### Hepatitis Diagnosis and Treatment

**OBJECTIVE**

The objective of this Clinical Practice Guideline (CPG) is to provide evidence-based practice recommendations for the diagnosis and treatment of Hepatitis. The CPG discusses goals of care management for the population and outlines the organizations that WellCare aligns with regarding Hepatitis and relevant Measureable Health Outcomes.

**OVERVIEW**

Viral hepatitis is an infection that causes liver inflammation and damage that leads to swelling that occurs when tissues of the body become injured or infected. This inflammation can damage organs. Viruses are the most common cause of hepatitis, but the condition can also be caused by other infections, heavy alcohol use, toxins, certain medications, and autoimmune disease.¹ There are five types of hepatitis:²

- Hepatitis A and E typically spread through contact with food or water that has been contaminated by an infected person’s stool. People may also get hepatitis E by eating undercooked pork, deer, or shellfish.
- Hepatitis B, C, and D spread through contact with an infected person’s blood; Hepatitis B and D can spread through contact with other body fluids (e.g., sharing drug needles, having unprotected sex).
- Hepatitis A and E viruses typically cause only acute, or short-term, infections and the virus goes away.
- Hepatitis B, C, and D viruses can cause acute and chronic, or long-lasting, infections.

When the cause of hepatitis is undetermined, it may be referred to as “non-A–E hepatitis” or “hepatitis X”; this type is often acute however it can become chronic. More information on the types of hepatitis are in the Addendum.

Hepatitis B, C, and D afflict more than half a billion people worldwide and are responsible for more than a million deaths a year. Chronic infection with these viruses can lead to cirrhosis of the liver, end-stage liver disease, and liver cancer.¹ The Centers for Disease Control and Prevention (CDC) report that in 2014* the number of new cases by type were: A – 1,239; B – 2,791; and C – 2,204. There were 8,081 deaths due to hepatitis in 2014.³

* The most current year’s data.

While some individuals are asymptomatic, common symptoms include:

- Loss of appetite
- Nausea and vomiting
- Diarrhea
- Dark-colored urine and pale bowel movements
- Stomach pain
- Jaundice, yellowing of skin and eyes

The severity of hepatitis varies from mild to serious; some may develop cirrhosis or liver cancer while hepatitis goes away by itself or have success with medication. Vaccines are available for some types of hepatitis as well.⁴

For screening information related to Hepatitis, visit the United States Preventive Services Task Force (USPSTF) website at [https://www.uspreventiveservicestaskforce.org](https://www.uspreventiveservicestaskforce.org). In addition, refer to the following preventive CPGs: *Adult (HS-1019)* and *Older Adults (HS-1063)*.
Hierarchy of Support

**GUIDELINE HIERARCHY**

CPGs are updated annually or as necessary due to updates made to guidelines or recommendations by the American Association for the Study of Liver Diseases (AASLD). When there are differing opinions noted by national organizations, WellCare will default to the member’s benefit structure as deemed by state contracts and Medicaid / Medicare regulations. If there is no specific language pertaining to the diagnosis and treatment of hepatitis, WellCare will default (in order) to the following:

- National Committee for Quality Assurance (NCQA);
- United States Preventive Services Task Force (USPSTF), National Quality Strategy (NQS), Agency for Healthcare Research and Quality (AHRQ);
- Specialty associations, colleges, societies, etc. (e.g., American Academy of Family Physicians, American Congress of Obstetricians and Gynecologists, American Cancer Society, etc.).

Links to websites within the CPGs are provided for the convenience of Providers. Listings do not imply endorsement by WellCare of the information contained on these websites. NOTE: All links are current and accessible at the time of MPC approval.

WellCare aligns with the AASLD on the topic of hepatitis diagnosis and treatment. Highlights from their respective publications are noted below.

**AMERICAN ASSOCIATION FOR THE STUDY OF LIVER DISEASES (AASLD)**

**Hepatitis B**

The American Association for the Study of Liver Diseases (AASLD) published a guideline for the treatment of chronic hepatitis B in adults and children. This guideline focuses on using antiviral therapy in chronic HBV infection and does not address other related and important issues, such as screening, prevention, and surveillance. The full AASLD guideline on Hepatitis B can be found [here].

