# National Medical Policy

**Subject:** **Vitamin D Screening**

**Policy Number:** **NMP499**

**Effective Date*:** **December 2009**

**Update:** **March 2011, January 2012, January 2013, January 2014**

---

**This National Medical Policy is subject to the terms in the IMPORTANT NOTICE at the end of this document**

**For Medicaid Plans: Please refer to the appropriate Medicaid Manuals for coverage guidelines prior to applying Health Net Medical Policies**

**The Centers for Medicare & Medicaid Services (CMS)**
For Medicare Advantage members please refer to the following for coverage guidelines first:

| Use | Source | Reference/Website Link |
|---|---|---|
| | National Coverage Determination (NCD) | |
| | National Coverage Manual Citation | |
| X | Local Coverage Determination (LCD)* | Vitamin D Assay Testing: (L31377) http://www.cms.gov/medicare-coverage-database/ |
| | Article (Local)* | |
| X | Other | 100-04, Medicare Claims Processing Manual, Chapter 30. (1.07 MB) Minor formatting and template changes were made: http://www.ngsmedicare.com/wps/wcm/connect/4858cf804c2a5457a231f310c8525603/2012-08+August+MMR+Final.pdf?MOD=AJPERES&CACHEID=4858cf804c2a5457a231f310c8525603 |
| | None | Use Health Net Policy |

Instructions

- Medicare NCDs and National Coverage Manuals apply to ALL Medicare members in ALL regions.
- Medicare LCDs and Articles apply to members in specific regions. To access your specific region, select the link provided under "Reference/Website" and follow the search instructions. Enter the topic and your specific state to find the coverage determinations for your region. *Note: Health Net must follow local coverage determinations (LCDs) of Medicare Administration Contractors (MACs) located outside their

service area when those MACs have exclusive coverage of an item or service. (CMS Manual Chapter 4 Section 90.2)

- If more than one source is checked, you need to access all sources as, on occasion; an LCD or article contains additional coverage information than contained in the NCD or National Coverage Manual.
- If there is no NCD, National Coverage Manual or region specific LCD/Article, follow the Health Net Hierarchy of Medical Resources for guidance.

## Current Policy Statement (Update January 2014 – A Medline search failed to reveal any studies that would cause Health Net, Inc. to change its current position)

Health Net, Inc. considers Vitamin D screening investigational and therefore not medically necessary for the general population. Vitamin D supplements, dietary recommendations and sensible sun exposure should be sufficient to fulfill the body's vitamin D requirement, unless there are extenuating circumstances (i.e. specific disorders that may cause vitamin D deficiency such as disorders of calcium metabolism, malnutrition/malabsorption, long term use of specific medication such as glucocorticosteroids, diseases of the bone, nutrition and renal disease.)

## Definitions

| | |
|---|---|
| PTH | Parathyroid hormone |
| VDR | Vitamin D receptors |
| VDBP | Vitamin D binding proteins |
| NHANES | National Health and Nutrition Examination Survey |
| 25-OH vitamin D | 25-hydroxyvitamin D test, 25-hydroxycholecalciferol, calcidiol |
| 1,25-(OH) 2D3 | 1,25-dihydroxycholecalciferol, calcitriol, active form of vitamin D found in the body (1,25(OH) 2D3) |
| Pg | Picograms |
| IU | International Units |
| ng/mL | Nanograms per milliliter |
| AAP | American Academy of Pediatrics |
| ng | Nanograms |
| DRI's | Dietary Reference Intakes |
| RDA | Recommended daily allowance |
| UL | Tolerable upper intake limits |

## Codes Related To This Policy

NOTE:
The codes listed in this policy are for reference purposes only. Listing of a code in this policy does not imply that the service described by this code is a covered or non-covered health service. Coverage is determined by the benefit documents and medical necessity criteria. This list of codes may not be all inclusive.

On October 1, 2014, the ICD-9 code sets used to report medical diagnoses and inpatient procedures will be replaced by ICD-10 code sets. Health Net National Medical Policies will now include the preliminary ICD-10 codes in preparation for this transition. Please note that these may not be the final versions of the codes and that will not be accepted for billing or payment purposes until the October 1, 2014 implementation date.

## ICD-9 Codes

| | |
|---|---|
| 252.00 | Hyperparathyroidism, unspecified |
| 252.01 | Primary hyperparathyroidism |
| 252.02 | Secondary hyperparathyroidism, non-renal |

| | |
|---|---|
| 252.08 | Other hyperparathyroidism |
| 252.1 | Hypoparathyroidism |
| 268.0 | Rickets active |
| 268.2 | Osteomalacia unspecified |
| 268.9 | Unspecified vitamin d deficiency |
| 275.3 | Disorders of phosphorus metabolism |
| 275.41 | Hypocalcemia |
| 275.42 | Hypercalcemia |
| 585.3 | Chronic kidney disease, stage iii (moderate) |
| 585.4 | Chronic kidney disease, stage iv (severe) |
| 585.5 | Chronic kidney disease, stage v |
| 585.6 | End stage renal disease |
| 588.81 | End stage renal disease |
| 733.00 | Osteoporosis unspecified |
| 733.01 | Senile osteoporosis |
| 733.02 | Idiopathic osteoporosis |
| 733.09 | Other osteoporosis |
| 733.90 | Disorder of bone and cartilage unspecified |

