GAMMA GLUTAMYL TRANSFERASE (GGT)

Policy Number: CMP-021
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Table of Contents

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>BACKGROUND</td>
<td>1</td>
</tr>
<tr>
<td>POLICY</td>
<td>3</td>
</tr>
<tr>
<td>REFERENCES</td>
<td>4</td>
</tr>
<tr>
<td>POLICY HISTORY/REVISION HISTORY</td>
<td>4</td>
</tr>
</tbody>
</table>

INSTRUCTIONS FOR USE

This Medical Policy provides assistance in interpreting UnitedHealthcare benefit plans. When deciding coverage, the enrollee specific document must be referenced. The terms of an enrollee's document (e.g., Certificate of Coverage (COC) or Summary Plan Description (SPD)) may differ greatly. In the event of a conflict, the enrollee's specific benefit document supersedes this Medical Policy. All reviewers must first identify enrollee eligibility, any federal or state regulatory requirements and the plan benefit coverage prior to use of this Medical Policy. Other Policies and Coverage Determination Guidelines may apply. UnitedHealthcare reserves the right, in its sole discretion, to modify its Policies and Guidelines as necessary. This Medical Policy is provided for informational purposes. It does not constitute medical advice.

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BACKGROUND

Gamma-glutamyltransferase (GGT) is an enzyme that transports amino acids; it is present in the cell membrane of nearly all human cells. It is most abundant in the kidney, liver, pancreas and intestine, but the majority of the GGT detected in serum derives from the liver. GGT is the most sensitive biomarker of hepatobiliary disease.

Obtaining a serum GGT can be useful to interpret liver enzyme alteration. Liver function tests provide an overall snapshot of liver health. The comprehensive blood chemistry profile generally includes alanine aminotransferase (ALT), aspartate aminotransferase (AST), and alkaline phosphatase (ALP), which means that liver enzyme studies are not only performed for patients with symptoms such as fatigue and pruritis suggestive of liver pathology but also patients undergoing routine examinations. Determining the significance of elevations of liver enzymes requires a comprehensive and logical approach. While the aforementioned liver enzymes do not have specificity for any particular disease, the degree of enzyme alteration and its pattern
relative to other enzymes is clinically useful. Certain patterns of liver enzyme alteration point to hepatocyte damage and some point to cholestasis. When ALT and AST rise relative to ALP and GGT, hepatocyte injury is more likely than biliary obstruction. In the case of alcoholic liver disease, GGT is elevated and the AST/ALT ratio is >2. Because biliary stasis increases the synthesis and release of ALP from bile duct epithelial cells, a preferential increase in ALP points to a cholestatic pattern, which could be seen, for example, in drug-induced liver injury.

Most of the serum ALP derives from bone and liver. Elevations can be seen with bone and liver pathology and also with sepsis. Although electrophoresis can be used to determine which ALP isoenzyme is elevated when total ALP is increased, obtaining a serum GGT is a relatively inexpensive way to gain additional information. An increase in GGT would support a liver origin for the increase in ALP, which can be seen in cholelithiasis, inflammatory diseases such as ulcerative colitis and primary sclerosing cholangitis, autoimmune diseases such as primary biliary cirrhosis, malignancy, amyloidosis and sarcoidosis. If the GGT is not elevated, a bone source for the elevated ALP is more likely, as would be the case with rickets.

GGT levels rise directly with increasing amounts of alcohol consumption and can remain elevated for weeks. For this reason, GGT levels have been used as a marker of alcohol abuse. In patients with altered mental status and those who will not quantify actual alcohol consumption, biomarkers of alcohol dependence can be helpful clinically. Nonetheless, increases in GGT related to comorbid conditions limit its specificity for this use.

Serum GGT can also be increased in other disease states including diabetes, hyperthyroidism, rheumatoid arthritis, myotonic dystrophy and obstructive pulmonary disease. It has been recommended that due to lack of specificity, GGT use be limited clinically to investigation of alkaline phosphatase elevations. Research studies are ongoing to determine its value as a biomarker for nephrotoxicity and cardiovascular disease risk.

Fasting morning specimens are preferred for laboratory measurement of serum GGT. In addition to liver injury and alcohol use, other factors, including race, body mass index, pregnancy, drugs, cigarette smoking, and age can alter serum GGT concentrations. Levels remain fairly steady with increasing age in men, although they increase with age in women.

GGT is indicated in the following circumstances:

1. To provide information about known or suspected hepatobiliary disease, for example:
   a. Following chronic alcohol or drug ingestion
   b. Following exposure to hepatotoxins
   c. When using medication known to have a potential for causing liver toxicity (e.g., following the drug manufacturer’s recommendations)
   d. Following infection (e.g., viral hepatitis and other specific infections such as amebiasis, tuberculosis, psittacosis, and similar infections)
2. To assess liver injury/function following diagnosis of primary or secondary malignant neoplasms
3. To assess liver injury/function in a wide variety of disorders and diseases known to cause liver involvement (e.g., diabetes mellitus, malnutrition, disorders of iron and mineral metabolism, sarcoidosis, amyloidosis, lupus, and hypertension)
4. To assess liver function related to gastrointestinal disease
5. To assess liver function related to pancreatic disease
6. To assess liver function in patients subsequent to liver transplantation
7. To differentiate between the different sources of elevated alkaline phosphatase activity

**POLICY**

For the following CPT code(s) in Table 1, the patient should have a diagnosis (ICD-10-CM) code(s) listed in the attached files below.

**Table 1. HCPCS Codes (Alphanumeric, CPT® AMA)**

<table>
<thead>
<tr>
<th>HCPCS Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>82977</td>
<td>Glutamyl transferase, gamma (GGT)</td>
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</tbody>
</table>

**ICD-10 Diagnosis Codes (Proven)**

When used to assess liver dysfunction secondary to existing non-hepatobiliary disease with no change in signs, symptoms, or treatment, it is generally not necessary to repeat a GGT determination after a normal result has been obtained unless new indications are present.

If the GGT is the only “liver” enzyme abnormally high, it is generally not necessary to pursue further evaluation for liver disease for this specific indication.

When used to determine if other abnormal enzyme tests reflect liver abnormality rather than other tissue, it generally is not necessary to repeat a GGT more than one time per week.

Because of the extreme sensitivity of GGT as a marker for cytochrome oxidase induction or cell membrane permeability, it is generally not useful in monitoring patients with known liver disease.
REFERENCES


POLICY HISTORY/REVISION HISTORY

<table>
<thead>
<tr>
<th>Date</th>
<th>Action/Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>01/21/2017</td>
<td>Updated ICD10 codes as per CMS recommendations. Removed ICD9 code file.</td>
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<tr>
<td>10/01/2015</td>
<td>Removed ICD9 table. Embedded ICD9/ICD10 PDF files.</td>
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</tbody>
</table>