Preemptive policy: This is a P&T approved policy and can be used after the drug is FDA approved until it is superseded by an updated policy

CENTENE® Corporation

Clinical Policy: Bulevirtide (Hepcludex)

Reference Number: CP.PHAR.589
Effective Date: FDA Approval Date
Last Review Date: 08.22
Line of Business: Commercial, HIM, Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

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Description

Bulevirtide (Hepcludex®) is a viral entry inhibitor.

FDA Approved Indication(s) [Pending]

Hepcludex is indicated for the treatment of chronic hepatitis delta virus (HDV) infection in plasma (or serum) HDV-RNA positive adults with compensated liver disease.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Hepcludex is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria*

**Criteria will mirror the clinical information from the prescribing information once FDA-approved*

A. Chronic Hepatitis D Infection (must meet all)**:**

1. Diagnosis of chronic HDV infection as evidenced by detectable serum HDV RNA levels by quantitative assay in the last 6 months;*
2. Prescribed by or in consultation with a gastroenterologist, hepatologist, or infectious disease specialist;
3. Age ≥ 18 years;*
4. Two elevated alanine transaminase (ALT) lab values within the past 12 months (≥ 70 IU/L for men, ≥ 50 IU/L for women);*
5. Child-Pugh hepatic insufficiency score < 7 (Child-Pugh Class A);*
6. No previous (within the last 2 years) or current decompensated liver disease, including coagulopathy, hepatic encephalopathy, and esophageal varices hemorrhage;*
7. Dose does not exceed 2 mg (1 vial) per day. *

Approval duration: 6 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):

a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy*

**Criteria will mirror the clinical information from the prescribing information once FDA-approved*

A. Chronic Hepatitis D Infection (must meet all)**:**

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. Member is responding positively to therapy as evidenced by both of the following (a and b):
   a. A reduction in HDV RNA levels or undetectable HDV RNA levels by quantitative assay;
   b. A reduction or normalization (≤ 35 IU/L for men, ≤ 25 IU/L for women) of ALT lab values;
3. If request is for a dose increase, new dose does not exceed 2 mg (1 vial) per day.*

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line

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of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

AASLD: American Association for the Study of Liver Diseases
ALT: alanine transaminase
FDA: Food and Drug Administration
HDV: hepatitis delta virus
IgG: immunoglobulinG
IgM: immunoglobulin M
PT: prothrombin time

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings [Pending]

- Contraindication(s): pending
- Boxed warning(s): pending

Appendix D: General Information

- According to the American Association for the Study of Liver Diseases (AASLD), the upper limit of normal for serum ALT concentrations for men and women are 35 IU/L and 25 IU/L, respectively.
- According to the World Health Organization, HDV infection is diagnosed by high levels of anti-HDV immunoglobulin G(IgG) and immunoglobulin M (IgM), and confirmed by detection of HDV RNA in serum. However, HDV diagnostics are not widely available and there is no standardization of HDV RNA assays, which are used for monitoring response to antiviral therapy.
- Child-Pugh Classification

Parameter	Points assigned		
	1	2	3
Ascites	Absent	Slight	Moderate
Bilirubin	< 2 mg/dL	2-3 mg/dL	> 3 mg/dL
Albumin	> 3.5 g/dL	2.8 – 3.5 g/dL	< 2.8 g/dL
Prothrombin time (PT) (seconds over control) or INR*	< 4 < 1.7	4-6 1.7 to 2.3	> 6 > 2.3
Encephalopathy	None	Grade 1 to 2	Grade 3 to 4

* Frequently INR will be used as a substitute for PT

- A (5-6 points): well-compensated disease
- B (7-8 points): significant functional compromise
- C (10-15 points): decompensated disease

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V. Dosage and Administration [Pending]

Indication	Dosing Regimen	Maximum Dose
Chronic HDV infection*	2 mg SC daily*	Pending

VI. Product Availability [Pending]

Pending

VII. References

1. ClinicalTrials.gov. Study to access efficacy and safety of bulevirtide in participants with chronic hepatitis delta (CHD). Available at: https://clinicaltrials.gov/ct2/show/NCT03852719?term=MYR301&draw=2&rank=1. Accessed April 22, 2022.
2. American Association for the Study of Liver Diseases (AASLD). Update on prevention, diagnosis, and treatment of chronic Hepatitis B: AASLD 2018 hepatitis B guidance. Hepatology. 2018; 67(4):1560-1599.
3. Hepatitis D. World Health Organization. July 28, 2021. Available at: https://www.who.int/news-room/fact-sheets/detail/hepatitis-d. Accessed April 22, 2022.
4. Tsoris A and Marla CA. Use of the child pugh score in liver disease. 2021 Mar 22. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK542308/

Coding Implications [Pending]

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
Pending	Pending

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created pre-emptively	05.24.22	08.22
Template changes applied to other diagnoses/indications and continued therapy section.	09.19.22	

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Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in

developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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