Hepatitis C Virus (HCV) Infection is an important cause of morbidity and mortality in the US and worldwide. Common disease outcomes of chronic HCV infection include end-stage liver disease and hepatocellular carcinoma, much of which can be avoided with early diagnosis and treatment. An estimated 3.2 million Americans are chronically infected with HCV. Of these, between 60% and 70% will develop chronic liver disease and between 4% and 24% will develop cirrhosis. Mortality due to cirrhosis or hepatocellular carcinoma will be an outcome for between 1% and 5%.1,2,3

HCV diagnostics and treatment has been a particularly dynamic field in medicine. Molecular testing for HCV virus has an important clinical role in diagnosing the infection and in selecting therapy and measuring the therapeutic response of treatment regimens. Molecular tests used to diagnose, determine therapy and measure response are listed as follows:

- **Hepatitis C Viral RNA Genotype, LIPA** analyzes areas of the HCV genome. Candidates for LIPA testing are candidates for HCV treatment whose regimens and length of therapy may be impacted by results.

- The qualitative HCV RNA tests use either polymerase chain reaction (PCR) or a transcription-mediated amplification (TMA) to report the presence of HCV virus in the blood. Qualitative tests report results as detected or not detected and are used to diagnose acute or chronic HCV infection or to determine a resolution of the virus following therapy or spontaneously.4

- **Hepatitis C Virus (HCV) RNA Detection and Quantification by Real-Time Reverse Transcription-PCR (RT-PCR)** may be used to diagnose patients with a recent exposure prior to the appearance of antibodies, confirm a diagnosis of chronic HCV infection, establish a baseline diagnosis, or monitor disease progression and/or therapeutic response.5
Nucleic acid testing (NAT) for HCV RNA is used to follow positive screening tests to confirm the presence of current infection. NAT uses reverse transcriptase polymerase chain reaction (RT-PCR) amplification for qualitative RNA detection. If NAT is nonreactive, the screening test may have been positive due to a previous exposure to the HCV virus in which infection has resolved or the screening test may have yielded a false positive result. A reactive RNA HCV test indicates the presence of current HCV infection. In some cases, it may be appropriate to follow HCV RNA testing with a second.6

**COVERAGE CRITERIA**

HCV screening is medically necessary for any of the following:

- Members with persistently elevated liver enzymes without an obvious explanation,
- One-time birth cohort screening for members born between the years 1945 and 1965,
- Members with risk factors including any of the following:
  - Injection drug users including members who have ever used injection drugs, or
  - Intranasal drug users including members who have ever used intranasal drugs, or
  - Recipients of clotting factor concentrates produced prior to 1987, or
  - Recipients of blood, blood products or organ transplantation prior to July 1992, or
  - Recipients of blood or blood products from a donor who later tested positive for HCV infection, or
  - Members born to HCV infected mothers, or
  - Known exposure to HCV-positive blood, or
  - Exposure through sexual contact, or
  - HIV infection, or
  - Long-term hemodialysis, or
  - History of incarceration, or
  - From immigrant populations who received blood products or underwent invasive medical procedures from low resource countries.7 8 9

HCV screening is recommended for members with any of the following undefined risk factors:

- Recipients of transplanted tissue after 1992, or
- Non-injection drug users, or
- Tattoos or body piercings, or
- Multiple sexual partners and/or a medical history significant for sexually transmitted diseases, or
- Long-term sexual partner with HCV infection.10 11

Coverage criteria for molecular tests for HCV are listed below:
For diagnostics, the CDC recommends antibody screening tests followed by confirmation tests. Current FDA approved HCV screening test kits available for use in the US include but may not be limited to the following:

- Enzyme immunoassays (EIA) using HCV-encoded recombinant antigens. The two available EIA tests include Abbott HCV EIA 2.0, Abbott Laboratories, Abbott Park, Illinois, and ORTHO® HCV Version 3.0 ELISA, Ortho-Clinical Diagnostics, Raritan, New Jersey.

- Enhanced chemiluminescence immunoassay (CIA) test kits. The two available CIA tests include (VITROS® Anti-HCV assay, Ortho-Clinical Diagnostics, Raritan, New Jersey) and Advia Centaur HCV (Bayer Laboratories). 

- OraQuick HCV Rapid Antibody Test (OraSure Technologies) is a recently developed rapid assay using fingerstick capillary blood and venipuncture whole blood with a sensitivity and specificity similar to EIA and CIA.

- Microparticle Immunoassay (MEIA) marketed under the trade name AxSYM Anti-HCV by Abbott Laboratories, Abbott Park, Illinois.