In addition, the following systematic reviews support the guideline and were published in January 2016:

- Antiviral therapy for chronic hepatitis B viral infection in adults: A systematic review and meta-analysis
- Antiviral therapy in management of chronic hepatitis B viral infection in children: A systematic review and meta-analysis
- Antiviral therapy in chronic hepatitis B viral infection during pregnancy: A systematic review and meta-analysis

**Hepatitis C**

The AASLD published a guideline on recommendations for testing, managing, and treating hepatitis C. Topics include:

- HCV Testing and Linkage to Care
- When and in Whom to Initiate HCV Therapy
- Overview of Cost, Reimbursement, and Cost-effectiveness Considerations for Hepatitis C Treatment Regimens
- Monitoring Patients Who Are Starting HCV Treatment, Are on Treatment, or Have Completed Therapy
- Not Recommended Regimens In HCV Treatment

The full AASLD guideline on Hepatitis C can be found [here].

**Evidence Based Practice**

**AGENCY FOR HEALTHCARE RESEARCH AND QUALITY (AHRQ)**

The Agency for Healthcare Research and Quality (AHRQ) has published the following report(s):

- Interventions To Improve Patient Adherence to Hepatitis C Treatment: Comparative Effectiveness

Patients with chronic hepatitis C often have difficulties adhering to antiviral therapy due to the complexities of treatment and the adverse events commonly experienced. This Comparative Effectiveness Review (CER) systematically assesses the comparative benefits and harms of treatment adherence interventions for adults.
receiving combination antiviral therapy for chronic hepatitis C.

- **Treatment for Hepatitis C Virus Infection in Adults**[1](click here)
  This report systematically reviews the comparative benefits and harms of current antiviral treatment regimens for chronic hepatitis C virus (HCV) infection in treatment-naive adults.

### MEASUREMENT OF COMPLIANCE

WellCare is committed to adhering to the measures and standards published by the Centers for Medicare and Medicaid Services (CMS) and the National Committee for Quality Assurance (NCQA). Please reference WellCare’s Clinical Policy Guiding Document titled *Quality Improvement*.

NOTE: To access Clinical Policy Guiding Documents visit [www.wellcare.com](http://www.wellcare.com) – select the Provider tab, then “Tools” and “Clinical Guidelines”.

### Care Management

The goals for Care Management is to support the member's ability to self-manage the underlying condition of Hepatitis, minimize symptoms and complications of Hepatitis, preventing the spread of infection, and remove barriers preventing the member from achieving those goals. Primary symptoms of Hepatitis to educate member on include:

- Abdominal discomfort (especially on the right side, below ribs)
- Bruising/bleeding
- Confusion
- Dark urine
- Distended abdomen
- Feeling tired
- Itchy skin
- Jaundice (yellow skin/whites of eyes)
- Joint pain
- Loss of appetite
- Muscle aches
- Nausea/vomiting
- Pale colored stools

Integrated care management of Hepatitis involves:

- Educate member on signs and symptoms to report to provider
- Educate member on preventing spread of infection
- Assess for and assist with barriers to adherence to treatment plan

### MEASURABLE HEALTH OUTCOMES

Targeted Health Outcomes (Extended Program Goals) result from successful member self-management (see Case Management Objectives).

1. The Member experiences no symptoms requiring acute medical care and intervention. The case manager compares the recent utilization frequency for Hepatitis to the frequency prior to CM engagement. CM monitors for ED and inpatient authorization/utilization related to the primary diagnosis of Hepatitis. In absence of ED and inpatient utilization, authorizations and claims data, or to otherwise demonstrate less frequent need for acute medical intervention, CM may use Provider and/or Member narrative.

2. The Member reports fewer or lessening symptoms over a specific period of time after the start of Case Management engagement. Member-specific goals should reference individual symptoms. Compare member's responses to gastrointestinal symptom assessment questions on initial and subsequent assessments.

### CASE MANAGEMENT GOALS

Case Goals should target specific care gaps and/or adherence issues, and measure the member’s progress towards self-management and adherence which will lead to the targeted health outcomes above. Examples:

1. The Member’s prescription refills demonstrate at least an 80% adherence rate (verified by claims or member/provider narrative) over last 30 days.

2. The Member is adherent to routine labs (such as serum testing and urinalysis), and other diagnostics prescribed by the physician (verified by claims or member/provider narrative) over last 30 days.

