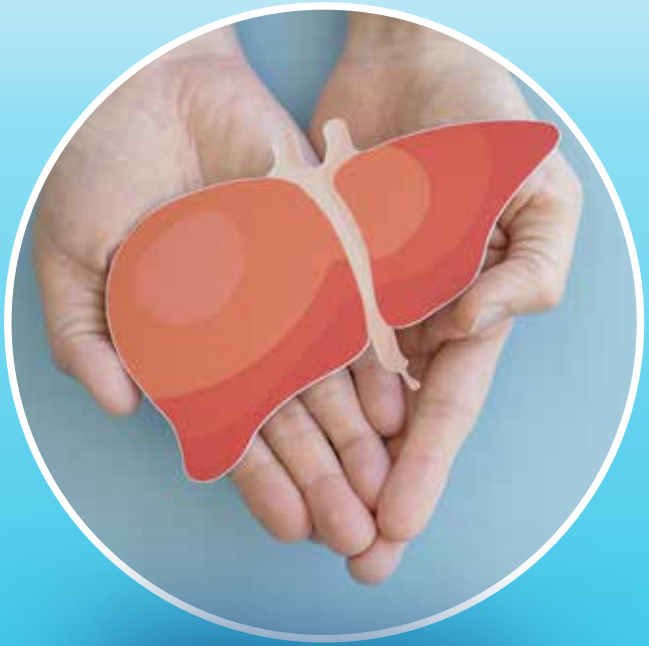
The Management of Hepatitis B

A Guide for Health Professionals



The Hepatitis Foundation of New Zealand

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The Hepatitis Foundation of New Zealand

The Hepatitis Foundation of New Zealand (HFNZ) is a charitable trust, contracted to Te Whatu Ora - Health New Zealand to provide a health monitoring programme that supports people living with hepatitis B (HBV).

Our Monitoring Programme

Our free, lifelong, national monitoring programme is for all people living with HBV in New Zealand an is proven to improve health outcomes. People registered with HFNZ receive regular HBV monitoring, assessment, education and support.

We work in partnership with General Practice, Secondary Care and other health providers to provide ongoing care of their patients living with HBV.

Delivery of our programme

Blood Tests: We provide six-monthly blood test monitoring for enrolled patients, in line with the gold standard of care for people living with hepatitis B.
Education: We deliver tailored hepatitis B education and health assessments directly to patients to support understanding and engagement in their care.
Engagement with Health Professionals: We work closely with GPs and other healthcare providers involved in our patients' care, offering hepatitis B education, clinical advice, and regular updates.
Clinical Oversight: We refer patients for further assessment or treatment in primary or secondary care when required, including copies of test results and clinical correspondence with providers.
Support: Our team of expert clinicians provides information and advice to both patients and healthcare professionals. We also offer home visits when necessary and free hepatitis B testing for eligible family members.

We operate a free nationwide helpline on 0800 33 20 10 and have email support at hepteam@hfnz.nz for all enquiries.

Hepatitis is one of the world's most common Infectious diseases

Over 250 million people worldwide live with chronic hepatitis B virus. Each year over one million people die of hepatitis B (HBV) related chronic hepatitis (CHB), cirrhosis or Hepatocellular Carcinoma (HCC) liver cancer.

In New Zealand approximately 94,000 people are estimated to be living with HBV, with 50% of these yet to be diagnosed. Hepatitis B is the predominant cause of hepatocellular carcinoma (HCC)—primary liver cancer—in New Zealand. An estimated 300 people die annually due to hepatitis B and C.

Regular six-monthly blood tests for individuals with chronic hepatitis B (CHB) are crucial for detecting early indicators of liver disease, such as cirrhosis and/or hepatocellular carcinoma (HCC). This early detection enables timely engagement with appropriate interventions, thereby reducing patient morbidity and mortality.

