**Coverage Policy**

**Pharmacy and Therapeutics Advisory Committee**

**Policy:** Liver Disease  
**Class:** Gastrointestinal Disorders  
**LOB:** MCL  
**P&T Date:** 9/11/2018  
**Review History:** 2/17, 9/15

This policy has been developed through review of medical literature, consideration of medical necessity, generally accepted medical practice standards, and approved by the HPSJ Pharmacy and Therapeutic Advisory Committee.

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**Overview**

Liver disease can be caused by various factors – infectious disease (hepatitis B, C), chronic alcoholism, nonalcoholic fatty liver disease, medications, etc. Chronic liver disease can progress to ascites and cirrhosis, which can lead to complications and eventually may require liver transplant. Hepatitis B and C medications can help reduce the risk of long-term complications from chronic hepatitis and transmission of disease to others. Certain antibiotics and blood pressure medications can treat or prevent liver disease complications, such as hepatic encephalopathy, variceal bleeding, ascites, and spontaneous bacterial peritonitis.

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**Table 1: Formulary Liver Disease Treatment Agents**

<table>
<thead>
<tr>
<th>Indication</th>
<th>Drug</th>
<th>Available Strengths</th>
<th>FML Limit</th>
<th>Notes</th>
<th>Cost Per Rx</th>
</tr>
</thead>
</table>
| Hepatic Encephalopathy Prophylaxis | Lactulose (Generlac/Kristalose) | 20g/30mL Oral Solution; 10g, 20g Powder Packet | --        | For HE: Xifaxan is reserved for treatment failure of compliant use of lactulose evidenced by consistent lactulose fills.  
For IBS-D: Restricted to 42 tablets per 14 days.  
Restricted to 3 fills per 365 days.  
Xifaxan is reserved for patients who have failed treatment with at least one antispasmodic, one TCA, and loperamide; or failed treatment with at least one antispasmodic and one TCA for use in abdominal pain relief. | $13.68      |
| Rifaximin (Xifaxan)         | 550mg Tablet        | PA                                                      |           |                                                                                           | $1,276.29   |
| Neomycin (Neo-Fradin)      | 500mg Tab           | --                                                      |           |                                                                                           | $7.84       |
| Bromocriptine (Parlodel)   | 2.5mg Tab, 5mg Capsule | --                                                    |           |                                                                                           | $135.14     |
| Metronidazole (Flagyl)     | 250mg, 500mg Tab    | --                                                      |           |                                                                                           | $7.82       |
| Propranolol (Inderal)      | 20mg/5mL, 40mg/5mL Oral Solution; 60mg, 80mg, 120mg, 160mg ER Cap.; 10mg, 20mg, 40mg, 60mg, 80mg Tab | --        |                                                                                           | $14.72      |
| Nadolol (Corgard)          | 20mg, 40mg, 80mg Tab | --                                                      |           |                                                                                           | $46.84      |
| Spironolactone (Aldactone) | 25mg, 50mg, 100mg Tab | --                                                      |           |                                                                                           | $8.55       |
| Furosemide (Lasix)         | 10mg/mL, 40mg/5mL Oral Solution; 20mg, 40mg, 80mg Tab | --        |                                                                                           | $0.79       |
EVALUATION CRITERIA FOR APPROVAL/EXCEPTION CONSIDERATION

Below are the coverage criteria and required information for each agent. These coverage criteria have been reviewed approved by the HPSJ Pharmacy & Therapeutics (P&T) Advisory Committee. For conditions not covered under this Coverage Policy, HPSJ will make the determination based on Medical Necessity as described in HPSJ Medical Review Guidelines (UM06).

**Hepatic Encephalopathy Prophylaxis**

*Lactulose (Generlac), Metronidazole (Flagyl), Neomycin (Neo-Fradin), Bromocriptine (Parlodel), Rifaximin (Xifaxan)*

- **Coverage Criteria:** None
- **Limits:** None
- **Required Information for Approval:** N/A

**Rifaximin (Xifaxan) 550 mg tablets**

- **Coverage Criteria:**
  - For use in Hepatic encephalopathy, Xifaxan is reserved for treatment failure of compliant use of lactulose evidenced by consistent lactulose fills.
  - For use in IBS-D, Xifaxan is reserved for patients who have failed treatment with at least one antispasmodic, one TCA, and loperamide; or failed treatment with at least one antispasmodic and one TCA for use in abdominal pain relief.

- **Limits:**
  - Quantity limit: Restricted to 42 tablets per 14 days.
  - Fill limit: Restricted to 3 fills per 365 days.

- **Required Information for Approval:** Proper chart note documentation and pharmacy fill history of at least one antispasmodic and one TCA for use in antispasmodic relief and at least one antispasmodic, one TCA, and loperamide for use in IBS-D.

