Oscar Clinical Guideline: entecavir (Baraclude) (PG085, Ver. 8)

entecavir (Baraclude)

Disclaimer

Clinical guidelines are developed and adopted to establish evidence-based clinical criteria for utilization management decisions. Clinical guidelines are applicable according to policy and plan type. The Plan may delegate utilization management decisions of certain services to third parties who may develop and adopt their own clinical criteria.

Coverage of services is subject to the terms, conditions, and limitations of a member's policy, as well as applicable state and federal law. Clinical guidelines are also subject to in-force criteria such as the Centers for Medicare & Medicaid Services (CMS) national coverage determination (NCD) or local coverage determination (LCD) for Medicare Advantage plans. Please refer to the member's policy documents (e.g., Certificate/Evidence of Coverage, Schedule of Benefits, Plan Formulary) or contact the Plan to confirm coverage.

Summary

Hepatitis B (HBV) is a viral infection that targets the liver, leading to either acute or chronic disease. Acute infections are often self-limiting and do not always require treatment; however, a small fraction can progress to chronic hepatitis B. Chronic infections, defined as the persistence of hepatitis B surface antigens present after 6 months, pose significant health risks as they can result in serious liver complications, such as cirrhosis and hepatocellular carcinoma (HCC). The goal of HBV treatment is to reduce the risk of HCC, however initiation of therapy is based on several factors including presence or absence of cirrhosis, alanine aminotransferase levels (a liver enzyme test, with higher levels indicating liver damage or disease) and HBV DNA levels. Management of chronic HBV includes treatment with either pegylated interferon or nucleoside/nucleotide analogs (i.e., entecavir [Baraclude] or Vemlidy [tenofovir alafenamide]). The American Association for the Study of Liver Diseases (AASLD) has published recommendations for management of HBV at https://www.aasld.org.

Entecavir (Baraclude) is a potent nucleoside analog reverse transcriptase inhibitor that inhibits HBV replication. It is available as tablets and oral solution, and is indicated for the treatment of chronic HBV infection in adults and children 2 years of age and older with evidence of active viral replication and either persistently elevated serum aminotransferases (aspartate aminotransferase [AST], alanine aminotransferase [ALT]) or histologically active disease.

In addition to its role in managing chronic hepatitis B, entecavir (Baraclude) also has an important place in prophylaxis against HBV reactivation in immunocompromised individuals, and HBV reinfection post liver transplant, further broadening its clinical utility. Reactivation of HBV can result in severe hepatitis and/or hepatic failure in up to 25-50% of cases. Management recommendations in the case of reactivation prophylaxis are the same as for initial chronic HBV infection.

Definitions

"ALT and AST" refer to alanine aminotransferase and aspartate aminotransferase, liver enzymes that indicate liver cell injury when elevated.

"HBeAg" refers to hepatitis B e antigen, a marker of HBV replication.

"HBsAg" refers to hepatitis B surface antigen, indicating current HBV infection.

"Anti-HBc" refers to antibody to hepatitis B core antigen, indicating current or past HBV infection.

"HBV DNA" refers to hepatitis B virus DNA, a measure of viral load and replication.

"Decompensated Liver Disease" is a severe stage of chronic liver disease characterized by the presence of complications such as variceal bleeding, ascites, hepatic encephalopathy, or abnormal liver function tests. It indicates a failure of the liver to perform its normal metabolic and synthetic functions.

"Documentation" refers to written information, including but not limited to:

- Up-to-date chart notes, relevant test results, and/or relevant imaging reports to support diagnoses; or
- Prescription claims records, and/or prescription receipts to support prior trials of formulary alternatives.

"Nucleos(t)ide analogue" refers to a class of antiviral medications that inhibit HBV replication by interfering with viral DNA synthesis.

"No evidence of" indicates that the reviewer has not identified any records of the specified item or condition within the submitted materials or claims history. In the absence of such evidence, the member is considered eligible. If any evidence of the item or condition is present upon review of the request, the member does not qualify.

"[s]" indicates state mandates may apply.

