



BlueCross BlueShield
of Alabama

Name of Policy:

Bone Mineral Density Testing

Policy #: 191
Category: Radiology

Latest Review Date: April 2017
Policy Grade: A

Background/Definitions:

As a general rule, benefits are payable under Blue Cross and Blue Shield of Alabama health plans only in cases of medical necessity and only if services or supplies are not investigational, provided the customer group contracts have such coverage.

The following Association Technology Evaluation Criteria must be met for a service/supply to be considered for coverage:

- 1. The technology must have final approval from the appropriate government regulatory bodies;*
- 2. The scientific evidence must permit conclusions concerning the effect of the technology on health outcomes;*
- 3. The technology must improve the net health outcome;*
- 4. The technology must be as beneficial as any established alternatives;*
- 5. The improvement must be attainable outside the investigational setting.*

Medical Necessity means that health care services (e.g., procedures, treatments, supplies, devices, equipment, facilities or drugs) that a physician, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury or disease or its symptoms, and that are:

- 1. In accordance with generally accepted standards of medical practice; and*
- 2. Clinically appropriate in terms of type, frequency, extent, site and duration and considered effective for the patient's illness, injury or disease; and*
- 3. Not primarily for the convenience of the patient, physician or other health care provider; and*
- 4. Not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.*

Description of Procedure or Service:

Bone density studies can be used to identify individuals with osteoporosis and monitor response to osteoporosis treatment, with the goal of reducing the risk of fracture. Bone density is most commonly evaluated with dual x-ray absorptiometry (DXA); other technologies are also available.

Bone Mineral Density

Risk factors for fracture include low bone mass, low bone strength, a personal history of fracture as an adult, or a history of fracture in a first-degree relative. Osteoporosis, defined as low bone mass leading to an increased risk of fragility fractures, is an extremely common disease in the elderly population due to age-related bone loss in both sexes and menopause-related bone loss in women. The World Health Organization (WHO) has diagnostic thresholds for osteoporosis based on bone mineral density (BMD) measurements compared with a T score, which is the standard deviation difference between an individual's BMD and that of a young-adult reference population. Conditions that can cause or contribute to osteoporosis include lifestyle factors such as low intake of calcium, high intake of alcohol or cigarette smoking, and thinness. Other risk factors for osteoporosis include certain endocrine, hematologic, gastrointestinal tract and genetic disorders, hypogonadal states, and medications.

BMD can be measured using different techniques in a variety of central (i.e., hip or spine) or peripheral (i.e., wrist, finger, heel) sites. While BMD measurements are predictive of fragility fractures at all sites, central measurements of the hip and spine are the most predictive. Fractures of the hip and spine (i.e., vertebral fractures) are also considered to be the most clinically relevant. BMD is typically expressed as a T score. The utility of screening BMD measurements can be established by demonstrating that screening identifies a population at increased risk of fracture and that, by treating those at-risk individuals, the rate of fractures is reduced thereby lowering fracture-related morbidity and mortality. These potential benefits of screening should outweigh the risks of screening (radiation exposure) or false positives (initiation of unnecessary treatment).

Osteoporosis Treatment

Treatment of osteoporosis includes both lifestyle measures (e.g., increased intake of calcium and vitamin D, exercise, smoking cessation) and pharmacologic measures. Current pharmacologic options include bisphosphonates such as alendronate (i.e., Fosamax), selective estrogen receptor modulators such as raloxifene (i.e., Evista), the recombinant human parathyroid hormone teriparatide (i.e., Forteo), and calcitonin. An updated 2014 systematic review funded by the Agency for Healthcare Research and Quality found good-quality evidence that bisphosphonates, denosumab, teriparatide, and raloxifene reduce fracture risk in postmenopausal women with BMD in the osteoporotic range and/or preexisting hip or vertebral fracture.