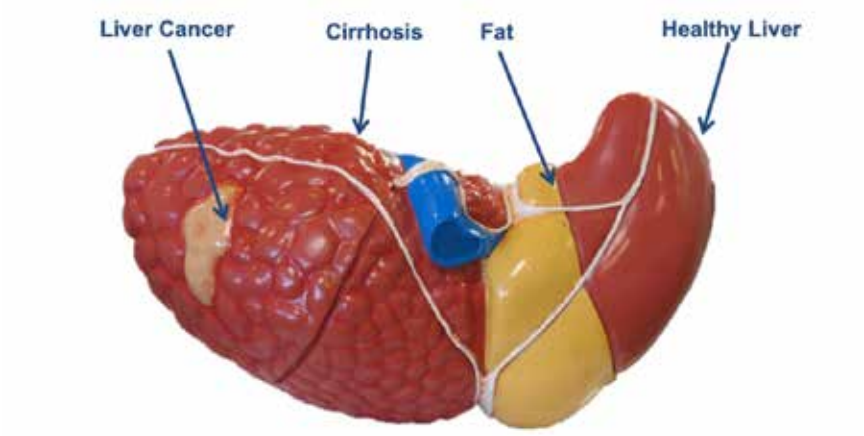
People with severe liver disease (severe fibrosis/cirrhosis and/or a family history of liver cancer) should also receive six monthly liver ultra-sound scans and should ideally be under Secondary Care.

Many people with the virus have no symptoms until the liver is damaged. This is why regular blood tests are so important, even for patients who feel well.

New Zealand is one of 196 countries participating in the World Health Organization's (WHO) initiative to eliminate viral hepatitis by 2030.

World Health Organization Elimination Targets

- Reducing new infections by 90%
- Diagnosing 90% of people with viral hepatitis
- Reducing mortality by 65%
- Treating 80% of eligible people



Key Terms

- Hepatitis B virus (HBV): Acute or Chronic
- Chronic hepatitis B virus (CHB): HBV present >6 months
- Fibrosis: Scarring of the liver
- Cirrhosis: Extreme scarring of the liver
- Hepatocellular carcinoma (HCC): Primary Liver cancer
- Steatosis: Fatty Liver

Hepatitis B Testing

Who to test:

- Anyone over 35 years of age born in New Zealand
- Especially Māori, Pasifika or Asian ethnicity
- Born outside New Zealand from a high risk country
- Have a mother or close family member with hepatitis B
- Live with someone who has hepatitis B
- Had unprotected sex with a person living with hepatitis B
- Have ever injected drugs
- Have received a tattoo using unsterilised equipment.

Diagnostic serology tests

1. **HBsAg** Hepatitis B surface Antigen
2. **Anti-HBs or HBsAb** Hepatitis B surface Antibody
3. **Anti-HBc or HBcAb** Hepatitis B core Antibody

If surface antigen is negative and antibody positive, the patient is immune and no further action is needed.

HBsAg Positive

Refer to The Hepatitis Foundation with results of: HBsAg (+), HBeAg (+/-), LFT's (Incl AST), AFP, HBV DNA, FBC and Patient Consent.

HBsAg Negative

Anti-HBs and Anti-HBc (-) consider HBV vaccination. If Anti-HBc (+) and HBsAg (-), indicates past infection/ exposure therefore natural immunity. NO Vaccination required.

HFNZ will organise:

- Additional blood tests and investigations
- Liver ultrasound (if required)
- Long term monitoring with HFNZ
- Referral to secondary care where appropriate
- GP's/Midwives can refer to secondary care when necessary.
- Refer to your 'Regional Health Pathway' for more information.

Please copy: HFNZ into any investigations or results relating to the management of hepatitis B; LFT's, hepatitis serology, AFP, liver ultrasounds that you might request).