- Chemiluminescent Immunoassay (CMIA) marketed under the trade name Architect Anti-HCV by Abbott Laboratories, Abbott Park, Illinois.

- Confirmation testing using HCV RNA testing is medically necessary as a follow up for all screening tests. Nucleic acid testing (NAT) for HCV RNA uses reverse transcriptase polymerase chain reaction (RT-PCR) amplification for qualitative RNA detection. If NAT is nonreactive, the screening test may have been positive due to a previous exposure to the HCV virus in which infection has resolved or the screening test may have yielded a false positive result. A reactive RNA HCV test indicates the presence of current HCV infection. In some cases, it may be appropriate to follow HCV RNA testing with a second. FDA-approved diagnostic NATs include AMPLICOR® Hepatitis C Virus (HCV) Test, version 2.0 and COBAS AMPLICOR® Hepatitis C Virus Test, version 2.0 (Roche Molecular Systems, Branchburg, New Jersey), which have a lower limit of detection of approximately 50 IU/mL.

- Qualitative HCV RNA tests using polymerase chain reaction (PCR) or a transcription-mediated amplification (TMA) report the presence of HCV in the blood as a qualitative value indicating chronic or acute HCV infection.

- Hepatitis C Virus (HCV) RNA Detection and Quantification by Real-Time RT-PCR may be used to diagnose patients with a recent exposure prior to the appearance of antibodies, confirm a diagnosis of chronic HCV infection, establish a baseline diagnosis, or monitor disease progression and/or therapeutic response.

- bDNA assay tests use signal amplification technology that hybridize viral nucleic acid to specific probes to facilitate amplification for detection. bDNA is less technical than other RNA methods but sensitivity is lower as compared to PCR techniques.

- HCV RNA testing is medically necessary for the following:
  - Members beginning a HCV treatment regimen, in which case quantitative RNA screening would be required to determine baseline values,
  - HCV diagnostics in the event of a recent exposure in which case a negative result on a screening tests could not be trusted. In most cases, detectable antibodies develop between two and six months following exposure,
- HCV diagnostics for members who are immunocompromised due to hemodialysis, post solid organ transplant, or advanced HIV infection in the event of negative screening tests or in lieu of antibody screening not expected to be diagnostic,

- Members currently receiving HCV treatment in which quantitative testing measures therapeutic response throughout treatment course,

- To determine whether a member has cleared HCV infection, either secondary to HCV therapy or spontaneously, in which case qualitative testing would report a viral load that is undetected.

The CDC recommends, testing for HCV RNA or follow-up testing for HCV antibody for persons who might have been exposed to HCV within the past 6-months.

The following molecular tests for HCV infection are not currently considered medically necessary or are considered experimental / investigational:

- Molecular RNA testing using Recombinant Immunoblot Assay (RIBA) HCV 3.0 Strip Immunoblot Assay (Novartis Vaccines and Diagnostics) is not medically necessary. RIBA was previously recommended by the CDC as a confirmatory test, but is no longer recommended and is no longer available.

- Antinuclear antibodies (ANA) are common in the HCV infection population; however, researchers have yet to determine the clinical importance of ANA in therapy selection and measuring therapeutic response.

MEDICAL BACKGROUND

Hepatitis has been a public health problem documented as early as 3000 B.C. In ancient Sumaria, jaundice was recorded on clay tablets in the first handbook of medicine attributable to an evil being named Aihazu who attacked the liver. The transmission of hepatitis was documented in ancient Greece and Rome during the Middle-Ages, and upon the discovery of the New World. In more recent history, epidemics of hepatitis were noted during the French Revolution, the American Civil War, and the Second World War.

Although hepatitis has a public health history spanning more than 5000 years, the Hepatitis C virus (HCV) as one of the several causes of transmissible hepatitis was only first identified in 1989. As a result, HCV has a relatively short history of scientific published research leaving many aspects of the disease still in question. Medical literature has currently identified six different HCV genotypes. In the US, around 75% of cases belong to the first genotype, followed by 2 and 3 in frequency. Treatment options are improving but vaccine studies have failed. Also, unknown factors seem to dictate the natural history of the disease. Typically, disease progression begins with liver inflammation and progresses to liver disease and liver cancer. This process often occurs with no symptoms, or symptoms like fatigue, loss of appetite and general malaise which are frequently overlooked or misattributed to other problems. For this reason, HCV is termed as a silent killer. However, the natural progression of HCV is highly variable in timeframe and severity. For example, an estimated 15-25% of patients clear the infection without medical intervention.