## ICD-10 Codes

| | |
|---|---|
| E20.0-E20.9 | Hypoparathroidism |
| E21.0-E21.5 | Hyperparathyroidism and other disorders of the parathyroid gland |
| E55.0 | Rickets, active |
| E55.9 | Vitamin D deficiency, unspecified |
| E83.30-E83.39 | Disorders of phosphorus metabolism and phosphatases |
| E83.51 | Hypocalcemia |
| E83.52 | Hypercalcemia |
| M80.00-M80.88 | Age-related osteoporosis with current pathological fracture |
| M81.000-M81.8 | Other osteoporosis without current pathological fracture |
| M83.0-M83.9 | Adult osteomalacia |
| M89.9 | Disorder of bone, unspecified |
| M94.9 | Disorder of cartilage, unspecified |
| N18.3 | Chronic kidney disease, stage 3 (moderate) |
| N18.4 | Chronic kidney disease, stage 4 (severe) |
| N18.5 | Chronic kidney disease, stage 5 |
| N18.6 | End stage renal disease |
| N25.81 | Secondary hyperparathyroidism of renal origin |

## CPT Codes

| | |
|---|---|
| 82306 | Vitamin D; 25 Hydroxy, includes fraction(s), if performed |
| 82652 | Vitamin D; 1, 25 Dihydroxy, includes fraction(s), if performed |

## HCPCS code

N/A

## Scientific Rationale – January 2014

There is a paucity of current peer-reviewed literature on Vitamin D screening for the general population. The United States Preventive Services Task force is currently in the process of finalizing recommendations for Vitamin D testing at this time. There is no change in the recommendations from the 2011 Endocrine Society, the 2010 Institute of Medicine and others.

## Scientific Rationale – January 2012

A clinical guideline from the Endocrine Society (2011) on the evaluation, treatment and prevention of Vitamin D deficiency recommends screening for vitamin D deficiency in individuals at risk for deficiency. They do not recommend population screening for vitamin D deficiency in individuals who are not at risk. Per the guideline, "There is no evidence demonstrating benefits of screening for vitamin D deficiency at a population level. Such evidence would require demonstration of the feasibility and cost-effectiveness of such a screening strategy, as well as benefits in terms of important health outcomes. In the absence of this evidence, it is premature to recommend screening at large at this time."

## Scientific Rationale Update – March 2011

### Institute of Medicine

On November 30, 2010, the Institute of Medicine published revised guidelines for vitamin D. The revisions include new recommendations for vitamin D intake as well as a new cutoff point for determining vitamin D deficiency.

The report's recommendations take into account nearly 1,000 published studies as well as testimony from scientists. A large amount of evidence, which formed the basis of the new intake values, confirms the roles of calcium and vitamin D in promoting skeletal growth and maintenance and the amounts needed to avoid poor bone health. The committee also reviewed hundreds of studies and reports on other possible health effects of vitamin D, such as protection against cancer, heart disease, autoimmune diseases, and diabetes. While these studies point to possibilities that warrant further investigation, they have yielded conflicting and mixed results and do not offer the evidence needed to confirm that vitamin D has these effects.

Although sunlight triggers the natural production of vitamin D in skin and contributes to people's vitamin D levels, individuals' sun exposure varies greatly and many people are told to minimize their exposure, so the committee assumed minimal sun exposure to establish the Dietary Reference Intakes (DRI's). The new intake levels of vitamin D cover the needs of individuals who get little sun.

Table 1, below, shows the Recommended Dietary Allowance (RDA) for Vitamin D, 1997 and 2010:

| **Life Stage Cycle** | **1997** | **2010** |
|---|---|---|
| Infants to 1 year | 200 IU | 400 IU |
| 1-18 years | 200 IU | 600 IU |
| 19-51 years | 200 IU | 600 IU |
| 51-70 years | 400 IU | 600 IU |
| 71+ years | 600 IU | 800 IU |
| Pregnant / Lactating | 200 IU | 600 IU |

The new report also updates the amount of vitamin D considered sufficient for bone health. The cutoff for a vitamin D deficiency is now less than 20 ng/mL; the former level was less than 15ng/mL.

The committee also increased the Tolerable Upper Intake Limits (UL), which represent the safe upper boundary of dietary intake and do not include vitamin D produced from exposure to sunlight. Rising rates of supplement use have increased the chances of overconsumption of vitamin D. Some signals suggest there are greater risks of death and chronic disease associated with long-term high vitamin D intake from supplements, which informed the committee's recommendations about excessive levels.

Table 2, below, shows upper limits vitamin D, 1997 verses 2010:

| **Age** | **1997** | **2010** |
|---|---|---|
| 1-3 years | 1,000 IU | 2,500 IU |
| 4-8 years | 2.000 IU | 3,000 IU |
| All others | 2,000 IU | 4,000 IU |

The 1997 UL used a different age-group classification for children: 0-12 months (1000 IU) and 1-13 years (2000 IU).

Cole et al. (2010) The goals of this study were to determine the prevalence of vitamin D deficiency among minority children in a southern U.S. city, to examine differences in serum 25-hydroxyvitamin D levels between non-Hispanic black and Hispanic children, and to determine dietary sources of vitamin D. Low-income, minority children (N = 290; mean age: 2.5 +/- 1.2 years) were recruited during well-child clinic visits. Serum 25-hydroxyvitamin D and calcium levels were measured and dietary information was assessed. The mean 25-hydroxyvitamin D(3) level was 26.2 +/- 7.6 ng/mL, whereas 25-hydroxyvitamin D(2) was not detected. Overall, 22.3% of children had deficient serum 25-hydroxyvitamin D (3) levels (<or =20 ng/mL), 73.6% had less-than-optimal serum 25-hydroxyvitamin D levels (<or =30 ng/mL), and 1.4% had low serum calcium levels (<or =9 mg/dL). A significantly larger proportion of non-Hispanic black children, compared with Hispanic children, had vitamin D deficiency (26% vs 18%; P<.05). Age and season of recruitment were significantly associated with vitamin D deficiency and low serum calcium levels. Older children (>or =3 years) were less likely to have vitamin D deficiency (odds ratio [OR]: 0.89 [95% confidence interval [CI]: 0.81-0.96]; P<.001). Study enrollment during spring and summer reduced the likelihood of vitamin D deficiency by approximately 20% (spring, OR: 0.85 [95% CI: 0.73-0.98]; P = .03; summer, OR: 0.82 [95% CI: 0.73-0.92]; P<.01). Fortified milk provided most dietary vitamin D (62%), with Hispanic children reporting greater intake. Suboptimal vitamin D status was common among apparently healthy, low-income, minority children. Age and season were significant predictors of vitamin D deficiency.

