Medical Policy
Serum Holotranscobalamin as a Marker of Vitamin B12 - Cobalamin Status

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Policy Number: 561
BCBSA Reference Number: 2.04.39

Related Policies
None

Policy
Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity Medicare HMO BlueSM and Medicare PPO BlueSM Members

Measurement of holo-transcobalamin in the diagnosis and management of Vitamin B12 deficiency is INVESTIGATIONAL.

Prior Authorization Information
Pre-service approval is required for all inpatient services for all products. See below for situations where prior authorization may be required or may not be required for outpatient services.
Yes indicates that prior authorization is required.
No indicates that prior authorization is not required.
N/A indicates that this service is primarily performed in an inpatient setting.

<table>
<thead>
<tr>
<th>Outpatient</th>
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<tbody>
<tr>
<td>Commercial Managed Care (HMO and POS)</td>
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<tr>
<td>Commercial PPO and Indemnity</td>
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<tr>
<td>Medicare HMO BlueSM</td>
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<td>Medicare PPO BlueSM</td>
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CPT Codes / HCPCS Codes / ICD Codes
Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement. Please refer to the member’s contract benefits in effect at the time of service to determine coverage or non-coverage as it applies to an individual member.
Providers should report all services using the most up-to-date industry-standard procedure, revenue, and diagnosis codes, including modifiers where applicable.

CPT Codes
There are not any specific CPT codes for this service.

Description
Vitamin B12 (cobalamin) is an essential vitamin that is required for DNA synthesis affecting red blood cell formation and methionine synthesis affecting neurologic functioning. Cobalamin deficiency can result from nutritional deficiencies or malabsorption. Clinical signs and symptoms of cobalamin deficiency include megaloblastic anemia, paresthesias and neuropathy, and psychiatric symptoms, such as irritability, dementia, depression, and psychosis. Hematologic abnormalities promptly disappear after treatment, while neurologic disorders may become permanent if treatment is delayed.

The diagnosis of cobalamin deficiency has traditionally been based on low levels of total serum cobalamin, in conjunction with clinical evidence of disease. However, this laboratory test has been found to be poorly sensitive and specific. Therefore, attention has turned to measuring metabolites of cobalamin as a surrogate marker. Holotranscobalamin (holo-TC) is a transcobalamin-vitamin B12 complex which has been investigated as a diagnostic test for vitamin B12 deficiency in symptomatic and at-risk populations, as well as an assay for monitoring response to therapy. Serum levels of holo-TC can be measured using a radioimmunoassay or enzyme immunoassay.

Examples of testing devices include HoloTC RIA and Axis-Shield HoloTC Assay from Axis-Shield. All devices used in the measurement of holotranscobalamin in the diagnosis and management of Vitamin B12 deficiency are considered investigational regardless of the commercial name, FDA status or the manufacturer.

Summary
There are inadequate data to establish holotranscobalamin testing as an alternative to either total serum cobalamin, or levels of methylmalonic acid or homocysteine in the diagnosis of vitamin B12 deficiency. While technically feasible, and likely to have diagnostic performance that approaches that of currently utilized tests, no evidence of clinical utility has been demonstrated. Since evidence of the clinical utility of the test is currently lacking, the test remains investigational.

Policy History

<table>
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<tr>
<th>Date</th>
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<tbody>
<tr>
<td>1/2016</td>
<td>Clarified coding information.</td>
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<tr>
<td>7/2014</td>
<td>Updated Coding section with ICD10 procedure and diagnosis codes, effective 10/2015.</td>
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<tr>
<td>12/2013</td>
<td>New references from BCBSA National medical policy.</td>
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<td></td>
<td>No changes to policy statements.</td>
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Information Pertaining to All Blue Cross Blue Shield Medical Policies
Click on any of the following terms to access the relevant information:

Medical Policy Terms of Use
Managed Care Guidelines
Indemnity/PPO Guidelines
Clinical Exception Process
Medical Technology Assessment Guidelines
References