DRAFT Medical Coverage Policy | Vitamin-D Testing

EFFECTIVE DATE: 09|01|2024
POLICY LAST REVIEWED: 05|01|2024

OVERVIEW
Hypovitaminosis D may result from inadequate intake, insufficient sunlight, malabsorption, liver, kidney and genetic disease. It results in the inadequate mineralization of bone. Vitamin D; 25 hydroxy and Vitamin D; 1, 25 dihydroxy laboratory assays are used in the medical management of patients with hypovitaminosis D.

MEDICAL CRITERIA
Not applicable

PRIOR AUTHORIZATION
Not applicable

POLICY STATEMENT
Medicare Advantage Plans and Commercial Products
Measurement of 25-OH Vitamin D level and Measurement of 1, 25-OH Vitamin D are covered when filed with a covered diagnosis (see coding section).

All other indications are not covered for Medicare Advantage and not medically necessary for Commercial Products as there is no indication that technology results in an improvement in the net health outcome.

Commercial Products
Some genetic testing services are not covered and a contract exclusion for any self-funded group that has excluded the expanded coverage of biomarker testing related to the state mandate, R.I.G.L. **§27-19-81** described in the Biomarker Testing Mandate policy. For these groups, a list of which genetic testing services are covered with prior authorization, are not medically necessary or are not covered because they are a contract exclusion can be found in the Coding section of the Genetic Testing Services or Proprietary Laboratory Analyses policies. Please refer to the appropriate Benefit Booklet to determine whether the member's plan has customized benefit coverage. Please refer to the list of Related Policies for more information.

COVERAGE
Benefits may vary between groups and contracts. Please refer to the appropriate Benefit Booklet, Evidence of Coverage or Subscriber Agreement for applicable laboratory testing or not medically necessary/not covered benefits/coverage.

BACKGROUND
Routine use of laboratory assays to document Vitamin D deficiency remains controversial. The current United States Preventive Health Service Task Force recommendations consider current medical evidence insufficient to assess the balance of benefits and harms of screening for Vitamin D deficiency in asymptomatic adults. However, one major meta-analysis (one with five pooled randomized controlled trials including 1237 patients) concluded that Vitamin D supplementation reduced the risk of falls among ambulatory and institutionalized older individuals with stable health by more than 20%.

A second meta-analysis pooled 12 randomized controlled trials, all using cholecalciferol supplementation therapy between 700-800 IU/d. The results demonstrated a reduction in fractures of the hip of 26%, and non-vertebral fractures of 23%, in both ambulatory and institutionalized elderly persons.

There is also controversy as to the definition of vitamin D sufficiency, although many authors accept a level of 25(OH)D of at least 30 ng/ml. Accepting this metric, 25-50% of nursing home or homebound patients, greater than 50% of hospitalized patients and 30% of women with osteoporosis may still have Vitamin D deficiency despite a growing societal awareness of that deficiency as a contributing factor.

In 2009, the Agency for Healthcare Research and Quality, through the Tufts Evidenced Based Practice Center, conducted a systematic review of the scientific literature on Vitamin D and calcium intake as related to status indicators and health outcomes. This original report summarized 165 articles and 11 systematic reviews that incorporated 200 additional primary articles. In 2013, in preparation for a project in conjunction with the NIH Office of Dietary Supplements, the report was updated to include 154 new articles. Despite this effort, disagreement exists regarding Vitamin D optimum dosing, target 25 (OH) vitamin D levels and the reported associations with health outcomes. Associations with cardiovascular disease, major cancers breast, prostate, colorectal and pancreatic were mixed and inconclusive.

A pragmatic approach for patients and their physicians was developed by the ABIM Foundation in its Choosing Wisely initiative. The patient friendly literature reassures individuals that healthy diet and exercise maintain most persons in an adequate range of Vitamin D level. It raises the possible justification of empiric vitamin D supplementation without testing for those patients without risk factors but may be thought to have inadequate sun exposure or dietary intake, while outlining those clinical risk factors that warrant baseline diagnostic assays.

It is established that 25-hydroxyvitamin D is more reflective of total body stores of vitamin D than the shorter lived, activemetabolite, 1,25 dihydroxyvitamin D. Although lack of laboratory standardization is commonly noted in most papers, it is the preferred initial assay in the evaluation of most patients with hypovitaminosis D. The 25-hydroxyvitamin D undergoes additional hydroxylation in the kidney by 1-alphahydroxylase under the influence of parathyroid hormone to produce the active metabolite. The 1,25 dihydroxyvitamin D assay is reserved for those patients where a contributory medical illness generally related to kidney disease, but also possibly related to liver, parathyroid or genetic diseases that may influence this normal metabolism.

