Clinical Policy: Adefovir (Hepsera)

Reference Number: ERX.SPA.276
Effective Date: 12.01.18
Last Review Date: 11.21
Line of Business: Commercial, Medicaid

Revision Log

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

Description
Adefovir (Hepsera®) is a nucleotide analogue and reverse transcriptase inhibitor with activity against human hepatitis B virus.

FDA Approved Indication(s)
Hepsera is indicated for the treatment of chronic hepatitis B in patients 12 years of age and older with evidence of active viral replication and either evidence of persistent elevations in serum aminotransferases (ALT or AST) or histologically active 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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Hepsera is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

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

1. Diagnosis of chronic hepatitis B virus infection;
2. Prescribed by or in consultation with a gastroenterologist, hepatologist, or infectious disease specialist;
3. Age ≥ 12 years;
4. Failure of one of the following, unless clinically significant adverse effects are experienced or all are contraindicated: Pegasys®, entecavir, tenofovir;
   **Prior authorization may be required for Pegasys, entecavir or tenofovir*
5. Hepsera is not prescribed concurrently with tenofovir;
6. Dose does not exceed 10 mg (1 tablet) per day.

Approval duration: 6 months

B. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

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

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. Hepsera is not prescribed concurrently with tenofovir;
4. If request is for a dose increase, new dose does not exceed 10 mg (1 tablet) per day.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 policy – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
ALT: alanine aminotransferase
AST: aspartate aminotransferase
FDA: Food and Drug Administration

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
entecavir (Baraclude®)	0.5 to 1 mg PO QD	1 mg/day
Pegasys (peginterferon alfa-2a)	180 mcg SC once weekly for 48 weeks	180 mcg/day
tenofovir disproxil fumarate (Viread®)	300 mg PO QD	300 mg/day
Vemlidy® (tenofovir alafenamide)	25 mg PO QD	25 mg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings
- Contraindication(s): hypersensitivity
- Boxed warning(s): severe acute exacerbations of hepatitis, nephrotoxicity, HIV resistance, lactic acidosis, and severe hepatomegaly with steatosis

Appendix D: General Information
- Hepsera labeling warns against coadministration of Hepsera with tenofovir-containing products. Hepsera may increase serum concentrations of tenofovir-containing products and vice versa, resulting in additive nephrotoxicity and diminishing therapeutic effect. In the treatment of chronic hepatitis B, tenofovir should not be administered with Hepsera to avoid multi-drug resistance. In patients with concomitant HIV and chronic hepatitis B, treatment with tenofovir is sufficient.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Chronic hepatitis B	CrCl ≥ 50 mL/min: 10 mg PO QD CrCl 30 to 49 mL/min: 10 mg PO Q48H CrCl 10 to 29 mL/min: 10 mg PO Q72H Hemodialysis: 10 mg every 7 days following dialysis	10 mg/day

VI. Product Availability

Tablet: 10 mg

VII. References

1. Hepsera Prescribing Information. Foster City, CA: Gilead Sciences, Inc.; December 2018. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/021449s024lbl.pdf. Accessed August 8, 2021.
2. Terrault NA, Lok ASF, McMahon BJ, et al. Update on prevention, diagnosis, and treatment of chronic hepatitis B: AASLD 2018 Hepatitis B Guidance. Hepatology 2018; 67(4):1560-1599.
3. World Health Organization. Guidelines for the prevention, care and treatment of persons with chronic hepatitis B infection. March 2015. Available at: http://apps.who.int/iris/bitstream/handle/10665/154590/9789241549059_eng.pdf;jsessionid=F33AA940563ABBB8DF1570D876EC494B?sequence=1. Accessed August 8, 2020.
4. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2021. Available at: http://www.clinicalpharmacology-ip.com/.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	08.28.18	11.18
4Q 2019 annual review: no significant changes; references reviewed and updated.	07.31.19	11.19
4Q 2020 annual review: no significant changes; references reviewed and updated.	08.08.20	11.20
4Q 2021 annual review: no significant changes; references reviewed and updated.	08.09.21	11.21

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.