Clinical Patient Management

HFNZ long term monitoring for HBV includes:

- New patient education, HBV assessment following HBV diagnosis and letter to GP.
- HBV education and support for patients and healthcare providers.
- Six-monthly blood tests - results of which are copied to GP's:
  - **HBsAg** hepatitis B surface antigen
  - **HBeAg** hepatitis B e antigen
  - **LFT** Liver function tests (All LFT's including AST)
  - **AFP** alpha-fetoprotein tests
  - **FBC** Full Blood Count
  - **HBV DNA** hepatitis B Viral Load (when required)
- Referrals for six-monthly liver ultrasound scans for patients with an increased risk of liver cancer (HCC), e.g:
  - History of HCC in first degree relatives
  - Severe liver fibrosis/cirrhosis.
  - Reach B>5% risk of HCC in ten years, for liver ultrasound scans.
- HFNZ specialist assessment which may result in referrals to primary care for engagement in anti-viral treatment and secondary care for further assessment and care if required.
- Copies of all relevant correspondence including referrals and electronic blood test results.
- Arranging liver Elastography/Fibroscan (when required).

Blood Tests

HBsAg
Hepatitis B surface antigen

A positive or reactive HBsAg test result means the patient is infected with hepatitis B and is HBV positive therefore at risk of liver damage. HBV is a blood borne virus. Further testing is needed to determine if this is a new (acute) or a long-standing (chronic) hepatitis B infection.

Anti-HBs or HBsAb
Hepatitis B surface antibody

A positive or reactive HBsAb test result indicates the immune system is active against the virus. A positive HBsAg and HBsAb can occur at the same time and still has active infection with HBV.

Anti-HBc or HBcAb
Hepatitis B core antibody

A positive or reactive HBcAb test result indicates a past or current hepatitis B infection. If HBsAg negative and HBcAb positive this person has natural immunity regardless of HBsAb level.

HBeAg
Hepatitis B e antigen

This checks the status of the infection. A positive or reactive result indicates the virus is in the more active form. The e-antigen is a protein from the hepatitis B virus that circulates in infected blood when the virus is actively replicating. Being HBeAg positive means

the patient is likely to have a high level of virus present, which is related to increased risk of transmission.

AFP
Alpha-fetoprotein

This biomarker is primarily an indicator for HCC. **AFP > 20 ng/mL will pick up approx. 40% of early stage HCC (liver ultrasound scans identify approximately 60% of early HCC and are added in high-risk cases).** Screen for AFP six-monthly. If AFP is elevated seek advice and request HBV DNA if AFP is raised.
NOTE: AFP is raised in pregnancy.

HBV DNA (Hepatitis B Viral Load)
- HBV DNA at least every three years >30yrs or six-monthly when on Anti Viral Treatment (HFNZ Guidelines).
- Request HBV DNA if ALT/AST is abnormal. Deranged LFT can indicate Liver inflammation, HBV flare or HCC and may need investigation of other causes.
- Depending on HBV DNA result consider Anti-Viral treatment.

Acute - hepatitis B
Acute HBV needs to be distinguished from a HBV Flare which can occur in Chronic Hepatitis B.

To diagnose acute HBV include request: **IgM anti-HBc.**

In acute cases if **HBV DNA >1,000 commence anti-viral and monitor synthetic function (Albumin, INR) and any signs or symptoms (i.e jaundice, fatigue, nausea, vomiting, dark urine, abdominal pain)**, consult secondary care if necessary.

IgM anti-HBc: IgM anti-HBc positivity indicates recent infection with HBV (within less than 6 months). Its presence usually indicates acute infection. IgM anti-HBc should be ordered only when acute HBV infection is a concern.