The benefits of treatment of Vitamin D supplementation may be modest, and those benefits made difficult to quantify by general health, habits such as exercise and smoking, and other contributory factors such as ethnicity and medication treatment regimens.

However, the prevalence of osteoporosis, fall risk and skeletal fractures, and the general tolerance of the current recommended daily requirements mitigate for early supplementation in any individual uncertain regarding adequate dietary intake and sunlight exposure.

Once a patient has been shown to be Vitamin D deficient, by assay or clinical findings, the correctly chosen assay (25 hydroxyvitamin D, or 1,25 di-hydroxyvitamin D) may be used to assure correct supplementation to attain the serum levels outlined above.

Hypovitaminosis D may result from inadequate intake, insufficient sunlight, malabsorption, liver, kidney and genetic disease. It results in the inadequate mineralization of bone. The CDC reported approximately 300,000 hip fractures, 60,000 fall-related deaths and 33 billion dollars in health care expenditures in 2014. This policy identifies the indications and limitations of Medicare coverage for Vitamin D; 25 hydroxy and Vitamin D; 1, 25 dihydroxy laboratory assays in the medical management of patients.

Indications:
Measurement of 25-OH Vitamin D level is indicated for patients with:

- chronic kidney disease stage III or greater
- cirrhosis

- hypocalcemia
- hypercalcemia
- hypercalciuria
- hypervitaminosis D
- parathyroid disorders
- malabsorption states
- obstructive jaundice
- osteomalacia
- osteoporosis if:
    i. T score on DEXA scan <-2.5 or
    ii. History of fragility fractures or
    iii. FRAX> 3% 10-year probability of hip fracture or 20% 10-year probability of other major osteoporotic fracture or
    iv. FRAX> 3% (any fracture) with T-score <-1.5 or
    v. Initiating bisphosphanate therapy (Vitamin D level and serum calcium levels should be determined and managed as necessary before bisphosphonate is initiated.)
- osteosclerosis/petrosis
- rickets
- vitamin D deficiency on replacement therapy related to a condition listed above; to monitor the efficacy of treatment.

Measurement of 1, 25-OH Vitamin D level is indicated for patients with:

- unexplained hypercalcemia (suspected granulomatous disease or lymphoma)
- unexplained hypercalciuria (suspected granulomatous disease or lymphoma)
- suspected genetic childhood rickets
- suspected tumor-induced osteomalacia
- nephrolithiasis or hypercalciuria

CODING

Medicare Advantage Plans and Commercial Products

The following code is considered medically necessary when filed with the one of the diagnosis codes in the attachment below:

82306 Vitamin D; 25 hydroxy, includes fraction(s), if performed

ICD10 Diagnosis list for 82306

The following code is considered medically necessary when filed with the one of the diagnosis codes in the attachment below:

82652 Vitamin D; 1, 25 dihydroxy, includes fraction(s), if performed

ICD10 Diagnosis for 82652

RELATED POLICIES

Biomarker Testing Mandate
Genetic Testing Services
Medicare Advantage Plans National and Local Coverage Determinations

PUBLISHED

Provider Update, July 2024
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REFERENCES