3. Specific for Members requiring hospitalization: The Member participates in provider follow-up visit within 7 days of hospital discharge.
CASE MANAGEMENT OBJECTIVES

Case Management Objectives should focus on improving the member’s self-management skills including:

- Frequent handwashing to prevent other infections
- Follow up visits as per treatment plan
- Taking medications as prescribed
- Maintain diet / fluid intake as recommended
- Report new or worsening symptoms to PCP/Specialist
- Assist member/caregiver with addressing identified barrier(s) to managing hepatitis (e.g., transportation, access to and follow up with Specialist appointments, obtaining medications)
- Identify, if appropriate, for and eligible for needle exchange program and refer if eligible

MEDICAL BEHAVIORAL INTEGRATION

There is a high prevalence of behavioral health and substance use disorders in people with Hepatitis C. In one study, 93% of Veterans with Hepatitis C had one or more psychiatric or substance use disorder.17 People with mental illness are at a greater risk for exposure to infectious diseases such as chronic hepatitis, due to poor judgement and risky behaviors such as needle sharing, which is the most common risk factor for Hepatitis C infection. Given the high rate of co-morbidity between opioid abuse and infectious hepatitis, people in treatment for opioid abuse should be screened for Hepatitis C and education on the virus should be given. Two other key pieces to preventing Hepatitis C transmission are having access to clean needles and having access to substance abuse treatment, including medication assisted treatment.18

Being diagnosed with a behavioral health or substance use disorder can affect the diagnosis, linkage to care, disease progression and candidacy for antiviral treatment, however it should not preclude antiviral treatment. While patients with psychotic symptoms may have a more difficult time coping with chronic disease, have an increased suicide risk and difficulty adhering to complex antiviral treatment, integration of behavioral health treatment with medical care can improve candidacy for antiviral treatment, increase adherence, decrease substance use and increase overall treatment outcomes through support, education and motivational interviewing.17

Another concern regarding those with behavioral health conditions and antiviral treatment is neuropsychiatric side effects of hepatitis treatment. These side effects include depressive symptoms, concentration and memory problems, fatigue, anger, irritability, sleep disturbances, anxiety and suicidal thoughts. These side effects can worsen behavioral health symptoms and so antiviral treatment may be deferred until depression can be stabilized or an increase in support system or stable housing can be found. Side effects of antiviral treatment are also similar to drug and alcohol withdrawal symptoms which can complicate substance use treatment.17 It is also important to note that alcohol use can accelerate the progression of Hepatitis C liver disease, so education and integrated substance use treatment is important in this regard as well.18 In addition, this population may need more frequent doctor appointments to monitor for liver function and to detect any dangerous medication interactions from psychotropic medications. Medications for behavioral health conditions may have to be changed to reduce liver toxicity that can occur with some psychotropic medications such as Depakote.17

MEMBER EDUCATIONAL RESOURCES

There are currently no Krames educational materials available for this topic.

Related WellCare Guidelines

In addition to the information contained in this document, please reference the following CPGs: HIV Screening and Antiretroviral Treatment (HS-1024); Opioid Use Disorder and Treatment (HS-1053); and Substance Use Disorders (HS-1031). NOTE: Clinical Policies can be accessed by going to www.wellcare.com – select the Provider tab, then “Tools” and “Clinical Guidelines”.

References

HEPATITIS DIAGNOSIS AND TREATMENT
HS-1050


Disclaimer

Clinical Practice Guidelines (CPGs) made available by WellCare are informational in nature and are not a substitute for the professional medical judgment of treating physicians or other health care practitioners. CPGs are based on information available at the time and may not be updated with the most current information available at subsequent times. Individuals should consult with their physician(s) regarding the appropriateness of care or treatment options to meet their specific needs or medical condition. Disclosure of a CPG is not a guarantee of coverage and is not intended to be used for Utilization Management Decisions or for claims. Members of WellCare Health Plans should consult their individual coverage documents for information regarding covered benefits. WellCare does not offer medical advice or provide medical care, and therefore cannot guarantee any results or outcomes. WellCare does not warrant or guarantee any results or outcomes. WellCare does not warrant or guarantee any results or outcomes. WellCare does not warrant or guarantee any results or outcomes.

Medical Policy Committee Approval History

Date History and Revisions by the Medical Policy Committee
5/3/2018 • Approved by MPC. No changes.
7/24/2017 • Approved by MPC. New.

