitative and qualitative) and HBV DNA, that supports a prospectively curative course of treatment with bepirovirsen (and ideally other likely future therapeutic options).

**Describe the key components and clinical steps involved in delivering the proposed health technology:**

The key components of the health technology are summarised in table 1.. Briefly:

- All patients in the initial target population would strictly require one baseline assessment of quantitative HBsAg (qHBsAg) and most would concurrently have one quantitative assessment of HBV DNA viral load, to establish eligibility for treatment with bepirovirsen;
- Those patients who proceed to treatment with bepirovirsen would require up to 4 tests for qHBsAg and HBV DNA over a structured 72-week treatment and assessment period;
- Those patients who are assessed to have achieved a functional cure[3] at the end of that period would further require tapered monitoring regimen for qHBsAG and HBV DNA over time;
- Patients who do not achieve a functional cure outcome would return to a standard of care (SOC) testing algorithm, as discussed further below.

[3] Functional cure defined as sustained HBsAg loss and HBV DNA less than the lower limit of quantitation (LLOQ) following 24 weeks off-treatment (Ghanny et al, 2023).

*Table 1: Summary of components of the intervention*

| Period | All patients | | Treated patients | | Functionally Cured patients | |
|---|---|---|---|---|---|---|
| Tests | qHBsAG | HBV DNA | qHBsAG | HBV DNA | qHBsAG | HBV DNA |
| Baseline | 1 | 1 | | | | |
| Weeks 0-72 | | | 4 | 4 | | |
| Year 1 FC | | | | | 2 | 4 |
| Year 2+ FC | | | | | 1 | 1-2 |
| Year X NFC | | | | | SOC | SOC |

Abbreviations: FC = functional cure; NFC = no functional cure; NR = Not relevant; SOC = standard of care; W = week;

**Identify how the proposed technology achieves the intended patient outcomes:**

The intended outcomes of the proposed testing algorithm are to:

- Identify patients who are suitable for prospectively curative treatment with bepirovirsen; and,
- Monitor those patients both during and after their course of treatment with bepirovirsen to: evaluate response; assess functional cure status; guide decision making regarding possible discontinuation of NA therapy and monitor these outcomes over long-term follow up.

In so doing, the updated testing algorithm would unlock the very significant patient outcomes associated with curative treatment options for CHB, which until now has been managed mainly through chronic/continuous NA therapy, aimed at sustained viral suppression.

**Does the proposed health technology include a registered trademark component with characteristics that distinguishes it from other similar health components?**

Yes. However, there are multiple brands of each the relevant tests listed on the Australian Register of Therapeutic Goods (ARTG), with these being considered broadly equivalent and interchangeable, by both the Therapeutic Goods Administration (TGA) and current MBS Items.

**Explain whether it is essential to have this trademark component or whether there would be other components that would be suitable:**

In the presence of a number of ARTG listed examples of the relevant laboratory tests, it is unlikely that any alternative bespoke assays would be considered suitable for use in this setting.

**Are there any proposed limitations on the provision of the proposed health technology delivered to the patient (For example: accessibility, dosage, quantity, duration or frequency):**

There are no major limitations on provision of these tests, however the applicant understands they are mainly conducted in larger laboratories based in the eastern states (VIC, NSW, QLD).

**If applicable, advise which health professionals will be needed to provide the proposed health technology:**

The main health professionals involved in providing the proposed health technology would be nurses and laboratory technicians.

**If applicable, advise whether delivery of the proposed health technology can be delegated to another health professional:**

No.

**If applicable, advise if there are any limitations on which health professionals might provide a referral for the proposed health technology:**

Referral for these tests, in the proposed clinical setting, would primarily be the preserve of relevant specialists, mainly gastroenterologists, hepatologists, infectious diseases physicians, as

well as some PBS Section 100 Highly Specialised Drugs (HSD) Community Access prescribers. However, it is not proposed that any limits should be placed on referral pathways.

**Is there specific training or qualifications required to provide or deliver the proposed service, and/or any accreditation requirements to support delivery of the health technology?**

No.