Interpretation of hepatitis B blood tests

HBsAg	Anti-HBc	Anti-HBs	IgM Anti-HBc	Result	Action Required
Negative	Negative	Negative Or: Low <10	N/A	Susceptible	Vaccinate?* (See below)
Negative	Positive	Positive	N/A	Immune due to natural infection	No action required
Negative	Negative	Positive	N/A	Immune due to hep B Vaccination	No action required
Positive	Positive	Negative	Positive	Acutely Infected	Retest in six months. Notify Public Health.
Positive	Positive	Negative	Negative	Chronically Infected	Refer to HFNZ
Negative	Positive	Negative	N/A	Previous Natural Infection	No action required
Positive	Positive	Positive	Negative	Chronic infection (even though antibodies are present)	Refer to HFNZ

**Previous full course of vaccine no booster needed unless required for occupation. If uncertain of vaccine history give single dose of vaccine and repeat anti-HBs 10 – 14 days later. If no response or no previous vaccine give full course if HBV risk of infection.*

Hepatocellular carcinoma (HCC)

Chronic hepatitis B leads to an increased risk of death from liver cirrhosis and liver cancer. Primary liver cancer is the seventh most common type of cancer globally (fifth for men) and the fourth leading cause of annual cancer deaths worldwide (second for men).

Men develop liver cancer more than twice as frequently as women. In settings with limited resources and a high burden of hepatitis B, people are often diagnosed with Hepatitis B at an advanced stage of disease (decompensated cirrhosis or HCC).

Although 80–90% of people with hepatitis B associated HCC already have cirrhosis when diagnosed, HCC may occur without cirrhosis. A further challenge is that HCC is usually asymptomatic until it is at a clinically advanced stage.

Treatment options for advanced HCC are limited, and overall survival is extremely poor. The prognosis of HCC is affected by the size and number of tumours and underlying liver function and is improved if treatment can begin at an early stage of the disease, when the tumour is small.

Treatments would include microwave ablation, radio frequency ablation or percutaneous ethanol injection of small tumours. Current surveillance is with ultrasound and AFP measurement but with a consensus that people with CHB should be monitored for HCC every six months.

HCC rates secondary to HBV in New Zealand are rising despite infant vaccination due to aging population and immigration from endemic areas, currently more than 80 cases per year.

WHO 2024

Detection of Hepatocellular Carcinoma

Patients with chronic HBV infection are at much increased risk of HCC, increasing with age, male gender, and especially with cirrhosis (those with cirrhosis should be under secondary care). Pre-clinical detection of HCC is essential for any prospect of cure.

We include AFP in our six-monthly blood tests, but this detects less than half of tumours at a very early stage (Barcelona 0/A who have high cure rates). Six-monthly ultrasounds are more sensitive, at approximately 60%, but are not logistically practical for all of the patients we monitor, and a pragmatic approach is to confine this to patients with REACH-B >5% for 10 yr risk of HCC, or family history of HCC or Cirrhosis.

Note: HFNZ have piloted the use of a more sensitive marker (protein induced by vitamin K absence or antagonist II; PIVKA II) in combination with AFP and a weighting for age and gender (GAAD) which is reported to be 73 per cent sensitive for early stage HCC, and this may become the standard of care in future.

Treatment

Dr Chris Moyes,
Medical Director
HFNZ

Hepatitis B Virus is endemic in New Zealand and many parts of the world including the Pacific, South-East Asia, the Middle East, and Africa. Although universal vaccination of infants has been the policy in New Zealand for over 35 years, there is still a substantial reservoir of chronic infection in older adults and in immigrants of all ages from many countries. In some cases, HBV infection is aggravated by hepatitis D (delta), which is prevalent in Samoa and Kiribati, some other Pacific Islands, parts of Asia and Africa and only found in people with HBV. Consequently, the complications of active hepatitis, cirrhosis, and HCC continues to increase.

Who should be treated?

