Testing Serum Vitamin D Levels

Description of Procedure or Service

Vitamin D, also known as calciferol, is a fat-soluble vitamin that has a variety of physiologic effects, most prominently in calcium homeostasis and bone metabolism. In addition to the role that it plays in bone metabolism, other physiologic effects include inhibition of smooth muscle proliferation, regulation of the renin-angiotensin system, decrease in coagulation, and a decrease in inflammatory markers.

Vitamin D Levels
Vitamin D deficiency is best assessed by measuring serum levels of 25-hydroxy vitamin D. However, there is no consensus on the minimum vitamin D level or on the optimal serum level for overall health. The Institute of Medicine (IOM) report concluded that a level of 20 ng/mL is sufficient for the majority of healthy adults. Some experts, such as the National Osteoporosis Foundation and the American Geriatrics Society, recommend a higher level of 30 ng/mL.

Vitamin D deficiency, as defined by suboptimal serum levels, is common in the United States. In the National Health and Nutrition Examination Survey (NHANES) survey covering the period of 2000-2004, a total of 30% of individuals over the age of 12 had 25OH vitamin D levels less than 20 ng/mL. Vitamin D deficiency occurs most commonly as a result of inadequate dietary intake coupled with inadequate sun exposure. Evidence from the National Nutrition Monitoring System (NNMS) and the NHANES indicate that the average consumption is below recommended levels of intake. Yetley estimated that the average daily intake for U.S. adults ranged from 228 to 335 IU/d depending on gender and ethnicity. This is below the average daily requirement, estimated by the IOM to be 400 IU/d for healthy adults, and well below the IOM’s required daily allowance, which was estimated to be 600 IU for nonelderly adults and 800 IU for elderly adults.

Vitamin D deficiency may less commonly for other reasons. Kidney or liver disease can cause deficiency as a result of impaired conversion of inactive vitamin D to its active products. In rare situations, there is vitamin D resistance at the tissue level, which causes a functional vitamin D deficiency despite “adequate” serum levels.

The safe upper level for serum vitamin D is also not standardized. The IOM report concluded that there is potential harm associated with levels greater than 50 ng/mL and recommended that serum levels be maintained in the 20 to 40 ng/mL range. However, other conclusions on this point have differed. The Agency for Healthcare Research and Quality systematic review on vitamin D and bone health concluded that “There is little evidence from existing trials that vitamin D above current reference intakes is harmful.” The Women’s Health Initiative (WHI) concluded that hypercalcemia and hypercalciuria in patients receiving calcium and vitamin D were not associated with adverse clinical events. The WHI did find a small increase in kidney stones for women aged 50 to 79 years who received vitamin D and calcium.
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Associations of vitamin D levels with various aspects of health have been noted over the last several decades, and these findings have led to the question of whether supplementation improves health outcomes. For example, a relationship between vitamin D levels and overall mortality has been reported in the majority of observational studies that examine this relationship. Mortality is lowest at levels of vitamin D in the 25 to 40 nmol/L range. At lower levels of serum vitamin D, mortality increases steeply, and overall mortality in the lowest quintile was greater than 3 times that in the middle quintiles.

Vitamin D Replacement

The IOM document provided recommended reference values for intake of vitamin D and serum levels, based on available literature and expert consensus.8 Recommended daily allowances are 600 IU/d for individuals between 1 and 70 years of age, and 800 IU/d for individuals older than 70 years.

Estimates of vitamin D requirements are complicated by the many other factors that affect serum levels. Sun exposure is the most prominent, because individuals can meet their vitamin D needs entirely through adequate sun exposure. Other factors such as age, skin pigmentation, obesity, physical activity, and nutritional status also affect vitamin D levels and can result in variable dietary intake requirements to maintain adequate serum levels.

On the other hand, excessive intake of vitamin D can lead to toxic effects. These toxic effects are usually due to hypercalcemia and may include confusion, weakness, polyuria, polydipsia, anorexia, and vomiting. In addition, high levels of vitamin D may promote calcium deposition and has the potential to exacerbate conditions such as calcium kidney stones, and atherosclerotic vascular disease.