**Indicate the proposed setting(s) in which the proposed health technology will be delivered:**

- ☐ Consulting rooms
- ☐ Day surgery centre
- ☐ Emergency Department
- ☐ Inpatient private hospital
- ☐ Inpatient public hospital
- ☒ Laboratory
- ☒ Outpatient clinic
- ☐ Patient's home
- ☐ Point of care testing
- ☐ Residential aged care facility
- ☐ Other (please specify)

**Is the proposed health technology intended to be entirely rendered inside Australia?**
Yes.

# Comparator

**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 healthcare system). This includes identifying healthcare resources that are needed to be delivered at the same time as the comparator service:**
The nominated comparator is the SOC laboratory testing algorithm for CHB patients receiving stable NA therapy, typically comprised of entecavir or tenofovir disoproxil and/or lamivudine. However, it is noted that this SOC laboratory testing algorithm is in a state of evolution, based on recent changes in international treatment guidelines (EASL 2025); (AASLD/IDSA 2025). A summary of the key components of the SOC algorithm, based respectively on current MBS criteria and recent European guidelines (EASL 2025) is provided in Table 2.

***Table 2: Summary of components of the comparator***

| Period | Current (GESA) | | Evolving (EASL 2025) | |
|---|---|---|---|---|
| Tests | qHBsAG | HBV DNA | qHBsAG | HBV DNA |
| Annual | 0 | 4 | 1 | 2 |

**List any existing MBS item numbers that are relevant for the nominated comparators:**
HBsAg testing is clearly covered and frequently claimed under current MBS Items 69475, 69478, 69481 and 69484.

HBV DNA (quantitative) testing is covered under 69482 and 69483.

**Provide a rationale for why this is a comparator:**

This is the clearly established but gradually evolving standard of care for patients receiving stable NA therapy for CHB in Australia.

**Pattern of substitution – Will the proposed health technology wholly replace the proposed comparator, partially replace the proposed comparator, displace the proposed comparator or be used in combination with the proposed comparator?**

☐ None (used with the comparator)
☐ Displaced (comparator used following the proposed technology in some patients)
☒ Partial (proposed technology will replace the comparator in some patients)
☐ Full (subjects who receive the proposed intervention will not receive the comparator)

**Outline and explain the extent to which the current comparator is expected to be substituted:**

The intervention and comparator comprise the same laboratory tests (qHBsAG and HBV DNA) and it is only the frequency with which these would be used over time that differs. A summary of expected patterns of utilisation of the respective tests, within the proposed bepirovirsen testing algorithm and current/emerging SOC, across the time horizon of interest is provided in table 3. Overall utilisation of the respective tests between the proposed algorithm and independently emerging SOC is expected to be similar, while both of these are expected to result in significant substitution of the HBV DNA test with the less costly qHBsAg test, thus generating potential cost savings.

*Table 3: Expected pattern of utilisation for an average eligible patient*

| Time | Comparator | | | | Intervention | |
|---|---|---|---|---|---|---|
| | Current (GESA) | | Emerging (EASL) | | Proposed | |
| Tests | qHBsAg | HBV DNA | qHBsAg | HBV DNA | qHBsAg | HBV DNA |
| Baseline eligibility assessment (all patients) | | | | | | |
| W0 | 0 | 1 | 1 | 1 | 1 | 1 |
| Treatment and assessment period (treated patients) | | | | | | |
| W1-23 | 0 | 1 | 0 | 0 | 0 | 0 |
| W24 | 0 | 1 | 0 | 1 | 1 | 1 |
| W25-47 | 0 | 1 | 0 | 0 | 0 | 0 |
| W48 | 0 | 1 | 1 | 1 | 1 | 1 |
| W49-71 | 0 | 1 | 0 | 0 | 0 | 0 |
| W72 | 0 | 1 | 0 | 1 | 1 | 1 |
| Total | 0 | 7 | 2 | 4 | 4 | 4 |
| Long term follow up | | | | | | |
| Functionally cured patients | | | | | | |
| Y1 FC | NR | | NR | | 2 | 4 |
| Y2+ FC | | | | | 1 | 1-2 (≈1.5) |
| Non-functionally cured patients | | | | | | |
| YX NFC | 0 | 4 | 1 | 2 | 1 | 2 |
| Mixed utilisation: Over 5 years assuming an arbitrary 30% functional cure rate | | | | | | |
| 5Y (@30% FC) | 0 | 20 | 5 | 20 | 5.3 | 10 |
| Combined periods | | | | | | |
| Grand total | 0.0 | 27.0 | 7.0 | 14.0 | 9.3 | 14 |