**Variceal Bleeding Prophylaxis**

*Propranolol (Inderal), Nadolol (Corgard)*

- **Coverage Criteria:** None
- **Limits:** None
- **Required Information for Approval:** N/A

**Treatment of Ascites**

*Spironolactone (Aldactone), Furosemide (Lasix)*

- **Coverage Criteria:** None
- **Limits:** None
- **Required Information for Approval:** N/A
Spontaneous Bacterial Peritonitis Prophylaxis

Sulfamethoxazole/Trimethoprim (Septra, Bactrim); Ciprofloxacin (Cipro) 500 mg, 750 mg tablets

- **Coverage Criteria:** None
- **Limits:** None
- **Required Information for Approval:** N/A

Ciprofloxacin (Cipro) 100 mg, 250 mg tablets

- **Coverage Criteria:** None
- **Limits:** 28 tablets per 30 days
- **Required Information for Approval:** N/A

Treatment of Hepatitis B

Entecavir (Baraclude), Adefovir Dipivoxil (Hepsera)

- **Coverage Criteria:** Documentation of appropriate diagnosis is required.
- **Limits:** None
- **Required Information for Approval:** Chart notes and titers indicating that the patient has an active Hepatitis B infection.
- **Other Notes:** Medication is to be dispensed by HPSJ’s designated specialty pharmacy.

#### CLINICAL JUSTIFICATION

Cirrhosis is an irreversible disease caused by various toxicants and infectious etiologies. While cirrhosis is irreversible, symptoms of ascites and progression of disease can be halted with abstinence from the offending toxicant, use of antivirals (if applicable), and use of prophylactic therapies.

According to the American Association for the Study of Liver Disease (AASLD), initial treatment for overt hepatic encephalopathy is lactulose; rifaximin was studied in patients concurrently using lactulose, and thus efficacy is only demonstrated in these patients.\(^1\) AASLD and EASL also recommend secondary prophylaxis after an episode of overt hepatic encephalopathy.\(^1\) For primary prophylaxis of variceal bleeding, AASLD recommends Non-Specific Beta-Blockers (NSBBs) such as propranolol or nadolol, carvedilol, or endoscopic variceal therapy; first-line therapy for secondary prophylaxis is combination of NSBB+EVL, unless the patient received transjugular intrahepatic portosystemic shunt (TIPS).\(^2\) AASLD guidelines for ascites name sodium restriction (2000 mg per day) and diuretics (oral spironolactone with or without oral furosemide) as first-line treatment in patients with cirrhosis and ascites.\(^3\) AALSD guidelines also recommend primary prophylaxis of SBP in patients with cirrhosis and ascites, if the ascitic fluid protein < 1.5 g/dL along with impaired renal function (SCR ≥ 1.2, BUN ≥ 25, or serum Na ≤ 130) or liver failure (Child Pugh Score ≥ 9 and bilirubin ≥ 3). These guidelines also recommend long-term use of antibiotics in patients who have survived an episode of SBP.\(^3\) First-line options include sulfamethoxazole/trimethoprim and norfloxacin; however, norfloxacin is no longer available in the United States due to manufacturer discontinuation.\(^4\) In patients with immune-active chronic hepatitis B (CHB)—defined as elevation of ALT > 2 ULN, or evidence of significant histological disease plus elevated HB DNA > 2,000 IU/mL (HBeAg negative) or above 20,000 IU/mL (HbeAg positive), AASLD recommends Peg-IFN, entecavir, or tenofovir.\(^5\)
REFERENCES


REVIEW & EDIT HISTORY

<table>
<thead>
<tr>
<th>Document Changes</th>
<th>Reference</th>
<th>Date</th>
<th>P&amp;T Chairman</th>
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</thead>
<tbody>
<tr>
<td>Creation of Policy</td>
<td>HPSJ Formulary Criteria</td>
<td>--</td>
<td>Allen Shek, PharmD, BCPS</td>
</tr>
<tr>
<td>Update to Policy</td>
<td>HPSJ Coverage Policy – Gastrointestinal Disorders – Liver Disease 2015-09.docx</td>
<td>9/2015</td>
<td>Jonathan Szkotak, PharmD, BCACP</td>
</tr>
<tr>
<td>Update to Policy</td>
<td>HPSJ Coverage Policy – Gastrointestinal Disorders – Liver Disease 2017-02.docx</td>
<td>2/2017</td>
<td>Johnathan Yeh, PharmD</td>
</tr>
<tr>
<td>Update to Policy</td>
<td>HPSJ Coverage Policy – Gastrointestinal Disorders – Liver Disease 2018-09.docx</td>
<td>9/2018</td>
<td>Johnathan Yeh, PharmD</td>
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</tbody>
</table>

Note: All changes are approved by the HPSJ P&T Committee before incorporation into the utilization policy

Please review the Hepatitis C Coverage Policy for coverage criteria of hepatitis C treatments.

All anti-retroviral and substance use disorder medications not mentioned in this coverage policy are specifically carved out from Medi-Cal Managed Care Plans, and should be billed directly to Medi-Cal Fee-For-Service. The Managed Medi-Cal Prescription Drug Carve-Out list can be found at www.hpsj.com/medication-coverage-policies/ or www.hpsj.com/pharmacy. Please note that Medi-Cal FFS may require submission of a Treatment Authorization Request (TAR) to determine appropriateness of the treatment prior to coverage.