Baz-Hecht, et al. (2010) conducted a study to determine the frequency of vitamin D deficiency and its correlation with different factors. Three hundred and thirteen healthy children and adolescents (192 females and 121 males aged 8-18 years, mean +/- SD, 12.7 +/- 2.3 years) were enrolled, and measurements of serum 25-hydroxyvitamin D [25(OH)D](using EIA) and intact parathyroid hormone (iPTH) (using immunoradiometric assay (IRMA)) were conducted. The grades of vitamin D status were defined according to blood level of 25(OH)D as follows: severely deficient<12.5; deficient,>or = 12.5 and<25; insufficient,>or = 25 and<50; normal>or = 50 and<250 nmol/L. Severe deficiency was detected in 25% of subjects (males 8%; females 92%), deficiency in 27% (males 34%; females 66%) and insufficiency in 26% (males 58%; females 42%). The mean 25(OH)D level in males was significantly greater than that in females (p<0.001), and this level was significantly higher in prepubertal compared to pubertal subjects (p<0.001). 25(OH)D had a negative correlation with iPTH (p<0.001). The curve of iPTH began to rise when 25(OH)D reached 75 nmol/L. The level of 25(OH)D had a negative correlation with BMI-SDS and height-SDS in females (p-value, 0.01 and 0.039, respectively). The subjects did not have any signs or symptoms of rickets. Frequency of vitamin D deficiency did not have any significant seasonal variation. Furthermore, vitamin D deficiency was not found to be related to the type or location of the subjects' homes. In this study, subclinical vitamin D deficiency was significantly more prevalent in females, particularly those undergoing puberty. Children who were obese and taller than average, had lower levels of 25(OH)D, and level of 25(OH)D should be maintained>75 nmol/L in order to prevent PTH rising.

## Scientific Rationale – Initial

Vitamins are a number of chemically unrelated families of organic substances that cannot be synthesized by humans but need to be ingested in the diet in small quantities to prevent disorders of metabolism. They are divided into water-soluble and fat-soluble vitamins.

Vitamin D, also known as calciferol, is a lipid or fat-soluble vitamin whose metabolites have a significant clinical role in the interrelationship of vitamin D with calcium homeostasis and bone metabolism. Vitamin D* and its metabolites may be categorized into the following two families of steroids:

- **Cholecalciferol** (vitamin D3, colecalciferol, calciol) is produced in the skin on exposure to sunlight. The UV-B portion of sunlight converts 7-dehydrocholesterol to previtamin D3, which undergoes thermal isomerization to form vitamin D3. Latitude, season, aging, sunscreen use, clothing and skin pigmentation influence production of vitamin D3 by the skin.

    → Vitamin D3 is a hormone that has an important role in calcium and phosphorus metabolism.
    → Vitamin D3 is also obtained from dietary sources.
    → This form is the most active form of vitamin D.

- **Ergocalciferol** (vitamin D2, ercalciol) is manufactured by irradiation of ergosterol previtamin D2) derived from yeast. Both vitamins are transferred from the skin to the blood, where they are bound to a Gc-globulin, which is called vitamin D-binding protein (VDBP).

    → Ergocalciferol is not naturally present in the human body.
    → This form is also the form used in very high dose supplements.

***Note** – Both vitamin D2 and vitamin D3 are metabolized to 25-hydroxyvitamin D (25- OH Vit D) and to 1,25-dihydroxyvitamin D (1,25-(OH) 2 Vit D).

The main biologic actions of Vitamin D are noted below:

1. Absorption of calcium from intestine;
2. Mineralization of bone matrix;
3. Osteoblast differentiation;
4. Inhibition of parathyroid hormone secretion;
5. Bone resorption at highly supraphysiological concentrations.

In the kidney, 25-hydroxyvitamin D changes into an active form of the vitamin. 25-hydroxyvitamin D, also known as 25-hydroxycholecalciferol, calcidiol or abbreviated 25-OH Vit D, is the main vitamin D metabolite circulating in plasma.

Vitamin D may be acquired by exposure of skin to sunlight, intestinal absorption through the ingestion of foods containing vitamin D, and from dietary supplements. Foods such as fortified milk, oily fish, egg yolks, and liver, naturally contain substantial amounts of vitamin D. In the United States, milk is fortified with vitamin D2 (ergocalciferol, a plant steroid) or vitamin D3 and is the principal source of dietary vitamin D. In other parts of the world, cereals and bread products are often fortified with vitamin D. Consequently, before foods were supplemented with vitamin D, most vitamin D was acquired by its synthesis in skin.

The recommended daily allowance of 400 IU/day (10 µg) is generally consumed in the diet except in certain groups at risk for developing vitamin D deficiency, including breast-fed infants, strict vegetarians abstaining from eggs and milk, and the elderly. The concentration of vitamin D in serum is generally from < 0.2 to 20 ng/ml (< 0.5 – 52 ng/mL/l), although higher levels are apparent after prolonged exposure to sunlight.

