Clinical Policy: Bulevirtide-gmod (Hepcludex)

Reference Number: CP.PHAR.589
Effective Date: 05.22.26
Last Review Date: 08.26
Line of Business: Commercial, HIM/ICHRA, Medicaid

Coding Implications
Revision Log

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

Description

Bulevirtide-gmod (Hepcludex®) is a sodium taurocholate co-transporting polypeptide (NTCP)-directed hepatitis delta virus (HDV) attachment inhibitor.

FDA Approved Indication(s)

Hepcludex is indicated for the treatment of chronic HDV infection in adults without cirrhosis or with compensated cirrhosis.

This indication is approved under accelerated approval based on participants who achieved a decrease in HDV ribonucleic acid (RNA) and alanine aminotransferase (ALT) normalization. Continued approval for this indication may be contingent upon verification and description of clinical benefit.

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

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

1. Diagnosis of chronic HDV infection;
2. Prescribed by or in consultation with a gastroenterologist, hepatologist, or infectious disease specialist;
3. Age ≥ 18 years;
4. Documentation of recent (within the last 60 days) detectable serum HDV RNA levels by quantitative assay;
5. Two elevated ALT lab values within the past 12 months (> 35 IU/L for men, > 25 IU/L for women);
6. If cirrhosis is present, confirmation of Child-Pugh Class A status (defined as a score < 7 on the Child-Pugh scoring system; *see Appendix D*);
7. Member does not have decompensated liver disease (including ascites, coagulopathy, hepatic encephalopathy, and esophageal varices hemorrhage);
8. Provider attestation that member is receiving appropriate hepatitis B virus (HBV) infection therapy (e.g., antivirals), if indicated per guidelines;
9. Dose does not exceed 8.5 mg (1 vial) per day.

Approval duration:
Medicaid/HIM/ICHRA – 12 months
Commercial – 6 months or to the member's renewal date, whichever is longer

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/ICHRA) 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/ICHRA, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace/ICHRA) 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/ICHRA, 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/ICHRA, and CP.PMN.53 for Medicaid.

II. Continued Therapy

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 one of the following (a or b):
   a. A reduction in HDV RNA levels or undetectable HDV RNA levels by quantitative assay;
   b. A reduction or normalization of ALT lab values (≤ 35 IU/L for men, ≤ 25 IU/L for women);
3. If request is for a dose increase, new dose does not exceed 8.5 mg (1 vial) per day.

Approval duration:
Medicaid/HIM/ICHRA – 12 months
Commercial – 6 months or to the member's renewal date, whichever is longer

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/ICHRA) 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/ICHRA, and CP.PMN.255 for Medicaid; or
b. For drugs NOT on the formulary (commercial, health insurance marketplace/ICHRA) 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/ICHRA, 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/ICHRA, 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/ICHRA, 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 aminotransferase
FDA: Food and Drug Administration
HBV: hepatitis B virus
HDV: hepatitis delta virus
IgG: immunoglobulinG
IgM: immunoglobulin M
INR: international normalized ratio
NTCP: sodium taurocholate co-transporting polypeptide
PT: prothrombin time
RNA: ribonucleic acid

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): none reported
- Boxed warning(s): posttreatment severe acute exacerbation of hepatitis D and B

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 is a clinical scoring system used to assess the severity of chronic liver disease, primarily cirrhosis.

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 international normalized ratio (INR) will be used as a substitute for PT

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

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Chronic HDV infection	8.5 mg SC QD	8.5 mg/day

VI. Product Availability

Single-dose vial for injection: 8.5 mg as lyophilized powder or cake

VII. References

1. Hepcludex Prescribing Information. Foster City, CA: Gilead Sciences, Inc.; May 2026. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2026/761468Orig1s000lbl.pdf. Accessed May 27, 2026.
2. ClinicalTrials.gov. Study to access efficacy and safety of bulevirtide in participants with chronic hepatitis delta (CHD). August 22, 2025 Available at: https://clinicaltrials.gov/ct2/show/NCT03852719. Accessed May 27, 2026.
3. Hepatitis D. World Health Organization. July 25, 2025. Available at: https://www.who.int/news-room/fact-sheets/detail/hepatitis-d. Accessed May 27, 2026.
4. Tsoris A and Marla CA. Use of the child Pugh score in liver disease. 2023 Mar 13. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK542308/. Accessed May 27, 2026.
5. Pan C, Gish R, Jacabson IM, et al. Diagnosis and management of hepatitis delta virus infection. Dig Dis Sci. 2023;68(8):3237-3248.
6. Kushner, T. AGA Clinical practice update on management of hepatitis delta: commentary. Gastroenterology 2025;169:1063-1069.
7. Wedemeyer H, Aleman S, Brunetto MR, et al. A phase 3, randomized trial of bulevirtide in chronic hepatitis D. N Engl J Med. 2023 Jul 6;389(1):22-32.

Coding Implications
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
J3590	Unclassified biologics
C9399	Unclassified drugs or biologicals

Reviews, Revisions, and Approvals	Date	P&T Approval Date
3Q 2023 annual review: no significant changes as drug is still not FDA approved; references reviewed and updated.	04.20.23	08.23
3Q 2024 annual review: no significant changes as drug is still not FDA approved; references reviewed and updated.	05.15.24	08.24
3Q 2025 annual review: no significant changes as drug is still not FDA approved; revised approval duration for Commercial line of business to standard language of 6 months or to the member's renewal date, whichever is longer; references reviewed and updated.	04.24.25	08.25
3Q 2026 annual review: RT4: drug is now FDA approved – criteria updated per FDA labeling: revised requirement for detectable HDV RNA levels to be recent (within the last 60 days); revised elevated ALT requirement from ≥ 70 IU/L for men and ≥ 50 IU/L for women to > 35 IU/L for men and > 25 IU/L for women per clinical trial eligibility and guidelines; clarified Child-Pugh Class A status for those with cirrhosis present; added provider attestation that member is receiving appropriate HBV infection therapy; revised positive response criterion from "both" to "one" of the following: reduction in HDV RNA or ALT normalization; added ICHRA line of business; for Medicaid and HIM, revised initial approval duration from 6 months to 12 months for this chronic disease; references reviewed and updated.	06.02.26	08.26

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.