Abbreviations: EASL = European Association for the Study of the Liver, FC = functional cure; NFC = no functional cure; NR = Not relevant; W = week; Y= year

# Outcomes

**List the key health outcomes that will need to be measured in assessing the clinical claim for the proposed medical service/technology (versus the comparator):**

The key outcome for the proposed testing algorithm is facilitation of treatment with bepirovirsen, and ideally other curative treatment options for CHB. Those therapies will in turn be measured by their ability to deliver a sustained functional cure for CHB, with acceptable safety and tolerability.

**Outcome description – include information about whether a change in patient management, or prognosis, occurs as a result of the test information:**

The new testing algorithm is being proposed for the explicit purpose of changing patient management: selecting patients who are eligible for treatment with bepirovirsen; assessing response and cure outcomes among bepirovirsen treated patients to determine their suitability for cessation of background NA therapy; and monitoring functionally cured patients over time to ensure that any instances of relapse can be quickly and appropriately managed.

# Proposed MBS items

**How is the technology/service funded at present? (e.g., research funding; State-based funding; self-funded by patients; no funding or payments):**

The relevant laboratory tests are all currently funded by the MBS under items 69475, 69478, 69481 and 69484 for HBsAg testing, and under 69482 and 69483 for HBV DNA testing. However, it is not clear that the current descriptors for these items will be appropriate and/or sufficient to accommodate the revised testing algorithm required for use alongside curative treatment regimens such as bepirovirsen.

**Provide at least one proposed item with their descriptor and associated costs, for each Population/Intervention:**

While details are still being finalised, the initially proposed TGA indication and PBS restriction for bepirovirsen will likely be for finite treatment of CHB (24 weeks) in patients already on stable NA therapy, with HBsAg levels ≤ 3,000 IU/mL.

Based on pre-submission consultation with the Department of Health and Ageing (DOHA), the applicant understands that assessment of qHBsAg for the purposes of determining eligibility for bepirovirsen, and monitoring outcomes both during and beyond treatment, will likely fall within the scope of current MBS Item 69481, in which case no changes to that item or descriptor are expected to be required in order to support the proposed intervention. The applicant further understands that the recommended assessments of HBV DNA prior to and during treatment with bepirovirsen will fall within the scope of the current MBS Item 69483.

However, DOHA has advised that the descriptors for MBS Items 69482 and 69483 are not likely to permit regular ongoing HBV DNA assessment in functionally cured (HBsAg negative) patients no longer receiving antiviral therapy after successful treatment with bepirovirsen, at the proposed (or any other) frequency. Indeed, these descriptors currently do not technically support the recommended SOC testing schedule for (rare) instances of functionally curative treatment outcomes with NA's and/or pegylated interferon.

As such, two indicative new item descriptors are provided in Table 4, which would facilitate the recommended monitoring HBV DNA schedule for bepirovirsen, and likely most other curative treatment regimens for CHB

***Table 4: Indicative new item descriptors for HBV DNA testing following discontinuation of antiviral therapy***

| | |
|---|---|
| MBS item numbers | TBC |
| Category number | 6 |
| Category description | Pathology services |
| Proposed item descriptors | Quantitation of Hepatitis B viral DNA in patients who have discontinued antiviral therapy for chronic hepatitis B within the previous 12 months - 1 test<br>Rule 25: Not more than 4 times in a 12-month period |
| | Quantitation of Hepatitis B viral DNA in patients who have discontinued antiviral therapy for chronic hepatitis B more than 12 months previously - 1 test<br>Rule 25: Not more than 2 times in a 12-month period |
| Proposed MBS fee | $152.10 |

