Premier Health Plan

POLICY AND PROCEDURE

POLICY TITLE: ***Hepatitis B Products (Hepsera, Baraclude, Epivir-HBV, Pegasys, Tyzeka)***
DEPARTMENT: **Clinical Pharmacy Services- Utilization Management**
ORIGINAL DATE: ***September 2013 (as adopted from UPMC Health Plan)***

Last P & T Committee Approval Date: *February 2018*

Product Applicability: *mark all applicable products below:*

COMMERCIAL	[ ] HMO [ ] PPO *Products*: [ ] Small [ ] Indiv. [ ] Large *Exchange*: [ ] Shop [ ] Indiv. [x] All
OTHER	[x] Self-funded/ASO

PURPOSE

The purpose of this policy is to define the prior authorization process for Hepsera (adefovir dipivoxil), Baraclude (entecavir), Epivir-HBV (lamivudine), Pegasys (peginterferon alfa-2a), and Tyzeka (telbivudine).

Hepsera (Adefovir dipivoxil) 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.

Baraclude (Entecavir) is indicated for the treatment of chronic hepatitis B virus infection in adults with evidence of active viral replication and either evidence of persistent elevations in serum aminotransferases (ALT or AST) or histologically active disease.

Epivir-HBV (Lamivudine) is indicated for the treatment of chronic hepatitis B associated with evidence of hepatitis B viral replication and active liver inflammation.

Pegasys (Peginterferon alfa-2a) monotherapy is indicated for treatment of adult patients with HBeAg positive and HBeAg negative chronic hepatitis B infection who have compensated liver disease and evidence of viral replication and liver inflammation.

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Tyzeka (Telbivudine) is indicated for the treatment of chronic hepatitis B in adult patients with evidence of viral replication and either evidence of persistent elevations in serum aminotransferases (ALT or AST) or histologically active disease.

DEFINITIONS

ALT – alanine aminotransferase

Anti-HBe – antibody to hepatitis Be antigen

Anti-HBs – antibody to hepatitis surface antigen

AST – aspartate aminotransferase

DNA – deoxyribonucleic acid

HBeAg – hepatitis B e antigen

HBsAg – hepatitis B surface antigen

POLICY

It is the policy of the Health Plan to maintain a prior authorization process that promotes appropriate utilization of specific drugs with potential for misuse or limited indications. This process involves a review using Food and Drug Administration (FDA) criteria to make a determination of Medical Necessity, and approval by the Pharmacy & Therapeutics Committee of the criteria for prior authorization, as described in RX.002 Pharmacy and Therapeutics Committee and RX.003-Prior Authorization Process.

The drugs, Hepsera (adefovir dipivoxil), Baraclude (entecavir), Epivir-HBV (lamivudine), Pegasys (peginterferon alfa-2a), and Tyzeka (telbivudine), are subject to the prior authorization process.

PROCEDURE

Initial Authorization Criteria:

Must meet all of the criteria listed under the applicable headers:

1. **All requests:**
   - Must be prescribed by an infectious disease physician, a gastroenterologist, a hepatologist, or a transplant physician
   - Must have a diagnosis of chronic hepatitis B

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- Must submit documentation of baseline evaluation and results for the following tests:
  - Hepatitis B virus (HBV) DNA viral load
  - HBe Ag
  - Anti-HBe
  - HBsAg
  - Anti-HBs
  - Liver biopsy (if available)
- Must have documentation of results of Hepatitis B Virus Drug Resistance panel if member has received previous anti-viral drug treatment for Hepatitis B

2. HBeAg-positive chronic hepatitis B (must meet ONE of the ALT criteria AND the HBV DNA criteria):

- ALT criteria (must have ONE of the following ALT criteria)
  - ALT ≥2 times the upper limit or normal
  - Have evidence of moderate/severe inflammation or significant fibrosis on biopsy
- HBV DNA criteria:
  - Must have a HBV DNA level >20,000 IU/mL
  - HBV DNA Criteria does not need to be met for pediatric patients if ALT
  - 2 times the upper limit or normal for longer than 6 months
- If the above criteria are met, Baraclude or Pegasys is approved for 1 year.
  - Hepsera, Epivir, and Tyzeka are non-preferred due to weak anti-viral activity and high rates of drug resistance. Any request for these non-preferred agents require the submission of clinical rationale from the provider to support the use of these agents over preferred treatment options.
  - Tyzeka can be approved for members who are currently pregnant.

3. HBeAg-negative chronic hepatitis B (must meet ONE of the ALT criteria AND ONE of the HBV DNA criteria):

- ALT criteria:
  - ALT ≥2 times the upper limit or normal
  - ALT >1 time the upper limit of normal AND have evidence of moderate/severe inflammation or significant fibrosis on biopsy
  - ALT ≤ the upper limit of normal AND ALT has increased over time
- HBV DNA criteria:
  - HBV DNA >20,000 IU/mL

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  - HBV DNA >2,000 IU/mL AND have evidence of moderate/severe inflammation or significant fibrosis on biopsy
  - HBV DNA ≤2,000 IU/mL AND HBV DNA has increased over time
- If the above criteria are met, Baraclude or Pegasys is approved for 1 year.
  - Hepsera, Epivir, and Tyzeka are non-preferred due to weak anti-viral activity and high rates of drug resistance. Any request for these non-preferred agents require the submission of clinical rationale from the provider to support the use of these agents over preferred treatment options.
  - Tyzeka can be approved for members who are currently pregnant.