**Vitamin D Deficiency**
Decreased levels of 25-OH Vitamin D could appear in patients with any of the following conditions:

- Nutritional rickets (i.e. Rare when due to Vitamin D deficiency except in populations with unusually low sun exposure and lack of vitamin D in fortified foods) / osteomalacia;
- Senile / postmenopausal osteoporosis
- Celiac disease
- Inflammatory bowel disease (e.g. Crohn's disease)
- Insufficiency of the exocrine pancreas
- Short bowel syndrome
- Biliary cirrhosis, liver dysfunction
- Renal osteodystrophy
- Nephrotic syndrome
- Neonatal hypocalcemia
- Hypocalcemia
- Treatment with anticonvulsant drugs (enhanced metabolism)

The U.S. Institute of Medicine recommends that 32 nanograms per milliliter of 25-hydroxyvitamin D, as measured in serum, is an adequate level of Vitamin D. Intestinal calcium transport increased by 45 to 65% in women when 25-OH vitamin D levels were increased from an average of 20 to 32 ng per milliliter (50 to 80 ng/mL per liter).

The synthesis of vitamin D and its metabolism is closely coupled to calcium homeostasis, and is regulated by the parathyroid hormone (PTH), serum calcium, and phosphorus levels. PTH also stimulates bone osteoclast activity to mobilize bone calcium stores, thereby increasing serum calcium.

Low concentrations of 25-OH vitamin D causes secondary hyperparathyroidism. An individual loses more calcium from his/her bones when the PTH is abnormally high (PTH>65 pg/ml) and has an even greater risk for bone loss. [Normal levels of PTH are 10-55 picograms per milliliter (pg/mL)].

Without vitamin D, only 10 to 15% of dietary calcium and about 60% of phosphorus is absorbed. The interaction of 1,25-dihydroxyvitamin D with the vitamin D receptor increases the efficiency of intestinal calcium absorption to 30 to 40% and phosphorus absorption to approximately 80%.

Subclinical vitamin D deficiency may contribute to the development of osteoporosis, and is also associated with an increased risk of fractures in the elderly, decreased immune function, bone pain, potential colon cancer and a decline in cardiovascular health. Disorders associated with fat malabsorption, such as celiac disease, Crohn disease, pancreatic insufficiency, cystic fibrosis, and cholestatic liver disease, are also associated with vitamin D deficiency.

Estrogen, placental growth hormone, and prolactin may also regulate vitamin D metabolism, playing a role during pregnancy to meet increased calcium demands. In

addition, more than 50% of postmenopausal women taking medication for osteoporosis had suboptimal levels of 25-hydroxyvitamin D.

The lowest levels of vitamin D were in non-whites and those with late-stage breast cancer. The researchers found that weekly supplementation with high doses of vitamin D (50,000 IU or more) boosted the levels of the vitamin among all the women.

**Elevated Levels of Vitamin D**
Elevated levels of 25-OH Vit D appear in patients with:

- Hypercalcemia
- Vitamin D intoxication

    - Because any excess previtamin D3 or vitamin D3 is destroyed by sunlight, excessive exposure to sunlight does <u>not</u> cause vitamin D3 intoxication.

Vitamin D intoxication is extremely rare but can be caused by inadvertent or intentional ingestion of excessively high doses. Doses of more than 50,000 IU per day raise levels of 25-hydroxyvitamin D to more than 150 ng per milliliter (374 ng/mL per liter) and are associated with hypercalcemia and perphosphatemia. Doses of 10,000 IU of vitamin D3 per day for up to 5 months, however, do not cause toxicity.

Patients with chronic granulomatous disorders are more sensitive to serum 25-hydroxyvitamin D levels above 30 ng per milliliter because of macrophage production of 1,25-dihydroxyvitamin D, which causes hypercalciuria and hypercalcemia. In these patients, however, 25-hydroxyvitamin D levels need to be maintained at approximately 20 to 30 ng per milliliter to prevent vitamin D deficiency and secondary hyperparathyroidism.

**Blood Test for Vitamin D**
The blood test for vitamin D is known as the 25-hydroxyvitamin D test (i.e. 25-OH vitamin D test, the Calcidiol 25-hydroxycholecalciferol test, or the 25[OH]D). 25-OH Vit D is the predominant circulating form of vitamin D in the blood, and it is considered to be the most reliable index of an individual's vitamin D nutritional status. This test reflected the total amount of vitamin D in the body that was coming from all sources (Eg. Diet, dietary supplements, and the sun). The vitamin D blood test should be offered from the fall season through winter when vitamin D blood levels are at their lowest. Spring and summer months can give patients and clinicians a false sense of vitamin D security.

Although most laboratories report the normal range of the 25-hydroxyvitamin D test to be 20 to 100 ng per milliliter [50 to 250 ng/mL per liter], the preferred range is 30 to 60 ng per milliliter [75 to 150 ng/mL per liter]. This type of Vitamin D testing became more accurate and widely utilized in the 1970's; however, there has more recently been a resurgence of it, due to various articles noting the importance of Vitamin D testing.

The newer focus of Vitamin D testing is on research into the possible usefulness of vitamin D for the following reasons:

- A screening parameter for risk estimation of osteoporosis;
- An aid in the treatment of cancers;
- An immune booster;

- Slowing of the aging process;
- Improving neuromuscular function;
- Treatment of dermal diseases, e.g. psoriasis.