The IOM defined 3 parameters of nutritional needs for vitamin D, under the assumption of minimal sun exposure. These were the estimated average requirement, defined as the minimum intake required to maintain adequate levels; the recommended daily allowance, defined as the optimal dose for replacement therapy; and the upper level intake, defined as the maximum daily dose to avoid toxicity. These recommendations are summarized in Table 1.

<table>
<thead>
<tr>
<th>Patient Group</th>
<th>Estimated Average Requirement, IU/d</th>
<th>Recommended Daily Allowance, IU/d</th>
<th>Upper Limit Intake, IU/d</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-3 years old</td>
<td>400</td>
<td>600</td>
<td>2500</td>
</tr>
<tr>
<td>4-8 years old</td>
<td>400</td>
<td>600</td>
<td>3000</td>
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<tr>
<td>9-70 years old</td>
<td>400</td>
<td>600</td>
<td>4000</td>
</tr>
<tr>
<td>&gt;70 years old</td>
<td>400</td>
<td>800</td>
<td>4000</td>
</tr>
</tbody>
</table>

***Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.

Policy

BCBSNC will provide coverage for testing serum vitamin D levels when it is determined to be medically necessary because the medical criteria and guidelines noted below are met.

Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.
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When Testing Serum Vitamin D Levels is covered

Testing vitamin D levels in patients with signs and/or symptoms of vitamin D deficiency or toxicity (see Policy Guidelines section) may be considered **medically necessary**.

Testing vitamin D levels in asymptomatic patients may be considered **medically necessary** in the following patient populations:

- Individuals who have risk factors for vitamin D deficiency (see Policy Guidelines section).
- Institutionalized patients (see Policy Guidelines section).

When Testing Serum Vitamin D Levels is not covered

Testing vitamin D levels in asymptomatic patients is considered **not medically necessary** when the above criteria are not met.

Policy Guidelines

Signs and symptoms of vitamin D deficiency are largely manifested by changes in bone health and biochemical markers associated with bone production and resorption. In most cases, a clinical diagnosis of an abnormality in bone health (e.g., rickets, osteomalacia, osteoporosis), will lead to a decision to test vitamin D levels. Symptoms related to the clinical condition may be present, such as pain or low-impact fractures, but these in themselves are usually not indications for testing prior to a specific diagnosis. Some biochemical markers of bone health may indicate an increased risk for vitamin D deficiency, and testing of vitamin D levels may therefore be appropriate. These biochemical markers include unexplained abnormalities in serum calcium, phosphorous, alkaline phosphatase, and/or parathyroid hormone.

Signs and symptoms of vitamin D toxicity (hypervitaminosis D) are generally the result of induced hypercalcemia. Acute intoxication can cause symptoms of confusion, anorexia, vomiting, weakness, polydipsia, and polyuria. Chronic intoxication can cause bone demineralization, kidney stones, and bone pain.

“Institutionalized” refers to patients who reside at long-term facilities where some degree of medical care is provided. These can include long-term hospital stays, nursing homes, assisted living facilities, and similar environments.

There are no standardized lists of factors denoting high risk for vitamin D deficiency, and published lists of high-risk factor differ considerably. Certain factors tend to be present on most lists, however, and these may constitute a core set of factors for which there is general agreement that testing is indicated. The following list is compiled from examination of lists from numerous sources, with the following high-risk factors appearing on the majority of these lists:

- Chronic kidney disease, stage ≥3
- Cirrhosis/chronic liver disease
- Malabsorption states
- Osteomalacia
- Osteoporosis
- Rickets
- Hypo- or hypercalcemia
- Granulomatous diseases
- Vitamin D deficiency, on replacement
- Obstructive jaundice/biliary tract disease
- Osteogenesis imperfecta
- Osteosclerosis/osteopetrosis
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- Chronic use of anticonvulsant medication or corticosteroids
- Parathyroid disorders
- Osteopenia

The need for repeat testing may vary according to condition. A single test may be indicated for diagnostic purposes, a repeat test may be appropriate to determine whether supplementation has been successful in restoring normal serum levels. More than 1 repeat test may be indicated occasionally, such as in cases where supplementation has not been successful in restoring levels, where there are continued or recurrent signs and symptoms that may indicate ongoing deficiency, and/or in cases where inadequate absorption or noncompliance with replacement therapy is suspected.