# Algorithms

**PREPARATION FOR USING THE HEALTH TECHNOLOGY**

**Define and summarise the clinical management algorithm, including any required tests or healthcare resources, before patients would be eligible for the proposed health technology:**

Prior to being assessed for eligibility for bepirovirsen, all patients must have received a confirmed diagnosis of CHB infection, based on laboratory assessment of HBsAg, anti-HBc and anti-HBc as previously described, as well as a stable regimen of antiviral (NA) therapy (≥6 months). Most patients will also have received a number of assessments of related laboratory parameters, such as HBV DNA, HBeAg, ALT/AST, FBE, HCC and cirrhosis/fibrosis during this treatment journey.

**Is there any expectation that the clinical management algorithm before the health technology is used will change due to the introduction of the proposed health technology?**

No.

**Describe and explain any differences in the clinical management algorithm prior to the use of the proposed health technology vs. the comparator health technology:**

Not applicable

**USE OF THE HEALTH TECHNOLOGY**

**Explain what other healthcare resources are used in conjunction with delivering the proposed health technology:**

As previously described, the proposed health technology is a revised laboratory testing algorithm which is specifically intended to be used in conjunction with a fixed duration (24 week) regimen of bepirovirsen, that is expected to result in a functionally curative outcome for some CHB patients, thus enabling them to discontinue chronic background NA therapy.

**Explain what other healthcare resources are used in conjunction with the comparator health technology:**

As previously described, the comparator health technology is the current SOC testing algorithm associated with chronic continuous NA therapy for CHB.

**Describe and explain any differences in the healthcare resources used in conjunction with the proposed health technology vs. the comparator health technology:**

The pharmacological treatment regimen used in conjunction with the proposed health technology is an intensive, but potentially curative one, whereas that used in conjunction with the comparator algorithm is chronic and continuous in nature, aimed at achieving sustained viral suppression rather than functionally curative outcomes.

**CLINICAL MANAGEMENT AFTER THE USE OF HEALTH TECHNOLOGY**

**Define and summarise the clinical management algorithm, including any required tests or healthcare resources, after the use of the proposed health technology:**

The revised testing algorithm includes different long-term follow-up schedules for functionally cured and uncured patients, that would ideally be adhered to throughout life. For functionally cured patients, the DNA (HBV DNA) and protein (HBsAg) of the hepatitis B virus will be reduced to undetectable levels and may help your immune system keep the virus under control. Therefore, bepirovirsen may remove the need for lifelong hepatitis B medicine. For patients who do not achieve a functionally curative outcome, use of other healthcare resources is expected to be

consistent with the comparator SOC algorithm, including in most instances chronic/continuous NA therapy.

**Define and summarise the clinical management algorithm, including any required tests or healthcare resources, after the use of the comparator health technology:**

The comparator testing algorithm comprises a stable continuous schedule of assessments that would ideally be adhered to throughout life and as such there is no relevant "after" period.