Clinical Indications

Medical Necessity Criteria for Clinical Review

General Medical Necessity Criteria

The Plan considers entecavir (Baraclude) medically necessary when ALL the following criteria are met:

1. The member is 2 years of age or older*; AND*
2. IF there is evidence the member is coinfected with human immunodeficiency virus (HIV) or chronic hepatitis C virus (HCV), the member meets ONE of the following:
    a. The member has hepatitis B and HIV coinfection AND will be or is currently receiving a fully suppressive antiretroviral (ARV) treatment regimen for HIV*; or*
    b. The member is coinfected with hepatitis B and chronic HCV and will be or is currently receiving a hepatitis C direct-acting antiviral (DAA) therapy*; AND*
3. IF the request is for brand Baraclude, the member is unable to use, or has tried and failed the corresponding generic entecavir from TWO manufacturers, when available[s]*; AND*
4. IF the request is for Baraclude (entecavir) oral solution, the member meets ONE (1) of the following:
    a. The member is unable to swallow tablets*; or*
    b. The member requires a dose that cannot be achieved with commercially available tablet strengths*; or*
    c. The prescriber provides a clinically valid reason why the oral solution is necessary instead of the tablet formulation*; AND*
5. Entecavir (Baraclude)is being prescribed at a dose and frequency that is within FDA approved labeling OR is supported by compendia or evidence-based published dosing guidelines for the requested indication*; AND*

The requested medication is being used within the Plan's Quantity Limit of:

- entecavir (Baraclude) 0.5 mg or 1 mg tablets: 30 tablets every 30 days*; or*
- Baraclude (entecavir) 0.05 mg/mL solution: 630 mL every 30 days.

6. The member meets the applicable Medical Necessity Criteria for Initial Clinical Review or Subsequent Clinical Review listed below.

Medical Necessity Criteria for Initial Clinical Review

Initial Indication-Specific Criteria

Chronic Hepatitis B Virus (HBV) Infection

The Plan considers **entecavir (Baraclude)** medically necessary when **ALL** the following criteria are met:

7. The member meets the above General Medical Necessity Criteria; *AND*
8. The member has a documented diagnosis of chronic hepatitis B virus (HBV) infection, confirmed by appropriate laboratory test(s).

If the above prior authorization criteria are met, the requested product will be approved for up to 12 months.[s]

Hepatitis B Virus (HBV) Reactivation Prophylaxis

The Plan considers **entecavir (Baraclude)** medically necessary when **ALL** the following criteria are met:

7. The member meets the above General Medical Necessity Criteria; *AND*
8. The medication is prescribed by or in consultation with an oncologist, gastroenterologist, hepatologist, infectious disease,transplant specialist, or those with experience managing hepatitis B virus reactivation prophylaxis*; AND*
9. Entecavir (Baraclude)being used for prophylaxis against hepatitis B reactivation*; AND*
10. The member meets **ONE** (1) of the following conditions:
    a. Is anti-HBc-positive, HBsAg-positive **AND** undergoing immunosuppressive or cytotoxic therapy (see moderate-to-high risk per the American Gastroenterology Association (AGA) guidelines (see Appendix A, Table 1); *or*
    b. Is anti-HBc-positive, HBsAg-negative **AND** undergoing stem cell transplantation or receiving anti-CD20 therapy such as rituximab **OR** immunosuppressive or cytotoxic therapy (see moderate-to-high risk assessment per the AGA guidelines Appendix A, Table 1); *or*
    c. Is a non-liver solid organ transplant recipient of **ONE** (1) of the following:
        i. A HBsAg-positive extrahepatic organ; *or*
        ii. An anti-HBc-positive, HBsAg-negative organ.

If the above prior authorization criteria are met, the requested product will be approved for up to 12 months.[s]

Hepatitis B Virus (HBV) Reinfection Prophylaxis Post Liver Transplant

The Plan considers entecavir (Baraclude) medically necessary when ALL the following criteria are met:

7. The member meets the above General Medical Necessity Criteria; *AND*
8. The medication is being prescribed by or in consultation with a gastroenterologist, hepatologist, infectious disease, or transplant specialist*; AND*
9. Entecavir (Baraclude) is being used for prophylaxis of hepatitis B virus (HBV) reinfection*; AND*
10. The member has a documented history of BOTH of the following:
    a. Hepatitis B infection*; and*
    b. Has undergone a liver transplant.