Vitamin D3 seemed more effective than D2 at raising this blood test. Enzymes in the liver and the final vitamin D receptors (VDR) in tissues, bind vitamin D3 more effectively. As humans age, these metabolic differences make a very large difference in terms of effectiveness. Almost all successful anti-fracture clinical trials have used vitamin D3 at a dosage of at least 800 IU/day (20 mcg per day).

**Studies**

Mansbach et al. (2009) performed a study with the objective to determine if the serum levels of 25-hydroxyvitamin D (25[OH]D) is a nationally representative sample of US children aged 1 to 11 years. Data was collected from the 2001–2006 National Health and Nutrition Examination Survey. Serum 25(OH)D levels were determined by radioimmunoassay and categorized as <25, <50, and <75 ng/mL/L. National estimates were obtained by using assigned patient visit weights and reported with 95% confidence intervals (Cis). : During the 2001–2006 time period, the mean serum 25(OH)D level for U.S. children aged 1 to 11 years was 68 ng/mL/L (95% CI: 66–70). Children aged 6 to 11 years had lower mean levels of 25(OH)D (66 ng/mL/L [95% CI: 64–68]) compared with children aged 1 to 5 years (70 ng/mL/L [95% CI: 68–73]). Overall, the prevalence of levels at <25 ng/mL/L was 1% (95% CI: 0.7–1.4), <50 ng/mL/L was 18% (95% CI: 16–21), and <75 ng/mL/L was 69% (95% CI: 65–73). The prevalence of serum 25(OH)D levels of <75 ng/mL/L was higher among children aged 6 to 11 years (73%) compared with children aged 1 to 5 years (63%); girls (71%) compared with boys (67%); and non-Hispanic black (92%) and Hispanic (80%) children compared with non-Hispanic white children (59%). On the basis of a nationally representative sample of US children aged 1 to 11 years, millions of children may have suboptimal levels of 25(OH)D, especially non-Hispanic black and Hispanic children. More data in children are needed not only to understand better the health implications of specific serum levels of 25(OH) D but also to determine the appropriate vitamin D supplement requirements for children.

Dr. Jonathan Mansbach of the Harvard Medical School and Children's Hospital in Boston says his study supports expert recommendations of children getting a healthy amount of 400 daily units of vitamin D for the prevention of rickets. A child could consume the daily, recommended amount of vitamin D by drinking four cups of fortified milk, or eating large amounts of fish, however, many children do neither. Another great source of vitamin D is natural sunlight. When the skin is exposed to sunlight, the body makes vitamin D. Many children don't spend enough time outdoors to absorb the sunlight necessary for the body to produce the vitamin. This is especially true for children who live in colder climates. In addition, the bodies of children with darker skin often do not produce enough vitamin D as their skin absorbs less sunlight. Until more research is performed, the safest bet is to take vitamin D supplements.

Many breast cancer patients are deficient in vitamin D, according to the results of a study presented at the American Society of Clinical Oncology breast cancer symposium on October 8, 2009 in San Francisco. This could lead to weaker bones and increased risk of fractures. Vitamin D is essential to maintaining bone health, and women with breast cancer have accelerated bone loss due to the nature of hormone therapy and chemotherapy. It's important for women and their doctors to work together to boost their vitamin D intake. Peppone et al. (2009) analyzed vitamin D levels in 166 women with non-metastatic breast cancer who were undergoing one or more of the following treatments: hormone therapy, radiation,

and chemotherapy. The authors found that nearly 70 percent had vitamin D deficiency. Although levels of 32 nanograms/ml are adequate, the average level among the women was 27 ng/mL of vitamin D. Previous studies have shown that nearly half of all women and men have vitamin D levels below 32 nanograms per milliliter. The researchers found that weekly high-dose vitamin D supplementation (50,000 IU or more) increased vitamin D levels more than conventional low-dose supplementation. (It is important to note that high doses of vitamin D are safe for short-term use in order to correct a deficiency; however, could potentially be dangerous for the long-term.) In summary, literature regarding breast cancer risk and vitamin D has increased substantially over the past 10 years; however, definitive evidence regarding a causal relationship between vitamin D deficiency and breast cancer risk is still lacking. The association between levels of vitamin D and risk for certain types of cancer continues to be evaluated.

Hendry (2009) et al. completed a study in which Dr. Annamari Kilkkinen et al., at the National Institute for Health and Welfare in Helsinki, Finland, compared blood levels of vitamin D and deaths from heart disease or stroke over time in 2,817 men and 3,402 women in Finland. At enrollment, participants were just over 49 years old on average, and had no indicators of cardiovascular disease, the researchers note in the American Journal of Epidemiology. During follow-up of about 27 years on average, 640 of the participants (358 men) died from heart disease and another 293 (122 men) died from stroke. Compared with participants' with the highest vitamin D, those with the lowest Vitamin D levels had 25 percent higher risk of dying from heart disease or stroke. Allowing for age, gender, and other demographic factors, plus alcohol intake, smoking, physical activity, and season in which vitamin D levels were obtained did not significantly alter these associations. In this study, vitamin D levels were "substantially lower" than levels thought to be sufficient, and "somewhat lower" than those reported in previous studies in other European and American populations. However, there is no "absolute consensus" as to what the optimal range of vitamin D should be, the investigators note. Also, it's not known whether low vitamin D actually causes increased risk for heart disease or stroke. Additional, larger randomized controlled studies are necessary.