1. American Gastroenterological Association medical position statement: guidelines on osteoporosis in gastrointestinal diseases. *Gastroenterology*. 2003;124(3):791-4.
2. In: Ross AC, Taylor CL, Yaktine AL, Del Valle HB, editors. Dietary Reference Intakes for Calcium and Vitamin D. The National Academies Collection: Reports funded by National Institutes of Health. Washington (DC): Institute of Medicine; 2011.
3. Vitamin D Testing in the General Population: A Review of the Clinical and Cost-Effectiveness and Guidelines. CADTH Rapid Response Reports. Ottawa (ON) 2015.
4. Autier P, Gandini S. Vitamin D Supplementation and Total Mortality. A Meta-analysis of Randomized Controlled Trials. *Arch Intern Med*. 2007;167(16);1730-1737.
5. Bernstein CN, Leslie WD, Leboff MS. AGA technical review on osteoporosis in gastrointestinal diseases. *Gastroenterology*. 2003;124(3):795-841.
6. Bikle DD. Vitamin D and bone. *Curr Osteoporos Rep*. 2012;10(2):151-9.
7. Bikle DD. Vitamin D metabolism, mechanism of action, and clinical applications. *Chem Biol*. 2014;21(3):319-29.
8. Binkley N, Krueger D, Gemar D, Drezner MK. Correlation among 25-hydroxy-vitamin D assays. *J Clin Endocrinol Metab*. 2008;93(5):1804-8.
9. Bischoff-Ferrari HA, Dawson-Hughs B, Willett W, et al. Effect of vitamin D on falls a meta-analysis. *JAMA*. April 2004;291:16:1999-2006.
10. Bischoff-Ferrari HA, Giovannucci E, Willett WC, Dietrich T, Dawson-Hughes B. Estimation of optimal serum concentrations of 25-hydroxyvitamin D for multiple health outcomes. *Am J Clin Nutr*. 2006;84(1):18-28.
11. Bischoff-Ferrari HA, Willett W, Wong J, Giovannucci E, Dietrich T, Dawson-Hughes B. Fracture prevention with vitamin D supplementation, a meta-analysis of randomized controlled trials. *JAMA*. May 2005;293:18:2257-2264.
12. Bjelakovic G, Gluud C. Vitamin and mineral supplement use in relation to all-cause mortality in the Iowa Women's Health Study. *Arch Intern Med*. 2011;171(18):1633-1634.
13. Bjelakovic G, Gluud LL, Nikolova D, Whitfield K, Krstic G, Wetterslev J, et al. Vitamin D supplementation for prevention of cancer in adults. *Cochrane Database Syst Rev*. 2014(6):CD007469.
14. Bjelakovic G, Gluud LL, Nikolova D, Whitfield K, Wetterslev J, Simonetti RG, et al. Vitamin D supplementation for prevention of mortality in adults. *Cochrane Database Syst Rev*. 2011(7):CD007470.
15. Bjelakovic G, Gluud LL, Nikolova D, Whitfield K, Wetterslev J, Simonetti RG, et al. Vitamin D supplementation for prevention of mortality in adults. *Cochrane Database Syst Rev*. 2014(1):CD007470.
16. Bjelakovic G, Nikolova D, Gluud LL, Simonetti RG, Gluud C. Antioxidant supplements for prevention of mortality in healthy participants and patients with various diseases. *Cochrane Database Syst Rev*. 2008(2):CD007176.
17. Bodnar LM, Simhan HN, Powers RW, Frank MP, Cooperstein E, Roberts JM. High prevalence of vitamin D insufficiency in black and white pregnant women residing in the northern United States and their neonates. *J Nutr*. 2007;137:447-452.
18. Bolland MJ, Bacon CJ, Horne AM, et al. Vitamin D insufficiency and health outcomes over 5 y in older women. *Am J Clin Nutr*. 2010;91(1):82-9.
19. Camacho PM, Petak SM, Binkley N, et al. American Association of Clinical Endocrinologists and American College of Endocrinology Clinical Practice Guidelines for the Diagnosis and Treatment of Postmenopausal Osteoporosis - 2016. *Endocr Pract*. 2016;22(Suppl 4):1-42.
20. Chapuy M, Arlot M, Duboeuf F, et al. Vitamin D3 and calcium to prevent hip fractures in elderly women. *N Engl J Med*. 1992;327:23:1637-1642.
21. Chung M, Balk EM, Brendel M, et al. Vitamin D and calcium: a systematic review of health outcomes. *Evid Rep Technol Assess (Full Rep)*. 2009(183):1-420.
22. Compston JE. Hepatic osteodystrophy: vitamin D metabolism in patients with liver disease. *Gut*. 1986;27(9):1073-1090.