4. **Hepatitis B members with cirrhosis, regardless of HBeAg status (must meet one of the following):**
   - HBV DNA >2,000 IU/mL
   - Detectable HBV DNA level AND elevated ALT
   - If the above criteria are met, Baraclude is approved for 1 year.
     - Hepsera, Epivir, and Tyzeka are non-preferred due to weak anti-viral activity and high rates of drug resistance. Any request for these non-preferred agents require the submission of clinical rationale from the provider to support the use of these agents over preferred treatment options.
     - Tyzeka can be approved for members who are currently pregnant.

5. **Hepatitis B members who have had a liver transplant for Hepatitis B OR for solid organ transplant recipients who have received organs from Hepatitis B positive donors:**
   - Members are approvable regardless of ALT or HBV DNA levels
   - If the above criteria are met, Baraclude is approved for 1 year.
     - Hepsera, Epivir, and Tyzeka are non-preferred due to weak anti-viral activity and high rates of drug resistance. Any request for these non-preferred agents require the submission of clinical rationale from the provider to support the use of these agents over preferred treatment options.
     - Tyzeka can be approved for members who are currently pregnant.

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6. **Hepatitis B carriers who require immunosuppressive or cytotoxic therapy:**
   - Member must be a hepatitis B carrier, as evidenced by HBsAg-positive status
   - Must have planned course of cancer chemotherapy or immunosuppressive therapy
   - Members are approvable regardless of ALT or HBV DNA levels
   - If the above criteria are met, Baraclude is approved for 1 year.
     - Hepsera, Epivir, and Tyzeka are non-preferred due to weak anti-viral activity and high rates of drug resistance. Any request for these non-preferred agents require the submission of clinical rationale from the provider to support the use of these agents over preferred treatment options.
     - Tyzeka can be approved for members who are currently pregnant.

7. **Hepatitis B members who are also co-infected with Hepatitis D:**
   - Members are approvable regardless of ALT or HBV DNA levels
   - If the above criteria are met, Pegasys is approved for 1 year.

8. **Hepatitis B members who are currently pregnant to reduce risk of vertical HBV transmission (must meet all of the following):**
   - Must be in third trimester of pregnancy
   - Must have a serum HBV DNA level $>10^8$ IU/mL
   - If the above criteria are met, Tyzeka is approved for 6 months.

Reauthorization Criteria:

All prior authorization renewals are reviewed on an annual basis (unless specified otherwise below) to determine the Medical Necessity for continuation of therapy. Authorization may be extended at 1-year intervals (unless specified otherwise below) based upon the following:

- Chart documentation from the prescriber that the member's condition continues to benefit from treatment based upon the prescriber's assessment while on therapy
- Documentation/claims history demonstrating that the member has been compliant with therapy
- Recent documentation of HBV DNA level (required for all indications)
- Documentation of all of the following for chronic hepatitis B HBeAg-positive and HBeAg-negative members not falling under any other indications:
  - HBe Ag

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  - Anti-HBe
  - HBsAg
  - Anti-HBs
- Documentation of Hepatitis B Virus Drug Resistance panel results if patient has evidence or virologic breakthrough (>1 log10 [10-fold] increase in serum HBV DNA from nadir during treatment in a patient that had an initial virologic response) while compliant with therapy
- Treatment is authorized for a length of time as follows:
  - Members with HBeAg-positive chronic hepatitis B treatment are authorized until member meets ALL of the following:
    - Loss of HBeAg
    - Undetectable serum HBV DNA
    - Completed 6 to 12 months of additional treatment after appearance of anti-HBe
- Members with HBeAg-negative chronic hepatitis B treatment are authorized until member has loss of HBsAg
- Members with cirrhosis or who have had a liver transplant for hepatitis B can receive long-term treatment
- Members who have had a liver transplant for hepatitis B OR for solid organ transplant recipients who have received organs from hepatitis B positive donors can receive long-term treatment
- Members who are hepatitis B carriers and require immunosuppressive or cytotoxic therapy
  - Members with baseline HBV DNA <2,000 IU/mL should continue treatment for 6 months after completion of chemotherapy or immunosuppressive therapy
  - Members with baseline HBV DNA >2,000 IU/mL should continue treatment until they reach therapeutic endpoints for immunocompetent hepatitis B members as listed above
- Members who are also co-infected with hepatitis D are authorized for 1 year
- Members on hepatitis B treatment to reduce risk of vertical HBV transmission during birth are authorized for 6 months only

Limitations:

Length of Authorization (if above criteria met)	
Initial Authorization	• Reducing vertical transmission during pregnancy: up to 6 months

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	• All other diagnoses: up to 1 year
Reauthorization	See above

If the established criteria are not met, the request is referred to a Medical Director for review.

REFERENCES

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5. Pegasys [prescribing information]. South San Francisco, CA: Genentech USA, Inc.; July 2013
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7. Lucey MR, Terrault N, Ojo L, et al. Long-term management of the successful adult liver transplant: 2012 practice guideline by the American Association for the Study of Liver Disease and the American Society of Transplantation. *Liver Transplantation* 2013;19:3-26
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10. European Association for the Study of the Liver. EASL clinical practice guidelines: management of chronic hepatitis B virus infection. *Journal of Hepatology* 2012;57:167-185

RECORD RETENTION

Records Retention for Evolent Health documents, regardless of medium, are provided within the Evolent Health records retention policy and as indicated in CORP.028.E Records Retention Policy and Procedure.

REVIEW HISTORY

DESCRIPTION OF REVIEW / REVISION	DATE APPROVED
Annual review	*02/17, 02/18*
Criteria update	*10/16*

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