Addendum

TYPES OF HEPATITIS

<table>
<thead>
<tr>
<th></th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basics</td>
<td>Transmitted by: eating food made by an infected person who did not wash his or her hands after using the bathroom; drinking untreated water or eating food washed in untreated water; placing a</td>
<td>Transmitted through contact with an infected person’s blood, semen, or other body fluids. This includes being born to a mother with HBV, unprotected sex with an infected person; sharing drug needles</td>
<td>Transmitted by sharing drug needles or other drug materials with an infected person; accidental stick with a needle that was used on an infected person; being tattooed or pierced with tools that were</td>
<td>Transmitted the same way that HBV is spread. It can be acute or chronic infection, or both.</td>
<td>Transmitted by Drinking contaminated water (common in developing countries, including parts of Africa, Asia, Central America, and the Middle East).</td>
</tr>
</tbody>
</table>

Clinical Practice Guideline

Original Effective Date: 7/24/2017 - Revised: 5/3/2018
| Prevalence | Relatively uncommon. Approximately 2,500 cases. Common in developing countries with poor sanitation and limited access to clean water (e.g., parts of Africa, Asia, Central and South America, and Eastern Europe). | Researchers estimate that about 850,000 to 2.2 million people in the U.S. A vaccine was introduced in 1991 which has helped lower new cases by 82%. Most with HBV were infected before the vaccine was available. In the United States, 47 to 95 percent of people with chronic HBV were born outside the U.S., in parts of the world where HBV is more common. Chronic hepatitis B is more common in Africa, Asia, and parts of the Middle East, Eastern Europe, South and Central America. | HCV is the most common chronic viral infection found in blood and spread through contact with blood. Around 2.7 to 3.9 million people in the U.S. have chronic HCV. Many don't have symptoms and don't know they are infected. About 75 percent of U.S. adults who have hepatitis C are Baby Boomers and born between 1945 -1965. The number of new HCV cases has increased since 2006, especially among people <age 30 who inject heroin or misuse prescription opioids and inject them. | Hepatitis D is not common in the U.S. and is more common in other parts of the world, including Eastern and Southern Europe; the Mediterranean region and Middle East; parts of Asia, including Mongolia; Central Africa; and the Amazon River basin in South America. Most cases are in developing countries; it spreads through drinking contaminated water. In developed countries, such as the U.S., HEV is typically spread from animals to people, when people eat undercooked pork or wild game, such as deer. Transmission through blood transfusion is rare. |
| --- | --- | --- | --- | --- | --- |
| | or other drug materials with an infected person; accidental stick with a needle that was used on an infected person; being tattooed or pierced with tools that were used on an infected person and weren't properly sterilized; contact with the blood or open sores of an infected person; or using an infected person's razor, toothbrush, or nail clippers. | used on an infected person and were not properly sterilized; contact with the blood or open sores of an infected person; using an infected person's razor, toothbrush, or nail clippers; being born to a mother with HCV; unprotected sex with an infected person. Acute hepatitis C is a short-term infection. Symptoms can last up to 6 months. Chronic hepatitis C is a long-lasting infection; 75-85% of people with acute hepatitis C develop chronic hepatitis C. In most cases, people are able to recover from acute HDV and HBV and the viruses go away. In <5% of people with a co-infection, both infections become chronic and do not go away. A superinfection occurs in those with chronic HBV and then become infected with HDV. Severe acute hepatitis symptoms occur. Up to 90% of people with a superinfection are not able to fight off the HDV and develop chronic HDV (and have chronic HDV and HBV). | eating undercooked pork or wild game. More common in developed countries, such as the U.S., Australia, Japan, and parts of Europe and East Asia. Hepatitis E typically causes acute, or short-term, infection. |
### Individuals At Risk

<table>
<thead>
<tr>
<th>America, Sub-Saharan Africa, parts of Asia, and the Pacific Islands.</th>
<th>Screening efforts and more effective HCV treatments are identifying and curing more people with HCV could be a rare disease by 2036.</th>
<th>HDV rarely spreads from mother to child during birth. HDV occurs only in people who have HBV. People are more likely to have HDV in addition to HBV if they are injection-drug users; have lived with or had sex with someone who has HDV; or are from an area of the world where HDV is more common.</th>
<th>Hepatitis E is more common in developing countries, where sanitation is poor and access to clean water is limited. About 20% of the U.S. population has had HEV. Severe infections can occur, especially in pregnant women. The types of HEV that are common in developed countries are often mild and cause no symptoms.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Those at most risk include those traveling to developing countries; having sex with an infected person; are a man who has sex with men; use illegal drugs, including drugs that are not injected; or live with or care for someone who has HAV.</td>
<td>People are more likely to get hepatitis B if they are born to a mother who has hepatitis B (spread from mother to child during birth). People are more likely to have HBV if they were born in a part of the world where hepatitis B is more common; were born in the U.S. and did not receive the HBV vaccine as an infant, and have parents who were born in an area where hepatitis B was especially common. Screening is recommended for those who are pregnant; were born in an area of the world where chronic HBV is more common; did not receive the HBV vaccine as an infant and have parents who were born in an area where chronic HBV was especially common (e.g., sub-Saharan Africa, parts of Asia, or the Pacific Islands); are HIV positive; have injected drugs; are a man who has sex with men; have lived with or had sex with a person who has HBV; have an increased chance of infection due to other factors.</td>
<td>In the U.S., injecting drugs is the most common way that people get HCV. Injection drug users, those who had a blood transfusion or organ transplant before July 1992; have hemophilia and received clotting factor before 1987; have been on kidney dialysis; have been in contact with blood or infected needles at work; have had tattoos, body piercings; worked / lived in a prison; born to a mother with HCV; infected with HIV; had &lt;1 sex partner in the last 6 months or have a history of sexually transmitted disease; or men who have sex with men.</td>
<td></td>
</tr>
</tbody>
</table>