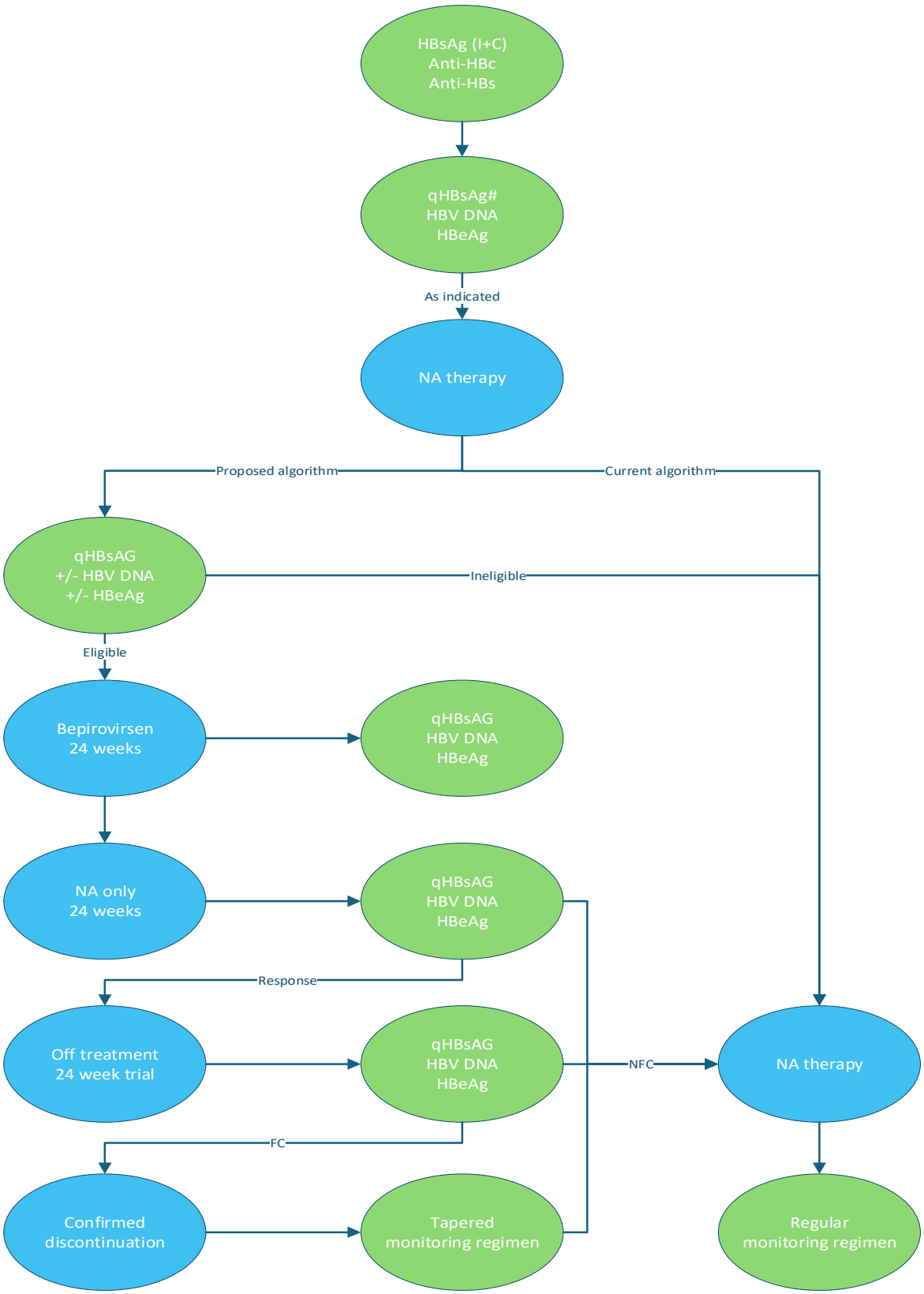
**Describe and explain any differences in the healthcare resources used after the proposed health technology vs. the comparator health technology:**

The purpose of the proposed testing algorithm is to facilitate functionally curative pharmacological treatment strategies that will enable patients to discontinue otherwise chronic background NA therapy. The purpose of the comparator testing algorithm by contrast is merely to support those chronic NA treatment regimens. The key difference in downstream healthcare resource use between the strategies is thus the cessation of NA therapy in a (much higher) proportion of patients who achieve functionally curative outcomes.

**Insert diagrams demonstrating the clinical management algorithm with and without the proposed health technology:**

A summary diagram capturing the differences in clinical management and likely healthcare resource use between the respective strategies is provided in **Figure 1**. For the purposes of this diagram, investigative procedures relevant to MSAC are depicted in green while pharmacological treatment approaches that will ultimately be considered by PBAC are highlighted in blue.