The CDC recommends the HCV screening process begin with any one of the four antibody screening tests. Three screening tests are laboratory based requiring venipuncture and a waiting period before results are reported. However, OraQuick HCV Rapid Antibody Test (OraSure Technologies) represents a revolution in HCV screening. The OraQuick test is
administered in a similar method as a blood glucose exam and results are reported within a few minutes. In 2011, a Clinical Laboratory Improvements Amendments waiver was granted to OraQuick test by FDA to expand the testing range. The waiver allows testing to be conducted in nontraditional settings such as physician offices, hospital emergency departments, health department clinics, and other freestanding counseling and testing sites. Following a positive screening test, the CDC recommends RNA testing to confirm the presence of current infection as well as to rule out a false positive. This step is especially important because it is now the transition to healthcare is facilitated. RNA tests are used not only as a diagnostic tool, but also throughout the treatment process. HCV RNA levels are measured at baseline, monitored throughout therapy as a measure of disease progression, and following the end of therapy to determine if the infection has cleared. RNA testing can also be used alone as a diagnostic tool in the event of a recent HCV exposure, or may be used to diagnose HCV in patients who are immunosuppressed who may not form detectable antibodies to the virus identifiable by screening tests. Also, important in HCV therapy is viral genotyping. Well-established data are available regarding the very specific expected therapeutic response to therapy by each HCV genotype. For this reason, molecular testing to determine the genotype of the HCV is very important in selecting antimicrobial agents, dosage, and determining length of treatment.35

**REGULATORY INFORMATION**

No legislative mandates were found for coverage of Hepatitis C Virus testing in either Kentucky or Indiana.36

Baptist Health Plan Coverage Guidelines are created to provide members and providers with peer-reviewed, current medical information.

State and federal laws/mandates and contract language have priority over Coverage Guidelines and must be taken into consideration before eligibility for coverage is determined.

Baptist Health Plan Coverage Guidelines may or may not mirror Centers for Medicare & Medicaid Services benefits or coverage offered by any other health insurance company.

For self-funded plans, consult individual plan documents. If there is a conflict between this policy and a self-funded plan document, the provisions of the plan document will govern. In addition, coverage for Medicare Advantage members may differ. This is a result of applicable coverage statements by the Center for Medicare and Medicaid Services (CMS). The National Coverage Determinations, Local Coverage Determinations, and Local Medical Review Policies may be found at the CMS website, [http://www.cms.gov](http://www.cms.gov). Please note that for all plans, the member’s health plan benefits that are in effect on the rendered date of service must be used in coverage determinations.
## COVERAGE DETAIL

CODES INCLUDE BUT MAY NOT BE LIMITED TO THE FOLLOWING:

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<thead>
<tr>
<th>CPT® Codes</th>
<th>Description</th>
<th>Coverage Information</th>
</tr>
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<tbody>
<tr>
<td>86803</td>
<td>Hepatitis C antibody</td>
<td>Is medically necessary when criteria are met</td>
</tr>
<tr>
<td>86804</td>
<td>Hepatitis C antibody; confirmatory test (eg, immunoblot)</td>
<td>Is medically necessary when criteria are met</td>
</tr>
<tr>
<td>87520</td>
<td>Infectious agent detection by nucleic acid (DNA or RNA); hepatitis C, direct probe technique</td>
<td>Is medically necessary when criteria are met</td>
</tr>
<tr>
<td>87521</td>
<td>Infectious agent detection by nucleic acid (DNA or RNA); hepatitis C, amplified probe technique, includes reverse transcription when performed</td>
<td>Is medically necessary when criteria are met</td>
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<tr>
<td>87522</td>
<td>Infectious agent detection by (DNA or RNA); hepatitis C, quantification, includes reverse transcription when performed</td>
<td>Is medically necessary when criteria are met</td>
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<tr>
<td>86803</td>
<td>Hepatitis C antibody</td>
<td>Is medically necessary when criteria are met</td>
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<tr>
<td>ICD.9© Diagnosis Codes</td>
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<td>Coverage Information</td>
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<tr>
<td>042</td>
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<td>286.0-286.9</td>
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<tr>
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<td>Drug dependence</td>
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<td>Donors</td>
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<td>ICD.10© Codes</td>
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<td>Coagulation defects, purpura and other hemorrhagic conditions</td>
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<td>Z99.2</td>
<td>Dependence on renal dialysis</td>
<td>Is medically necessary when criteria are met</td>
</tr>
</tbody>
</table>

## REFERENCES


9. Recommendations for Testing, Managing, and Treating Hepatitis C.  Joint panel from the


25 UpToDate website. Diagnosis and evaluation of chronic hepatitis C virus infection.


SEARCH TERMS

Carcinoma
Cirrhosis
Infection
Liver
Molecular