23. Giovannucci E. Vitamin D and cancer incidence in the Harvard cohorts. *Ann Epidemiol*. 2009;19(2):84-88.
24. Giovannucci E, Liu Y, Hollis BW, Rimm EB. 25-Hydroxyvitamin D and Risk of Myocardial Infarction in Men; A Prospective Study. *Arch Intern Med*. 2008:168(11):1174-1180.
25. Gordon PL, Sakkas GK, Doyle JW, Shubert T, Johansen KL. Relationship between vitamin D and muscle size and strength in patients on hemodialysis. *J Ren Nutr*. 2007;17(6):397-407.
26. Hanley DA, Cranney A, Jones G, et al. Vitamin D in adult health and disease: a review and guideline statement from Osteoporosis Canada. *CMAJ*. 2010;182(12):E610-8.
27. Hanley DA, Cranney A, Jones G, Whiting SJ, Leslie WD, Guidelines Committee of the Scientific Advisory Council of Osteoporosis C. Vitamin D in adult health and disease: a review and guideline statement from Osteoporosis Canada (summary). *CMAJ*. 2010;182(12):1315-9.
28. Holick MF. High Prevalence of Vitamin D Inadequacy and Implications for Health. *Mayo Clin Proc*. 2006;81(3):353-373.
29. Holick MF. Vitamin D deficiency. *N Engl J Med*. 2007; 357:266.
30. Holick MF. Vitamin D status: measurement, interpretation, and clinical application. *Ann Epidemiol*. 2009;19(2):73-8.
31. Holick MF, Binkley NC, Bischoff-Ferrari HA, Gordon CM, Hanley DA, Heaney RP, et al. Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab*. 2011;96(7):1911-30.
32. Holick MF, Gordon CM. The Hormone Foundation's: Patient guide to vitamin D deficiency. *J Clin Endocrinol Metab*. 2011;96(7):1-2.
33. Inker LA, Astor BC, Fox CH, et al. KDOQI US commentary on the 2012 KDIGO clinical practice guideline for the evaluation and management of CKD. *Am J Kidney Dis*. 2014;63(5):713-35.
34. Jacobus, CH, Holick, MF, Shao, Q, et al. Hypervitaminosis D associated with drinking milk. *N Engl J Med*. 1992;326:1173.
35. Johnson JM, Maher JW, DeMaria EJ, Downs RW, Wolfe LG, Kellum JM. The long-term effects of gastric bypass on vitamin D metabolism. *Ann Surg*. 2006 243(5):701-704;discussion 4-5.
36. Kennel K, Drake M, Hurley D. Vitamin D deficiency in adults: when to test and how to treat. *Mayo Clin Proc*. 2010;85(8):752-757;quiz 7-8.
37. Kidney Disease: Improving Global Outcomes CKDMBDWG. KDIGO clinical practice guideline for the diagnosis, evaluation, prevention, and treatment of Chronic Kidney Disease-Mineral and Bone Disorder (CKD-MBD). *Kidney Int Suppl*. 2009;76(113):S1-130.
38. Lafferty, FW. Differential diagnosis of hypercalcemia. *J Bone Miner Res*. 1991;6 Suppl 2:S51-59;discussion S61.
39. LeBlanc E, Chou R, Zakher B, Daeges M, Pappas M. Screening for Vitamin D Deficiency: Systematic Review for the US Preventive Services Task Force Recommendation. U.S. Preventive Services Task Force Evidence Syntheses, formerly Systematic Evidence Reviews. Rockville (MD)2014.
40. LeBlanc E, Zakher B, Daeges M, Pappas M, Chou R. Screening for vitamin D deficiency: a systematic review for the U.S. Preventive Services Task Force. *Ann Intern Med*. 2015;162(2):109-122.
41. Lee JH, O'Keefe JH, Bell D, Hensrud DD, Holick MF. Vitamin D deficiency an important, common, and easily treatable cardiovascular risk factor? *J Am Coll Cardiol*. 2008;52(24):1949-1956.
42. LeFevre ML, Force USPST. Screening for vitamin D deficiency in adults: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med*. 2015;162(2):133-140.
43. MacLean C, Alexander A, Carter J, et al. Comparative Effectiveness of Treatments To Prevent Fractures in Men and Women With Low Bone Density or Osteoporosis. AHRQ Comparative Effectiveness Reviews. Rockville (MD)2007.
44. MacLean C, Newberry S, Maglione M, McMahon M, Ranganath V, Suttorp M, et al. Systematic review: comparative effectiveness of treatments to prevent fractures in men and women with low bone density or osteoporosis. *Ann Intern Med*. 2008;148(3):197-213.
45. Moyer VA, Force USPST. Vitamin, mineral, and multivitamin supplements for the primary prevention of cardiovascular disease and cancer: U.S. Preventive services Task Force recommendation statement. *Ann Intern Med*. 2014;160(8):558-64.
46. Newberry. Vitamin D and Calcium: A Systematic Review of Health Outcomes (Update) 2014.

