Medicines Management Programme

Managed Access Protocol – Bulevirtide (Hepcludex®) for the treatment of chronic hepatitis delta virus (HDV) infection in plasma (or serum) HDV-RNA positive adult patients with compensated liver disease.

Medicine	Date of addition to Managed Access Protocol
Bulevirtide (Hepcludex®)	01/05/2025

Approved by	**Professor Michael Barry, Clinical Lead, MMP**	
Date approved	Version 1.0	24/04/2025

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List of abbreviations

HBV	Hepatitis B virus
HBsAg	Hepatitis B surface antigen
HDV	Hepatitis delta virus
HSE	Health Service Executive
HTH	High Tech Hub
MAP	Managed Access Protocol
MMP	Medicines Management Programme
NTCP	Sodium taurocholate co-transporting polypeptide
PCR	Polymerase chain reaction
PCRS	Primary Care Reimbursement Service
PegIFNα	Pegylated-interferon alfa-2a
RNA	Ribonucleic acid
SmPC	Summary of product characteristics

1. Bulevirtide

Hepcludex® contains bulevirtide. Bulevirtide is an antiviral that blocks the entry of hepatitis B virus (HBV) and hepatitis delta virus (HDV) into hepatocytes by binding to and inactivating sodium taurocholate co-transporting polypeptide (NTCP), a bile salt liver transporter serving as essential HBV/HDV entry receptor.

From May 2025, one presentation of bulevirtide is available on the High Tech Arrangement.

- Hepcludex® 2 mg powder for solution for injection

1.1 Licensed indication

Bulevirtide (Hepcludex®) is indicated for the treatment of chronic HDV infection in plasma (or serum) HDV-ribonucleic acid (RNA) positive adult patients with compensated liver disease.

1.2 Reimbursement

Reimbursement of bulevirtide on the High Tech Arrangement is supported only for patients who meet the criteria outlined in this managed access protocol (MAP), i.e. chronic HDV infection in plasma (or serum) HDV-RNA positive adult patients with compensated liver disease, with evidence of significant fibrosis, with an inadequate response to pegylated-interferon alfa-2a (PegIFNα) treatment, or who are ineligible to receive PegIFNα treatment due to intolerance or contraindication. All criteria must be satisfied in order for reimbursement to be supported.

An application for reimbursement approval is required to be submitted on an individual patient basis. The *Bulevirtide Application Form* should be completed and sent by secure email to the Health Service Executive (HSE)-Medicines Management Programme (MMP) at mmp@hse.ie.

Table 1 outlines the licensed therapeutic dosage of bulevirtide for chronic HDV infection in plasma (or serum) HDV-RNA positive adult patients with compensated liver disease. Please refer to the Summary of Product Characteristics (SmPC) for further prescribing information.

Table 1: Licensed therapeutic dosage of bulevirtide

Medicinal product (medicine)	Route of administration	Dosage
Hepcludex® (bulevirtide) 2 mg powder for solution for injection	Subcutaneous Injection	2 mg once daily (every 24 hours ± 4 hours) by subcutaneous injection

mg: milligrams

If a patient is recommended for reimbursement of bulevirtide, reimbursement is supported in line with the licensed therapeutic dosage specified in Table 1. Reimbursement of dosages in excess of the licensed therapeutic dosage (as outlined in Table 1) is not supported.

See Section 3 for further details on Reimbursement criteria – Requirement for outcome data.

1.3 Reimbursement price

The reimbursement price of the presentation of bulevirtide available on the High Tech Arrangement is outlined in Table 2. A commercial-in-confidence arrangement is in place with the marketing authorisation holder to reduce the net acquisition cost of bulevirtide to the HSE.

Table 2: Reimbursement code and price for the presentation of bulevirtide available on the High Tech Arrangement

Medicinal product (pack size)	Code	Reimbursement price*
Hepcludex® 2 mg powder for solution for injection (30 vials)	89415	€8,846.48

mg: milligrams

*Correct as at 01/05/2025

2. Reimbursement criteria – Initiation

This section outlines the criteria that must be satisfied in order for patients to be recommended for reimbursement of bulevirtide under the High Tech Arrangement.

2.1 Prescribers

Applications for reimbursement approval for bulevirtide under the High Tech Arrangement will only be considered from consultants in infectious diseases or consultant hepatologists and gastroenterologists, that are registered with the Irish Medical Council, who are experienced in the treatment of patients with HDV infection, and who have agreed to the terms of this MAP and been approved by the HSE ('approved consultants').