Recent updates of guidelines and WHO recommendations have considerably increased the criteria for treatment.
Anti-viral medication should be offered to all patients with high viral load **HBeAg positive or HBVDNA > 2000 IU/mL** with:-

- ACTIVE liver disease (ALT raised)
- Established liver disease – **Fibrosis or Cirrhosis** (can be screened for with FIB-4/APRI or fibroscan in non-obese)
- Other major risk factors eg co-infection, diabetes, family history of HCC, or risk of HCC within 10 yrs exceeding 2% (use REACH-B score on MDCalc App see *Useful links*) – this includes many patients with normal ALT

- BPAC also recommends offering treatment to ALL patients over 30 yrs with raised viral load > 2000 IU/mL to reduce integration of viral sequences into host DNA to reduce long-term risk of HCC

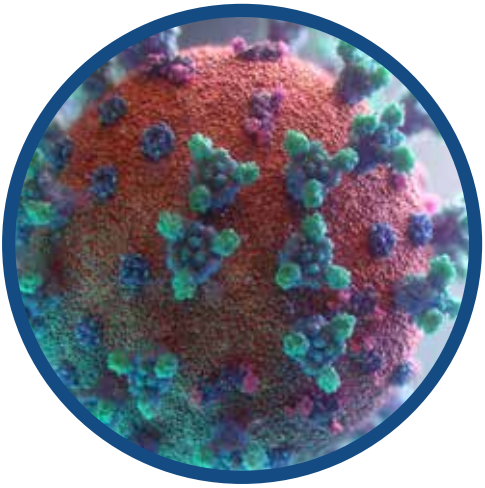
Treatment is still not recommended for immune tolerant patients under 30 yrs with very high HBVDNA and normal ALT unless there are other risk factors as above.

Only patients at high risk of HCC, or with established liver disease or co-morbidities need secondary referral – other cases can be managed in primary care.

How long should treatment last?

All patients with chronic HBV once commenced on Anti-Viral treatment until HBsAg negative (often life-long), unless otherwise advised and further assessed under a Specialist.

Chronic HBV patients may need regular lifelong monitoring for any possible hepatocellular carcinoma and/or progression to cirrhosis despite losing HBsAg.



Anti-viral Medications

Recommended medications for most patients in NZ are either **Entecavir 0.5mg daily** or **Tenofovir Disoproxil 245mg daily**, both of which can be prescribed by General practitioners.

Entecavir is an oral tablet used in adults who have active virus and liver damage. Entecavir is funded as a first-line therapy for patients with chronic hepatitis B.

Almost all patients achieve viral suppression (undetectable HBV DNA) and biochemical response (ALT below the upper limit of normal). Entecavir resistance is rare at less than one percent after six years.