**American Academy of Pediatrics (AAP)**

In November 2008, the American Academy of Pediatrics (AAP) released a guidance paper on the prevention of rickets and vitamin D deficiency in infants, children, and adolescents. This new report replaces their 2003 statement, which recommended a daily intake of 200 International Units (IU). The 2008 AAP statement recommends that the daily vitamin D intake for all pediatric patients be increased to 400 International Units (10 mcg), with a goal 25 (OH)D level of at least 20 ng/mL. The AAP statement also recommends that breastfed infants receive a vitamin D supplement at a dose of 400 International Units/day beginning shortly after birth and continuing until they are weaned and consuming at least 1 L of vitamin D-fortified formula or milk per day. Daily supplementation is also recommended for older children and adolescents who do not consume at least 400 International Units of vitamin D with their usual diet. The AAP guidelines were based on studies documenting the safety of vitamin D at this higher dose as well as new evidence suggesting a possible role for vitamin D in preventing cancer, cardiovascular disease, and diabetes.

The American Academy of Pediatrics recommends that children attain blood levels of vitamin D of at least 50 nanomoles per liter (nmol/L), while for adults, studies have found at least 75 nmol/L and perhaps up to 100 nmol/L could lower the risk of heart disease and specific cancers, researchers say.

However, much debate remains as to just how much daily vitamin D one should get for the amount to be deemed healthy. While 400 daily units may be enough to prevent rickets, it may not be a large enough quantity to promote general good health and prevent illness. Some experts suggest that newborns should start out getting 400 units of vitamin D a day, and up to 1,000 units per day after the age of 1 year. For teens, the amount suggested is 2,000 units per day, while for adults the various amounts deemed healthy by experts are up to 10,000 units daily. Working to establish standards needs to be a priority.

**Medicare Members**
Centers for Medicare & Medicaid (CMS). LCD for Vitamin D Assay Testing (L29510). Per local Medicare coverage, measurement of vitamin D levels is indicated for patients with:

- Chronic kidney Disease stage III or greater;
- Osteoporosis;
- Osteomalacia;
- Osteopenia;
- Hypocalcemia;
- Hypercalcemia;
- Hypoparathyroidism;
- HyperparathyroiDism;
- Rickets; and
- To monitor the efficacy of replacement therapy.

Limitations of Vitamin D testing per Local Medicare regulations:

- For Medicare beneficiaries, screening tests are governed by statute (Social Security Act 1861 {nn}). Vitamin D testing may not be used for routine screening.
- Once a beneficiary has been shown to be Vitamin D deficient, further testing is medically necessary **only** to ensure adequate replacement has been accomplished. Thereafter, annual testing may be appropriate depending upon the indication and other mitigating factors.

**Summary**

There has been an increase in tests for Vitamin D levels, noted within the past couple of years in the U.S. In 2008 there was an article from an investigator at Johns Hopkins that measured Vitamin D levels and correlated them with overall mortality. It has been followed by studies in various journals noting various benefits for vitamin D testing; however, most of these have not been backed up with randomized, controlled studies. An article in the American Journal of Epidemiology has just been published that ties Vitamin D levels to heart and stroke deaths. A recent article was also published on Vitamin D levels in children that appear low. The implications of all three are that there is inadequate Vitamin D intake and that Vitamin D levels may correlate with disease.

Undiagnosed vitamin D deficiency is not uncommon, and 25-hydroxyvitamin D is the barometer for vitamin D status. Serum 25-hydroxyvitamin D is not only a predictor of bone health but is also an independent predictor of risk for cancer and other chronic diseases. The report that postmenopausal women who increased their vitamin D intake by 1100 IU of vitamin D3 reduced their relative risk of cancer by 60 to 77% is a compelling reason to be vitamin D–sufficient.

Most commercial assays for 25-hydroxyvitamin D are good for detecting vitamin D deficiency. Radioimmunoassays measure total 25-hydroxyvitamin D, which includes levels of both 25-hydroxyvitamin D2 and 25-hydroxyvitamin D3. Some commercial laboratories measure 25-hydroxyvitamin D2 and 25-hydroxyvitamin D3 with liquid chromatography and tandem mass spectroscopy and report the values separately. As long as the combined total is 30 ng per milliliter or more, the patient has sufficient vitamin D.

The 1,25-dihydroxyvitamin D assay should never be used for detecting vitamin D deficiency because levels will be normal or even elevated as a result of secondary hyperparathyroidism. Because the 25-hydroxyvitamin D assay may not always be available, providing children and adults vitamin D supplements should guarantee vitamin D sufficiency unless there are mitigating circumstances. The majority of evidence suggests that the recommended dietary intakes alone are actually inadequate. Therefore, sensible sun exposure (or ultraviolet B irradiation), the use of vitamin D supplements, as well as dietary sources, are all needed to fulfill the body's vitamin D requirement.

Local Medicare coverage has specific guidelines for Vitamin D testing noted within the scientific rationale of this policy.

## Review History

| | |
|---|---|
| December 2009 | Medical Advisory Council Initial Approval |
| March 2011 | Update. Added Medicare Table with link to LCD. No revisions. |
| January 2012 | Update – no revisio U Update – no revisions |
| January 2013 | Update - no revisions. Codes updated. |

January 2014 Update – no revisions

**Patient Education Websites**

**English**

1. MedlinePlus. 25-hydroxy vitamin D test. Available at: http://www.nlm.nih.gov/medlineplus/ency/article/003569.htm
2. MedlinePlus.

**Spanish**

1. MedlinePlus. Examen de 25-hidroxi vitamina D. Acesso en: http://www.nlm.nih.gov/medlineplus/spanish/ency/article/003569.htm
2. MedlinePlus.