### Symptomology

| Symptoms may not develop for 2-6 weeks after contact with the virus. Older children and adults are more likely to have symptoms. People with HAV typically get better without treatment after a few weeks. In some cases, some may no symptoms while some have symptoms of acute HBV within 2 to 5 months after they come in contact with the virus. Symptoms may include: dark yellow urine; feeling tired; fever; gray-colored stools; joint pain; loss of appetite; nausea; abdominal pain; vomiting; | Some may no symptoms of acute HBV within 2 to 5 months after they come in contact with the virus. Symptoms may include: dark yellow urine; feeling tired; fever; gray-colored stools; joint pain; loss of appetite; nausea; abdominal pain; vomiting; | Most do not have symptoms. For this reason, HCV screening is important. Some with an acute HCV infection may have symptoms within 1 to 3 months after exposure. Symptoms may include: dark yellow urine; feeling tired; fever; gray-colored stools; joint pain; loss of appetite; nausea; abdominal pain; vomiting; | Symptoms include feeling tired; nausea and vomiting; poor appetite; pain over the liver (upper abdomen); darkening of the color of urine; lightening of the color of stool; yellowish tinge to the whites of the eyes, skin. Most people with chronic HDV have few symptoms. Most do not have symptoms while some people have symptoms 15 to 60 days after infections. Symptoms may include feeling tired; nausea and vomiting; poor appetite; pain over the liver; darkening of the color of urine; lightening of the color of stool; yellowish tinge to the |
symptoms last up to 6 months and can include:
dark yellow urine; feeling tired; fever;
gray-colored stools; joint pain; loss of appetite; nausea; pain in the abdomen; vomiting; yellowish eyes/skin

yellowish eyes, skin. Infants and children younger than age 5 typically don't have symptoms of acute HBV. Older children and adults are likely to have symptoms.

The chances of developing chronic HBV are greater if the person was infected as a young child. About 90% of infants infected with HBV develop a chronic infection. About 25-50% of children infected between the ages of 1 and 5 years develop chronic infections. Among people infected during adulthood, only about 5% develop chronic HBV.

Complications

Infection does not lead to long-term complications because the infection only lasts a short time. Complications can include:
- Transplant
- Liver Failure

Cirrhosis
Liver failure
Liver cancer

Cirrhosis
Liver failure
Liver cancer

Acute
Liver failure; hepatitis D and B infections are more likely to lead to acute liver failure than hepatitis B infection alone.

Chronic
Cirrhosis
Liver failure
Liver cancer

Acute
Most recover from acute hepatitis E without complications.

Acute liver failure; more common in pregnant women* and people who have other liver diseases

Chronic
People with weakened immune systems may develop cirrhosis, liver failure

Complications

Infection does not lead to long-term complications because the infection only lasts a short time. Complications can include:
- Transplant
- Liver Failure

Cirrhosis
Liver failure
Liver cancer

Cirrhosis
Liver failure
Liver cancer

Acute
Liver failure; hepatitis D and B infections are more likely to lead to acute liver failure than hepatitis B infection alone.

Chronic
Cirrhosis
Liver failure
Liver cancer

Acute
Most recover from acute hepatitis E without complications.

Acute liver failure; more common in pregnant women* and people who have other liver diseases

Chronic
People with weakened immune systems may develop cirrhosis, liver failure

Vaccine
Available
Yes
Yes
No
No
No

Diagnosis

Symptoms and blood test.
Medical and family history, physical exam, and blood tests.
Medical history, physical exam, and blood tests.
Medical history, a physical exam, and blood tests.
Symptoms and blood tests.