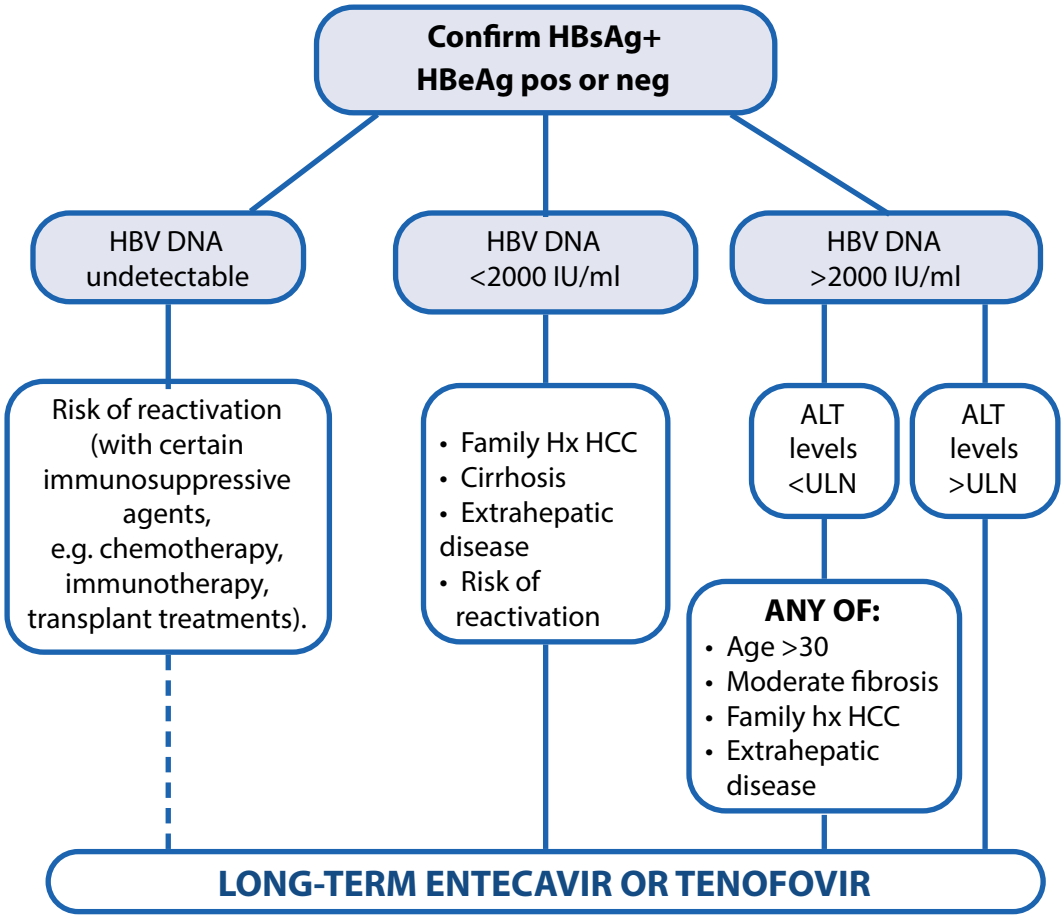
Tenofovir is an oral tablet and is considered to be safest for pregnancy and is the preferred treatment during pregnancy/ breastfeeding and dramatically reduces the risk of vertical transmission. Tenofovir is the first choice for women of reproductive age.

Note: Tenofovir can aggravate renal failure and very occasionally causes renal tubular problems so creatinine, calcium, and phosphorus levels should be monitored, along with periodic liver function and viral load (HBV DNA quantification). **Patients with renal impairment should be prescribed Entecavir rather than Tenofovir and may need a reduction in dose if GfR <50ml/min.**

No resistance to Tenofovir has been observed after five years of therapy. Renal function (creatinine, calcium, and phosphorus) should be assessed before commencement of Tenofovir and periodically while on treatment.

Both are extremely effective at suppressing HBV and reduce liver damage and HCC risk with very few side effects and no interaction with other medications, but need to be continued long-term.

Recommendations for HBV Therapy



Seroconversion of hepatitis B surface antigen

HBsAg seroconversion when a patient has cleared the Hepatitis B Virus (HBV) from their blood. (**HBsAg** is negative or not detected).

About one percent of people with hepatitis B will spontaneously lose **HBsAg** per year (seroconvert). Following seroconversion from HBsAg + to HBsAg - the HBV infection is usually no longer active and they are immune from further infection, but can still be at risk of HCC.

HBV reactivation can occur with potent immunosuppressive therapy and may need cover with prophylactic antiviral treatment.

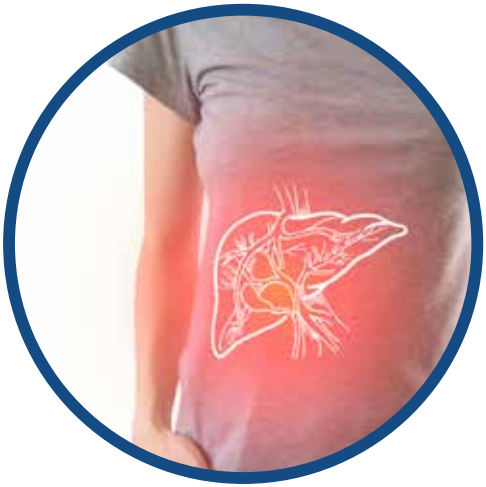
People who seroconvert >50 years old may still be at risk of hepatocellular carcinoma (HCC), although this risk is reduced compared to being HBsAg positive. The Hepatitis Foundation will monitor these people indefinitely.