## This policy is based on the following evidence-based guidelines:

1. Hayes Webinar. Vitamin D and Disease Prevention: Unraveling the Evidence. 11/18/2010.
2. Holick MF, Binkley NC, Bischoff-Ferrari HA, et al. Evaluation, Treatment, and Prevention of Vitamin D Deficiency: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2011 Jul;96(7):1911-30. Available at: http://www.endo-society.org/guidelines/final/upload/FINAL-Standalone-Vitamin-D-Guideline.pdf

## References – January 2014


1. Kopes-Kerr, C. Should family physicians routinely screen for vitamin D deficiency? No: screening is unnecessary, and routine supplementation makes more sense. *Am Fam Physician*. 2013 Apr 15;87(8):od2.


## References Update – January 2013


1. Misra M. Vitamin D insufficiency and deficiency in children and adolescents. UpToDate. December 10, 2012.
2. Ferri: Ferri's Clinical Advisor 2013, 1st ed. Laboratory Tests. 2012 Mosby, An Imprint of Elsevier
3. Tangpricha V. An update on the screening, diagnosis, management, and treatment of vitamin D deficiency in individuals with cystic fibrosis: evidence-based recommendations from the Cystic Fibrosis Foundation. J Clin Endocrinol Metab - 01-APR-2012; 97(4): 1082-93


## References Update – January 2012


1. Glendenning P, Inderjeeth CA. Screening for vitamin D deficiency: defining vitamin D deficiency, target thresholds of treatment and estimating the benefits of treatment. Pathology. 2011 Dec 19


## References Update – March 2011


1. Institute of Medicine (IOM). Dietary References for Calcium and Vitamin D. Washington D.C.: The National Acadamies Press. 2010. Available at: http://www.iom.edu/Reports/2010/Dietary-Reference-Intakes-for-Calcium-and-Vitamin-D.aspx.
2. Pazirandeh S, Burns DL. Overview of vitamin D. May 19, 2010.
3. Cole CR, Grant FK, Tangpricha V, et al. 25-hydroxyvitamin D status of healthy, low-income, minority children in Atlanta, Georgia. Pediatrics. 2010;125(4):633-9.

4. Baz-Hecht M, Goldfine A. The impact of vitamin D deficiency on diabetes and cardiovascular risk. Curr Opin Endocrinol Diab Obesity. 2010;17(2):113-119.
5. Razzaghy-Azar M, Shakiba M. Assessment of vitamin D status in healthy children and adolescents living in Tehran and its relation to iPTH, gender, weight and height. Ann Hum Biol. 2010;37(5):692-701.
6. Bischoff-Ferrari HA, Dawson-Hughes B, Staehelin HB, et al. Fall prevention with supplemental and active forms of vitamin D: a meta-analysis of randomised controlled trials, BMJ. 2009;339:b3692.
7. Freeedman DM, Looker A, Abnet CC, et al. Serum 25-hydroxyvitamin D and cancer mortality in the NHANES III Study (1998-2006). Cancer Res. 2010;70(21):8587-8597.
8. Gandini S, Boniol M, Haukka J, et al. Meta-analysis of observational studies of serum 25-hyroxyvitamin D levels and colorectal, breast and prostate cancer and colorectal adenoma. Int J Cancer. 2010. July 21; (epub ahead of print).

## References Initial

1. Mansbach JM, Ginde AA, Camargo CA. Serum 25-Hydroxyvitamin D Levels Among US Children Aged 1 to 11 Years: Do Children Need More Vitamin D? PEDIATRICS Vol. 124 No. 5 November 2009, pp. 1404-1410.
2. Hendry J. Low Vitamin D Tied to Heart, Stroke Deaths. American Journal of Epidemiology, October 15, 2009.
3. Freedman OC, Goodwin PJ. The Role of Vitamin D in Breast Cancer Recurrence. American Society of Clinical Oncology. ASCO Educational Book; 2009.
4. Centers for Medicare & Medicaid (CMS). LCD for D">VITAMIN D Assay TESTING (L29510). National Government Services. 9/1/2009. Available at: http://www.cms.hhs.gov/mcd/viewlcd_pdf.asp?lcd_id=29510&lcd_version=8&contractor_id=178
5. Centers for Medicare & Medicaid (CMS). Article for D">VITAMIN D Assay TESTING - Supplemental Instructions Article (A49254).
6. Peppone LJ, et al. Vitamin D deficiency prevalent in women being treated for breast cancer; High-dose supplementation can increase vitamin D blood levels. American Society of Clinical Oncology Breast Cancer Symposium, Abstract 211. October 8, 2009.
7. Cauley J, LaCroix AZ, Wu L, el al. Serum 25-Hydroxyvitamin D Concentrations and Risk for Hip Fractures. 19 August 2008 Annals of Internal Medicine Volume, 149. Number 4.
8. Goodwin P, Ennis M, Pritchard K, Koo J, Hood N. Vitamin D is common at breast cancer diagnosis and is associated with a significantly higher risk of distant recurrence and death in a prospective cohort study of T1-3, N0-1, M0 BC. Early Release Proceedings from the 2008 American Society of Clinical Oncology. #511.
9. Misra M, Pacaud D, Petryk A, et al. Vitamin D deficiency in children and its management: review of current knowledge and recommendations. Pediatrics. 2008 Aug;122(2):398-417.
10. Wagner CL, Greer FR, American Academy of Pediatrics Section on Breastfeeding, American Academy of Pediatrics Committee on Nutrition. Prevention of rickets and vitamin D deficiency in infants, children, and adolescents. Pediatrics 2008;122:1142–52.
11. Weng FL, Shults J, Leonard MB, et al. Risk factors for low serum 25-hydroxyvitamin D concentrations in otherwise healthy children and adolescents. Am J Clin Nutr. 2007; 86(1):150-158.
12. Lappe JM, Travers-Gustafson D, Davies KM, et al. Vitamin D and calcium supplementation reduces cancer risk: results of a randomized trial. Am J Clin Nutr. 2007; 85(6):1586-1591.
13. Holick, MF. Vitamin D deficiency. N Engl J Med 2007; 357:266. Available at: http://content.nejm.org/cgi/content/full/357/3/266