Approved consultants are responsible for ensuring that the patient or their representative/guardian is aware that the application for reimbursement approval is being made on their behalf.

The prescribing of Hepcludex® for approved patients under the High Tech Arrangement will be confined to the approved consultants and their teams. The governance of the team on the High Tech Hub (HTH), including access, rests with the approved consultant.

2.2 Patient age

Applications for reimbursement approval will only be considered for individuals aged 18 to 65 years at time of application.

2.3 Patient diagnosis

Reimbursement under the High Tech Arrangement will only be supported for the treatment of chronic HDV infection in plasma (or serum) HDV-RNA positive adult patients, with compensated liver disease, with evidence of significant fibrosis, with an inadequate response to PegIFNα treatment, or who are ineligible to receive PegIFNα treatment due to intolerance or contraindication.

2.3.1 Confirmation of chronic HDV infection

Individuals should have a positive serum anti-HDV antibody result. For reimbursement approval, clinicians are required to submit evidence (including date of measurement) of:

- A positive polymerase chain reaction (PCR) result for serum/plasma HDV RNA, the result must be within six months of the date of the application.

2.3.2. Compensated liver disease

For reimbursement approval, clinicians are required to confirm the patient has compensated liver disease and submit a Child-Pugh Score to support a diagnosis of compensated liver disease.

2.3.3 Confirmation of significant fibrosis

For reimbursement approval, clinicians are required to submit either a liver biopsy report to support the diagnosis of significant fibrosis defined as METAVIR stage greater than or equal to F2, or a transient elastography (Fibroscan) score of greater than or equal to 7.25 kPA. [1]

1. Qi X, An M, Wu T et al. Transient Elastography for Significant Liver Fibrosis and Cirrhosis in Chronic Hepatitis B: A Meta-Analysis. Canadian Journal of Gastroenterology and Hepatology. 2018; 2018:3406789. DOI: 10.1155/2018/3406789

2.4 Patient clinical history/status

2.4.1 Contraindications

In line with SmPC for Hepcludex®, applications for reimbursement approval will not be considered for individuals who meet any of the contraindications for treatment as outlined in the SmPC.

2.5 Patient's medical treatment

2.5.1. PegIFNα treatment

When reviewing applications, the MMP may request evidence to validate that the patient has been in receipt of PegIFNα treatment with an inadequate response (e.g. printout of dispensed medicinal products) or evidence to validate that the patient is ineligible to receive PegIFNα treatment due to intolerance or contraindication.

2.5.1.1 PegIFNα response inadequate

Reimbursement will be supported for patients with an inadequate response to a treatment course of PegIFNα.

2.5.1.2 PegIFNα not tolerated

In cases where a patient did not tolerate PegIFNα and experienced a clinically significant adverse reaction which led to discontinuation of treatment prior to completion of an adequate trial, or following a period of treatment at the maximum tolerated dose, information in relation to the duration of treatment and the adverse reaction experienced should be provided.

2.5.1.3 PegIFNα is contraindicated

For patients in whom treatment with PegIFNα is contraindicated, details of the contraindication, including any supporting evidence, must be provided at the time of application for reimbursement approval.

2.5.2 Treatment of underlying HBV infection

The underlying HBV infection should be simultaneously managed according to current treatment guidelines.

3. Reimbursement criteria – Requirement for outcome data

Follow-up data may be requested by the MMP for audit purposes and provision of same is a condition of ongoing reimbursement. It is the responsibility of the approved consultant to ensure

that the patient or their representative/guardian is aware that the provision of follow-up data is a condition of reimbursement, and that audits may occur during which their personal data will be reviewed.

3.1 Treatment discontinuation

The optimal treatment duration is unknown. Treatment should be continued as long as there is an associated clinical benefit. Consideration to discontinue the treatment should be given in cases of sustained (6 months) hepatitis B virus surface antigen (HBsAg) seroconversion or loss of virological and biochemical response.

4. Prescribing of bulevirtide for approved patients

Please refer to the SmPC for Hepcludex® for full prescribing information including monitoring and patient counselling requirements.

If a patient is recommended for reimbursement by the HSE-MMP, the High Tech prescription should be generated on the HTH. High Tech prescriptions which are not hub generated for bulevirtide will not be eligible for reimbursement by the HSE Primary Care Reimbursement Service (PCRS). Only approved consultants and their teams will have access to generate prescriptions.