Patients with close family history for HCC and/or cirrhosis will require six monthly liver ultrasound scans in addition to these 6 monthly bloods indefinitely. Cirrhotic Patients should be monitored under Secondary Care Gastroenterology indefinitely and be registered with HFNZ.

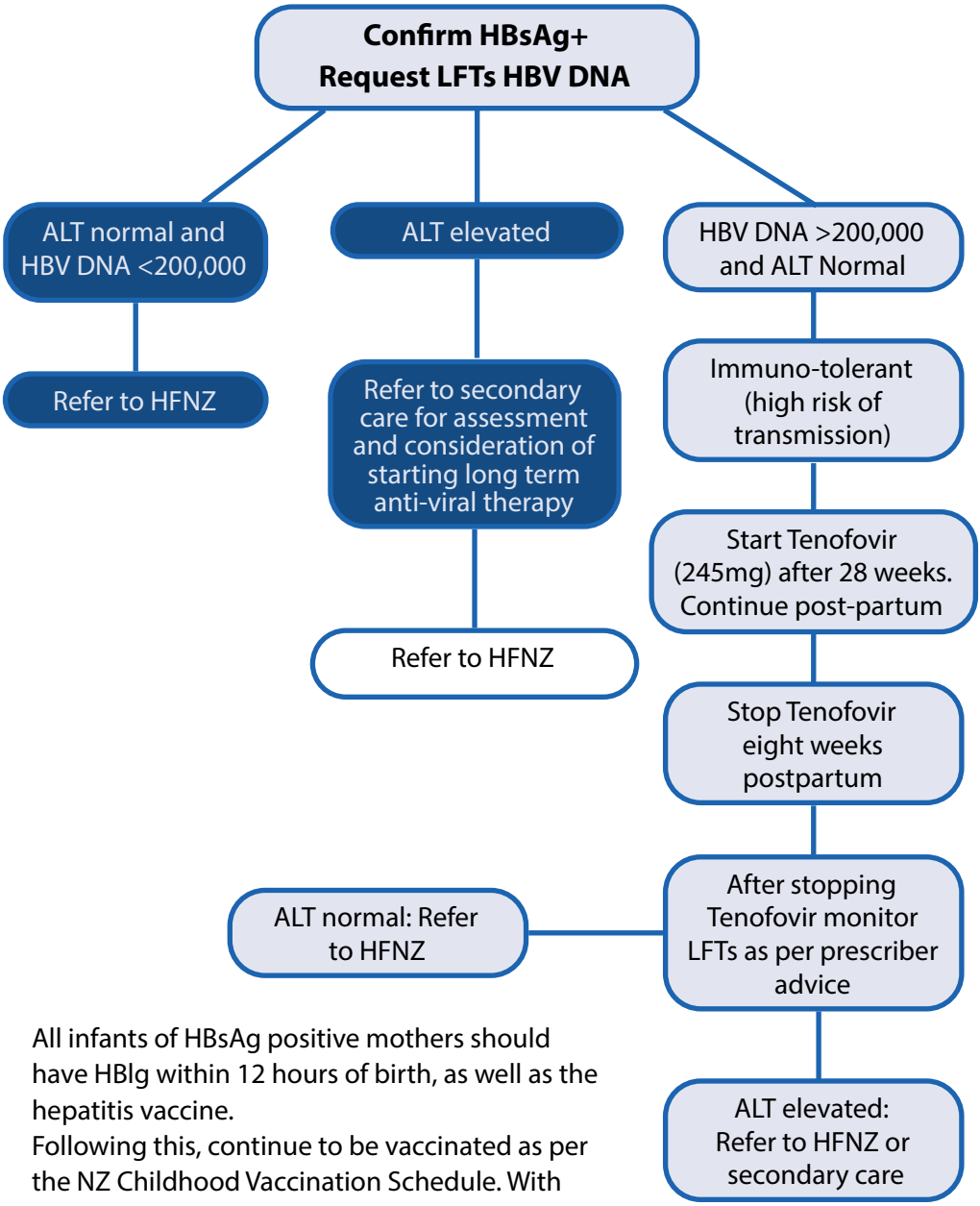
HBsAg becomes negative

High-risk: Cirrhosis or family history of HBV-related HCC	Continue monitoring blood tests and USS indefinitely
HBsAg-seroconversion at: <50 years old	Discharge from monitoring blood tests unless Fhx HCC/ Cirrhosis
HBsAg-seroconversion at: >50 years old	Continue monitoring indefinitely

Six-monthly liver function tests (LFTs) and alpha-fetoprotein (AFP)
12-monthly full blood count (FBC)



Antenatal Screening



All infants of HBsAg positive mothers should have HBIg within 12 hours of birth, as well as the hepatitis vaccine.
Following this, continue to be vaccinated as per the NZ Childhood Vaccination Schedule. With serology testing at 9 months of age, and referral to a specialist if HBsAg positive.

Referrals to The Hepatitis Foundation

We encourage you to refer hepatitis B patients to The Foundation for our free monitoring programme.

Verbal consent for referral is required.

We receive referrals through **Healthlink (CareSelect)** (Our EDI is nzhepfnd), **Best Practice, ERMS or Medtech Outbox.**

We also receive referrals by downloading our enrolment form at **www.hepatitisfoundation.org.nz** and emailing to **hepteam@hfnz.nz** or call **0800 33 20 10**

Ideally include in referral:

- Blood test results must include a positive HBsAg (hepatitis B surface antigen). Other relevant tests are: LFT, AFP, HBeAg, HBV DNA and FBC.
- The patient must be a New Zealand resident or eligible for free health care in NZ. If on Healthlink please provide proof of residency or eligibility of health care (see next page for more details on non resident/immigration patients).
- If under hospital care for hepatitis B, include ultrasound reports and clinic letters.