***Figure 1: Summary current/proposed clinical management algorithm***




Abbreviations: (I+C) = initial + confirmatory; FC = functional cure; NFC = no functional cure; (q)HBsAG = (quantitative) hepatitis B surface antigen test; HBeAg = hepatitis B e antigen test; HBV DNA = hepatitis B PCR DNA test; # = Emerging SOC (EASL 2025)
Tapered monitoring regimen – see

## Claims

**In terms of health outcomes (comparative benefits and harms), is the proposed technology claimed to be superior, non-inferior or inferior to the comparator(s)?**

☒ Superior
☐ Non-inferior
☐ Inferior

**Please state what the overall claim is, and provide a rationale:**

The overall claim is that the proposed testing algorithm for patients with CHB receiving stable NA therapy will be superior in terms of health outcomes than the comparator (current SOC testing) in that it will facilitate treatment with bepirovirsen, and ideally other functionally curative treatment options for CHB. Those therapies will in turn deliver superior clinical outcomes, specifically greatly increased rates of functional cure, for patients with CHB, with acceptable safety and tolerability.

**Why would the requestor seek to use the proposed investigative technology rather than the comparator(s)?**

The revised testing algorithm will facilitate patient selection and monitoring as required for prospectively curative treatment with bepirovirsen in a way that the current algorithm does not.

**Identify how the proposed technology achieves the intended patient outcomes:**

The revised testing algorithm facilitates a potentially curative pharmacological treatment regimen.

**For some people, compared with the comparator(s), does the test information result in:**

| | |
|---|---|
| A change in clinical management? | Yes |
| A change in health outcome? | Yes |
| Other benefits? | Yes |

**In terms of the immediate costs of the proposed technology (and immediate cost consequences, such as procedural costs, testing costs etc.), is the proposed technology claimed to be more costly, the same cost or less costly than the comparator?**

☐ More costly
☐ Same cost
☒ Less costly

**Provide a brief rationale for the claim:**

As previously described, the revised treatment algorithm includes greater use of qHBsAg testing and less use of HBV DNA testing than the current MBS standard of care and is thus likely to be moderately cost saving, due to differences in the fees associated with the respective tests. Some of this shift in emphasis will likely occur independently of the proposed algorithm due to the evolution of clinical guidelines and practice. However, there are no circumstances apparent to the applicant in which the revised testing algorithm could be more costly than current practice over an extended period of assessment (See

Table **3**– example over 5 years).

## Summary of Evidence

The applicant does not propose to prepare or present any summary of clinical evidence for the various investigative procedures considered herein. These are all established laboratory tests, with essentially known characteristics and performance, that have been listed on the ARTG and funded through the MBS for many years. Of particular note in this regard, the TGA has specifically advised the applicant that there are a number of registered quantitative hepatitis B tests and these would be suitable for use with bepirovirsen and that an application to register a particular test as a companion diagnostic for bepirovirsen is not required.

The clinical development program for bepirovirsen is extensive and ongoing. A comprehensive and up to date overview of this will be provided to PBAC for evaluation in due course. However, for the purposes of the current application, it is sufficient to note that the key evidence for the proposed intervention will come from two parallel phase III, randomised, placebo controlled trials, that assessed the efficacy and safety of the proposed bepirovirsen regimen, within the proposed target population of CHB patients on stable NA therapy with HBsAg levels ≤3,000 IU/mL (B-Well 1/2 trials - NCT05630807/ NCT05630820) and a longer term open label extension study that includes patients recruited from across the broader clinical development program (B-Sure trial - NCT04954859). None of these studies have yet been published and only preliminary headline results are currently available.

# References

EASL 2025: European Association for the Study of the Liver. EASL Clinical Practice Guidelines on the management of hepatitis B virus infection. J Hepatol. 2025 Aug;83(2):502-583.

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Towell V, Cowie B. Hepatitis B serology. Aust Fam Physician. 2012 Apr;41(4):212-4.

B-Well 1. https://clinicaltrials.gov/study/NCT05630807

B-Well 2. https://clinicaltrials.gov/study/NCT05630820

B-Sure. https://clinicaltrials.gov/study/NCT04954859