BlueCross BlueShield Federal Employee Program.

FEP Medical Policy Manual

FEP 2.04.135 Testing Serum Vitamin D Levels

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Related Policies:

None

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Description

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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 it plays in bone metabolism, other physiologic effects include inhibition of smooth muscle proliferation, regulation of the renin-angiotensin system, a decrease in coagulation, and a decrease in inflammatory markers.

OBJECTIVE

The objective of this evidence review is to examine whether testing for vitamin D deficiency improves net health outcomes in asymptomatic individuals.

POLICY STATEMENT

Testing vitamin D levels in individuals 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 individuals may be considered **medically necessary** in the following populations:

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

Testing vitamin D levels in asymptomatic individuals is considered **investigational** 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 (eg, rickets, osteomalacia, osteoporosis) will lead to a decision to test vitamin D levels. Symptoms related to the clinical condition may be present (eg, pain, low-impact fractures), but these symptoms 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, phosphorus, alkaline phosphatase, and/or parathyroid hormone.

Signs and symptoms of vitamin D toxicity (hypervitaminosis D) generally result from 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" as used herein refers to individuals who reside at long-term facilities where some degree of medical care is provided. These circumstances and facilities 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 factors differ considerably. Certain factors tend to be present on most lists, however, and they may constitute a core set of factors for which there is general agreement that testing is indicated. The Endocrine Society guidelines form the basis for the following list of high-risk factors for vitamin D deficiency. (see also Appendix 1)

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

- Osteopenia

The need for repeat testing may vary by 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 occasionally be indicated, such as in cases where supplementation has not been successful in restoring levels (another example might include an instance in which continued or recurrent signs and symptoms may indicate ongoing deficiency, and/or when inadequate absorption or noncompliance with replacement therapy is suspected).

BENEFIT APPLICATION

Experimental or investigational procedures, treatments, drugs, or devices are not covered (See General Exclusion Section of brochure).

FDA REGULATORY STATUS

The U.S. Food and Drug Administration (FDA) has cleared a number of immunoassays for in vitro diagnostic devices for the quantitative measurement of total 25-hydroxyvitamin D through the 510(k) process.

Clinical laboratories may develop and validate tests in-house and market them as a laboratory service; laboratory-developed tests must meet the general regulatory standards of the Clinical Laboratory Improvement Amendments (CLIA). Lab tests for vitamin D are available under the auspices of CLIA. Laboratories that offer laboratory-developed tests must be licensed by CLIA for high-complexity testing. To date, the FDA has chosen not to require any regulatory review of this test.

RATIONALE

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 randomized controlled trials (RCTs) of clinical utility (ie, evidence that patient care including testing vitamin D levels versus care without testing vitamin D levels improves outcomes). Relevant outcomes are overall survival, test validity, symptoms, morbid events, and treatment-related morbidity. Indirect evidence of the potential utility of testing includes many RCTs and systematic reviews of vitamin D supplementation. 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-hydroxyvitamin D level. Nonwhite race/ethnic groups are underrepresented in RCTs, but have an 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. However, high doses of vitamin D may be associated with safety concerns in patients at risk for falls. 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 patients who are pregnant, vitamin D supplementation may improve maternal and fetal outcomes. For overall mortality, there is also no benefit to 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 that the technology results in an improvement in the net health outcome.

SUPPLEMENTAL INFORMATION

Practice Guidelines and Position Statements

Guidelines or position statements will be considered for inclusion in 'Supplemental Information" if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

Bone Health and Osteoporosis Foundation

The Bone Health and Osteoporosis Foundation updated recommendations for the prevention and treatment of osteoporosis in 2021.[3,] They recommended monitoring serum 25-hydroxy vitamin D levels in postmenopausal women and men 50 years of age and older, and vitamin D supplementation as necessary to maintain levels between 30 and 50 ng/mL.

Endocrine Society

In 2011, the Endocrine Society published clinical practice guidelines on the evaluation, treatment, and prevention of vitamin D deficiency.[113,] The following recommendations were made regarding testing vitamin D levels:

- 25-hydroxy vitamin D serum level testing is recommended: "to evaluate vitamin D status only in patients who are at risk of deficiency." The guideline did not recommend screening of individuals not at risk of vitamin D deficiency.
- 1,25-dihydroxyvitamin D testing was not recommended to evaluate vitamin D status. However, the guideline did recommend monitoring calcitriol levels under certain conditions.

American College of Obstetrics and Gynecology

The American College of Obstetrics and Gynecology (2011, reaffirmed 2021) issued a committee opinion on the testing of vitamin D levels and vitamin D supplementation in pregnant women.[114,] The following recommendation was made concerning testing vitamin D levels:

"At this time there is insufficient evidence to support a recommendation for screening all pregnant women for vitamin D deficiency. For pregnant women thought to be at increased risk of vitamin D deficiency, maternal serum 25-hydroxyvitamin D levels can be considered and should be interpreted in the context of the individual clinical circumstance. When vitamin D deficiency is identified during pregnancy, most experts agree that 1,000-2,000 international units per day of vitamin D is safe."

American Academy of Family Physicians

The American Academy of Family Physicians supports the U.S. Preventative Task Force recommendation on vitamin D screening.[115,]

In 2018, key recommendations for practice concluded that there was insufficient information to recommend screening the general population for vitamin D deficiency and that treating asymptomatic individuals with identified deficiency has not been shown to improve health.[116,]

National Osteoporosis Society

The National Osteoporosis Society issued a patient management clinical guideline for vitamin D and bone health in 2014. [117,] It recommended that serum 25-hydroxyvitamin D levels should be measured to estimate vitamin D status in certain clinical scenarios such as: bone diseases that may improve with vitamin D treatment; bone diseases, prior to specific treatment where correcting vitamin D deficiency is appropriate; and musculoskeletal symptoms that could be due to vitamin D deficiency.

U.S. Preventive Services Task Force Recommendations

The **U.S. Preventive Services Task Force** published an updated recommendation[118,] and associated evidence report and systematic review in 2021 [119,] on vitamin D screening. The **Task Force** concluded that the current evidence was insufficient to assess the balance of benefits and harms of screening for vitamin D deficiency in asymptomatic individuals (grade I [insufficient evidence]).

Medicare National Coverage

There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

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POLICY HISTORY - THIS POLICY WAS APPROVED BY THE FEP® PHARMACY AND MEDICAL POLICY COMMITTEE ACCORDING TO THE HISTORY BELOW:

Date	Action	Description
December 2023	New policy	Policy updated with literature review through October 24, 2022; references added. Not Medically Necessary language changed to Investigational and other minor editorial refinements to policy statements; intent unchanged. FEP new policy.