Referral Process

A registered nurse will be in contact with your patient to answer all questions on HBV; a thorough education and assessment can be provided in-person, virtually or over the phone, and, if required, testing of family members.

The patient must be a New Zealand resident or be eligible for free healthcare in NZ. If they are resident on Healthlink, please provide proof of residency or eligibility of health care.

If they are under hospital care for hepatitis B, please include ultrasound reports and clinic letters.

Once referral is received, we'll send you a letter, advising we have received the referral.

A welcome pack will be sent to your patient, including a result letter, hepatitis B pamphlets and a consent form, if not already signed.

Note: We can accept referrals for non-resident or immigration patients but please advise them they may have to pay for other health services if they don't meet eligibility requirements for free care.

Useful Links

The Hepatitis Foundation of New Zealand
www.hepatitisfoundation.org.nz/health-professionals

Information for Health Professionals, MD Calc App - REACH-B Score,
www.mdcalc.com
Reach-B Score for Hepatocellular Carcinoma (HCC)
Fibrosis-4 (FIB-4) Index for Liver Fibrosis
AST to Platelet Ratio Index (APRI)

Immunisation Handbook
www.tewhatuora.govt.nz/for-health-professionals/clinical-guidance/immunisation-handbook

University of Liverpool – Drug Interactions
www.hep-druginteractions.org

Get in Touch

If you would like one of our Community Hepatitis Nurses to visit your practice to provide education, resource and advice regarding hepatitis B you can contact us and we will connect with you.

Or you can request Hepatitis B resources anytime by contacting the HFNZ team:

The Hepatitis Foundation of New Zealand
61 Alexander Avenue, Whakatāne 3120
0800 33 20 10
hepteam@hfnz.nz
www.hepatitisfoundation.org.nz
@HepatitisfoundationNZ

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