Summary of Evidence
For individuals who are asymptomatic without conditions or risk factors for which vitamin D treatment is recommended who receive testing of vitamin D levels, the evidence includes no RCTs of clinical utility (ie, evidence that patient care including testing vitamin D levels vs care without testing vitamin D levels improves outcomes). Indirect evidence of the potential utility of testing includes many RCTs and systematic reviews of vitamin D supplementation. Relevant outcomes are overall survival, test accuracy and validity, symptoms, morbidity events, and treatment-related morbidity. There is a lack of standardized vitamin D testing strategies and cutoffs for vitamin D deficiency are not standardized or evidence-based. In addition, despite the large quantity of evidence, considerable uncertainty remains about the beneficial health effects of vitamin D supplementation. Many RCTs have included participants who were not vitamin D deficient at baseline and did not stratify results by baseline 25(OH)D level. Nonwhite race/ethnic groups are underrepresented in RCTs but have increased risk of vitamin D deficiency.

For skeletal health, there may be a small effect of vitamin D supplementation on falls, but there does not appear to be an impact on reducing fractures for the general population. The effect on fracture reduction may be significant in elderly women, and with higher doses of vitamin D. For patients with asthma, there may be a reduction in severe exacerbations with vitamin D supplementation, but there does not appear to be an effect on other asthma outcomes. For overall mortality, there is also no benefit for the general population. RCTs evaluating extraskeletal, cancer, cardiovascular, and multiple sclerosis outcomes have not reported a statistically significant benefit for vitamin D supplementation. Although vitamin D toxicity and adverse events appear to be rare, few data on risks have been reported. The evidence is insufficient to determine the effects of the technology on health outcomes.

The U.S. Preventive Services Task Force (USPSTF) published a recommendation statement in 2014 and associated guidelines in 2015 on vitamin D screening. USPSTF concluded that the current evidence is insufficient to assess the balance of benefits and harms of screening for vitamin D deficiency in asymptomatic individuals (grade I [insufficient evidence]).

Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

*Applicable service codes: 82306, 82652, 0038U*

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources
Testing Serum Vitamin D Levels


Sr. Medical Director review 9/2015.


United States Preventive Services Task Force (USPSTF). Vitamin D Deficiency: Screening 2014. [Hyperlink to full reference]


Policy Implementation/Update Information

<table>
<thead>
<tr>
<th>Date</th>
<th>Changes</th>
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<tbody>
<tr>
<td>10/30/15</td>
<td>New medical policy issued. Testing vitamin D levels in patients with signs and/or symptoms of vitamin D deficiency or toxicity (see Policy Guidelines section) may be considered medically necessary. Testing vitamin D levels in asymptomatic patients may be considered medically necessary in the following patient populations: Individuals who have risk factors for vitamin D deficiency and Institutionalized patients. Sr. Medical director review 9/2015. Notification given 10/30/15 for effective date 12/30/15. (lpr)</td>
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<tr>
<td>4/1/16</td>
<td>Specialty Matched Consultant Advisory Panel review 2/24/2016. No change to policy. (an)</td>
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<tr>
<td>9/30/16</td>
<td>Statement in the non-covered section referring to routine screening was deleted. The screening diagnosis codes were removed from the Billing/Coding section. (an)</td>
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<tr>
<td>12/30/16</td>
<td>Minor change to description section. Policy statement unchanged. (an)</td>
</tr>
<tr>
<td>3/31/17</td>
<td>Added USPSTF recommendation to Policy Guidelines section. Specialty Matched Consultant Advisory Panel review 2/22/2017. No change to policy statement. (an)</td>
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Medical policy is not an authorization, certification, explanation of benefits or a contract. Benefits and eligibility are determined before medical guidelines and payment guidelines are applied. Benefits are determined by the group contract and subscriber certificate that is in effect at the time services are rendered. This document is solely provided for informational purposes only and is based on research of current medical literature and review of common medical practices in the treatment and diagnosis of disease. Medical practices and knowledge are constantly changing and BCBSNC reserves the right to review and revise its medical policies periodically.