If the above prior authorization criteria are met, the requested product will be approved for up to 12 months.[s]

Continued Care

Medical Necessity Criteria for Subsequent Clinical Review

Subsequent Indication-Specific Criteria

Chronic Hepatitis B Virus (HBV) Infection

The Plan considers entecavir (Baraclude) medically necessary when ALL the following criteria are met:

1. The member meets the above applicable General Medical Necessity Criteria and/or Initial Clinical Review; *AND*
2. The member has documented clinical improvement from baseline or maintenance of disease activity as evidenced by ONE of the following:
    a. Decrease or normalization of serum aminotransferases (ALT or AST) levels*; or*
    b. Loss or reduction of HBeAg or HBsAg*; or*
    c. Minimal histologic evidence of liver injury*; or*
    d. Reduction, suppression, or undetectable levels of serum HBV DNA levels.

If the above reauthorization criteria are met, the requested product will be authorized for up to 12-months.[s]

Hepatitis B Virus (HBV) Reactivation Prophylaxis

The Plan considers entecavir (Baraclude) medically necessary when ALL the following criteria are met:

1. The member meets the above applicable General Medical Necessity Criteria and/or Initial Clinical Review; *AND*
2. The member has no evidence of Hepatitis B reactivation.

If the above reauthorization criteria are met, the requested product will be authorized for up to 12-months.[s]

Hepatitis B Virus (HBV) Reinfection Prophylaxis Post Liver Transplant

The Plan considers **entecavir (Baraclude)** medically necessary when **ALL** the following criteria are met:

1. The member meets the above applicable General Medical Necessity Criteria and/or Initial Clinical Review; *AND*
2. The member has no evidence of Hepatitis B virus reinfection.

If the above reauthorization criteria are met, the requested product will be authorized for up to 12-months.[s]

Experimental / Investigational, or unproven[s]

Entecavir (Baraclude) for any other use is considered experimental, investigational, or unproven.

References

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Appendix A

Table 1: American Gastroenterology Association Risk Classification for Hepatitis B Virus Reactivation

	Low risk (<1%)	Moderate Risk (1-10%)	High Risk (>10%)
HBsAg positive	• Corticosteroid therapy (≤ 1 week, dose: low, moderate or high) ↔ • Intra-articular corticosteroid therapy	• Anti-T cell therapy • Corticosteroid therapy (Duration ≥ 4 weeks, dose: low)	• Anthracycline derivatives • Anti-TNF therapy • Anti-IL 6 therapy • B cell-depleting agents • CAR-T cell therapy • Cytokine/integrin inhibitors

	Low risk (<1%)	Moderate Risk (1-10%)	High Risk (>10%)
			• TACE • TKI therapy • JAK inhibitor therapy • HCV co-infection undergoing DAA therapy • Corticosteroids (Duration ≥ 4 weeks, dose: moderate/high) ↔
HBsAg negative; anti-HBc positive	• Immune checkpoint inhibitors • Anti-TNF therapy • HCV co-infection undergoing DAA therapy • Corticosteroids (Duration≥ 4 weeks, dose: low) • Intra-articular corticosteroid therapy • Corticosteroid therapy (≤ 1 week, dose: low, moderate or high) ↔	• Anthracycline derivatives • Anti-IL 6 therapy • Anti-T cell therapy • CAR-T cell therapy • Cytokine/integrin inhibitors • TKI therapy • JAK inhibitor therapy • TACE • Corticosteroids (Duration ≥ 4 weeks, dose: moderate/high) ↔	• B cell-depleting agents
TNF, tumor necrosis factor; HCV, hepatitis C virus; DAA, direct acting antiviral agent(s); IL-6, interleuken-6; TKI, tyrosine kinase inhibitors; JAK, janus kinase; TACE, transcatheter arterial chemoembolization. *↔ Glucocorticoids (prednisone or equivalent): low dose, <10 mg; moderate dose, 10-20 mg; high dose > 20 mg.* *A note on duration of use: Antiviral prophylaxis should be started before the start of the risk-imposing therapy and continued for at least 6 months after discontinuation of risk-imposing therapy (at least 12 months for B cell-depleting agents).*			

Clinical Guideline Revision / History Information

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