47. Orwoll ES. Clinical Practice Guidelines for Osteoporosis: Translating Data to Patients? *Ann Intern Med*. 2017;166(11):852-853.
48. Rosen CJ, Abrams SA, Aloia JF, et al. IOM committee members respond to Endocrine Society vitamin D guideline. *J Clin Endocrinol Metab*. 2012;97(4):1146-1152.
49. Silverberg SJ. Vitamin D deficiency and primary hyperparathyroidism. *J Bone Miner Res*. 2007;22 Suppl 2:V100-4.
50. Silverberg SJ, Clarke BL, Peacock M, et al. Current issues in the presentation of asymptomatic primary hyperparathyroidism: proceedings of the Fourth International Workshop. *J Clin Endocrinol Metab*. 2014;99(10):3580-3594.
51. Sotaniemi, EA, Hakkarainen, HK, Puranen, JA, Lahti, RO. Radiologic bone changes and hypocalcemia with anticonvulsant therapy in epilepsy. *Ann Intern Med*. 1972;77(3):389-394.
52. Wagner CL, Greer FR, and the Section on Breastfeeding and Committee on Nutrition. Prevention of Rickets and Vitamin D Deficiency in Infants, Children, and Adolescents. *Pediatrics*. 2008;122;1142-1152.
53. Ward KA, Das G, Berry JL, Roberts SA, Rawer R, Adams JE, Mughal Z. Vitamin D status and muscle function in post-menarchal adolescent girls. *J Clin Endocrinol Metab*. 2009 Feb;94(2):559-563.
54. Woolcott CG, Wilkens LR, Nomura AM et al. Plasma 25-hydroxyvitamin D levels and the risk of colorectal cancer: the multiethnic cohort study. *Cancer Epidemiol Biomarkers Prev*. 2010;19(1):130-134.
55. ABIM Foundation. Choosing Wisely (developed with the American Society of Clinical Pathology) Vitamin D tests- when you need them- and when you don't. Feb 2014, ChoosingWisely.org.
56. Other Contractor(s)' Policies.
57. Bazzano AN, Littrell L, Lambert S, Roi C. Factors associated with vitamin D status of low-income, hospitalized psychiatric patients: results of a retrospective study. *Neuropsychiatr Dis Treat*. 2016;12:2973-2980.
58. Dall'Ara F, Cutolo M, Andreoli L, Tincani A, Paolino S. Vitamin D and systemic lupus erythematous: a review of immunological and clinical aspects. *Clin Exp Rheumatol*. 2017.
59. Falkiewicz K, Boratynska M, Speichert-Bidzinska B, et al. 1,25-dihydroxyvitamin D deficiency predicts poorer outcome after renal transplantation. *Transplant Proc*. 2009;41(8):3002-3005.
60. Karimzadeh H, Shirzadi M, Karimifar M. The effect of Vitamin D supplementation in disease activity of systemic lupus erythematosus patients with Vitamin D deficiency: A randomized clinical trial. *J Res Med Sci*. 2017;22:4.
61. Lima GL, Paupitz JA, Aikawa NE, Alvarenga JC, Pereira RMR. A randomized double-blind placebo-controlled trial of vitamin D supplementation in juvenile-onset systemic lupus erythematosus: positive effect on trabecular microarchitecture using HR-pQCT. *Osteoporos Int*. 2017.
62. Pereira-Santos M, Costa PR, Assis AM, Santos CA, Santos DB. Obesity and vitamin D deficiency: a systematic review and meta-analysis. *Obes Rev*. 2015;16(4):341-349.
63. Rossini M, Gatti D, Viapiana O, et al. Vitamin D and rheumatic diseases. *Reumatismo*. 2014;66(2):153-170.
64. Sahebari M, Nabavi N, Salehi M. Correlation between serum 25(OH)D values and lupus disease activity: an original article and a systematic review with meta-analysis focusing on serum VitD confounders. *Lupus*. 2014;23(11):1164-1177.
65. Sakthiswary R, Raymond AA. The clinical significance of vitamin D in systemic lupus erythematosus: a systematic review. *PLoS One*. 2013;8(1):e55275.
66. Salman-Monte TC, Torrente-Segarra V, Vega-Vidal AL, et al. Bone mineral density and vitamin D status in systemic lupus erythematosus (SLE): A systematic review. *Autoimmun Rev*. 2017;16(11):1155-1159.
67. Sousa JR, Rosa EPC, Nunes I, Carvalho C. Effect of vitamin D supplementation on patients with systemic lupus erythematosus: a systematic review. *Rev Bras Reumatol Engl Ed*. 2017;57(5):466-471.
68. Wilkins CH, Sheline YI, Roe CM, Birge SJ, Morris JC. Vitamin D deficiency is associated with low mood and worse cognitive performance in older adults. *Am J Geriatr Psychiatry*. 2006;14(12):1032-1040.

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