14. Das G, Crocombe S, McGrath M, et al. Hypovitaminosis D among healthy adolescent girls attending an inner city school. Arch Dis Child 2006; 91:569.
15. Lips P, Hosking D, Lippuner K, et al. The prevalence of vitamin D inadequacy amongst women with osteoporosis: an international epidemiological investigation. J Intern Med 2006; 260:245.
16. Holick MF. High prevalence of vitamin D inadequacy and implications for health. Mayo Clin Proc 2006; 81:353.
17. Bischoff-Ferrari HA, Giovannucci E, Willett WC, et al. Estimation of optimal serum concentrations of 25-hydroxyvitamin D for multiple health outcomes. Am J Clin Nutr 2006; 84:18.
18. Bischoff-Ferrari HA, Willett WC, Wong JB, et al. Fracture Prevention With Vitamin D Supplementation. A Meta-analysis of Randomized Controlled Trials. JAMA, Vol. 293 No. 18, May 11, 2005. Available at: http://jama.ama-assn.org/cgi/content/full/293/18/2257
19. Gordon CM, DePeter KC, Feldman HA, et al. Prevalence of vitamin D deficiency among healthy adolescents. Arch Pediatr Adolesc Med 2004; 158:531.

**Important Notice**

**General Purpose**
Health Net's National Medical Policies (the "Policies") are developed to assist Health Net in administering plan benefits and determining whether a particular procedure, drug, service or supply is medically necessary. The Policies are based upon a review of the available clinical information including clinical outcome studies in the peer-reviewed published medical literature, regulatory status of the drug or device, evidence-based guidelines of governmental bodies, and evidence-based guidelines and positions of select national health professional organizations. Coverage determinations are made on a case-by-case basis and are subject to all of the terms, conditions, limitations, and exclusions of the member's contract, including medical necessity requirements. Health Net may use the Policies to determine whether under the facts and circumstances of a particular case, the proposed procedure, drug, service or supply is medically necessary. The conclusion that a procedure, drug, service or supply is medically necessary does not constitute coverage. The member's contract defines which procedure, drug, service or supply is covered, excluded, limited, or subject to dollar caps. The policy provides for clearly written, reasonable and current criteria that have been approved by Health Net's National Medical Advisory Council (MAC). The clinical criteria and medical policies provide guidelines for determining the medical necessity criteria for specific procedures, equipment, and services. In order to be eligible, all services must be medically necessary and otherwise defined in the member's benefits contract as described this "Important Notice" disclaimer. In all cases, final benefit determinations are based on the applicable contract language. To the extent there are any conflicts between medical policy guidelines and applicable contract language, the contract language prevails. Medical policy is not intended to override the policy that defines the member's benefits, nor is it intended to dictate to providers how to practice medicine.

**Policy Effective Date and Defined Terms.**
The date of posting is not the effective date of the Policy. The Policy is effective as of the date determined by Health Net. All policies are subject to applicable legal and regulatory mandates and requirements for prior notification. If there is a discrepancy between the policy effective date and legal mandates and regulatory requirements, the requirements of law and regulation shall govern. * In some states, new or revised policies require prior notice or posting on the website before a policy is deemed effective. For information regarding the effective dates of Policies, contact your provider representative. The Policies do not include definitions. All terms are defined by Health Net. For information regarding the definitions of terms used in the Policies, contact your provider representative.

**Policy Amendment without Notice.**
Health Net reserves the right to amend the Policies without notice to providers or Members. In some states, new or revised policies require prior notice or website posting before an amendment is deemed effective.

**No Medical Advice.**
The Policies do not constitute medical advice. Health Net does not provide or recommend treatment to members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

**No Authorization or Guarantee of Coverage.**
The Policies do not constitute authorization or guarantee of coverage of particular procedure, drug, service

or supply. Members and providers should refer to the Member contract to determine if exclusions, limitations, and dollar caps apply to a particular procedure, drug, service or supply.

**Policy Limitation: Member's Contract Controls Coverage Determinations.**
The determination of coverage for a particular procedure, drug, service or supply is not based upon the Policies, but rather is subject to the facts of the individual clinical case, terms and conditions of the member's contract, and requirements of applicable laws and regulations. The contract language contains specific terms and conditions, including pre-existing conditions, limitations, exclusions, benefit maximums, eligibility, and other relevant terms and conditions of coverage. In the event the Member's contract (also known as the benefit contract, coverage document, or evidence of coverage) conflicts with the Policies, the Member's contract shall govern. Coverage decisions are the result of the terms and conditions of the Member's benefit contract. The Policies do not replace or amend the Member's contract. If there is a discrepancy between the Policies and the Member's contract, the Member's contract shall govern.

**Policy Limitation: Legal and Regulatory Mandates and Requirements.**
The determinations of coverage for a particular procedure, drug, service or supply is subject to applicable legal and regulatory mandates and requirements. If there is a discrepancy between the Policies and legal mandates and regulatory requirements, the requirements of law and regulation shall govern.

**Policy Limitations: Medicare and Medicaid.**
Policies specifically developed to assist Health Net in administering Medicare or Medicaid plan benefits and determining coverage for a particular procedure, drug, service or supply for Medicare or Medicaid members shall not be construed to apply to any other Health Net plans and members. The Policies shall not be interpreted to limit the benefits afforded Medicare and Medicaid members by law and regulation.