The decision to perform bone density assessment should be based on an individual's fracture risk profile and skeletal health assessment. In addition to age, sex, and BMD, risk factors included in the World Health Organization Fracture Risk Assessment (FRAX) Tool are:

- Low body mass index;
- Parental history of hip fracture;

- Previous fragility fracture in adult life (i.e., occurring spontaneously or a fracture arising from trauma which, in a healthy individual, would not have resulted in a fracture);
- Current smoking or alcohol three or more units per day, where a unit is equivalent to a standard glass of beer (285 mL), a single measure of spirits (30 mL), a medium-sized glass of wine (120 mL), or one measure of an aperitif (60 mL);
- A disorder strongly associated with osteoporosis. These include rheumatoid arthritis, type I (insulin dependent) diabetes, osteogenesis imperfecta in adults, untreated long-standing hyperthyroidism, hypogonadism or premature menopause (<45 years), chronic malnutrition or malabsorption, and chronic liver disease;
- Current exposure to oral glucocorticoids or the patient has been exposed to oral glucocorticoids for more than three months at a dose of prednisolone of 5 mg daily or more (or equivalent doses of other glucocorticoids).

A 2011 joint position statement from the International Society for Clinical Densitometry and the International Osteoporosis Foundation includes the official position that FRAX with BMD predicts risk of fracture better than clinical risk factors or BMD alone. In addition, the joint position statement states that measurements other than BMD or T score at the femoral neck by DXA are not recommended for use with FRAX. The FRAX tool does not include a recommendation about which patients to further assess or treat. The FRAX website states that this is a matter of clinical judgment and recommendations may vary by country.

The following technologies are most commonly used to measure BMD.

1. Dual X-ray Absorptiometry (DXA)

DXA is probably the most commonly used technique to measure BMD, because of its ease of use, low radiation exposure, and its ability to measure BMD at both the hip and spine. DXA can also be used to measure peripheral sites, such as the wrist and finger. DXA generates two x-ray beams of different energy levels to scan the region of interest and measure the difference in attenuation as the beam passes through the bone and soft tissue. The low-energy beam is preferentially attenuated by bone, while the high-energy beam is attenuated by both bone and soft tissue. This differential attenuation between the two beams allows for correction for the irregular masses of soft tissue, which surround the spine and hip, and therefore the measurement of bone density at those sites.

2. Quantitative Computed Tomography (QCT)

QCT depends on the differential absorption of ionizing radiation by calcified tissue and is used for central measurements only. Compared to DXA, QCT is less readily available and associated with relatively high radiation exposure and relatively high cost.

3. Ultrasound Densitometry

Ultrasound densitometry is a technique for measuring BMD at peripheral sites, typically the heel, but also the tibia and phalanges. Compared to osteoporotic bone, normal bone demonstrates higher attenuation of the ultrasound wave, and is associated with a greater velocity of the wave passing through bone. Ultrasound densitometry has no radiation exposure, and machines may be purchased for use in an office setting.

The above techniques dominate BMD testing. Single- and dual-photon absorptiometry and radiographic absorptiometry are now rarely used and may be considered obsolete.

Lunar iDXA is a DEXA machine that measures the bone density and also the body composition in one scan. This should be coded as a DEXA scan and subject to the same coverage criteria and limitations.

Policy:

❖ Children and Adolescents

Bone mineral density testing meets Blue Cross and Blue Shield of Alabama's medical criteria for coverage for any of the following risk factors:

- A child or adolescent patient who has been treated for cancer with agents that predispose to reduced bone mineral density, including glucocorticoids, cranial radiation, methotrexate, or hematopoietic cell transplant (HCT). These patients may have one test that is usually done within two years post-treatment.

❖ Females

Bone mineral density testing meets Blue Cross and Blue Shield of Alabama's medical criteria for coverage for **any** of the following risk factors when the results of the testing will affect a treatment or regimen program:

- Women age 65 and older, regardless of other risk factors;
- A woman with breast cancer who becomes menopausal due to treatment of breast cancer;
- A woman with breast cancer who is being treated with aromatase inhibitors ;
- A patient with a recent fracture when the fracture is suspected to be associated with osteoporosis;
- A patient with long-term corticosteroid therapy which is defined as greater than three months on the equivalent of 30 mg of cortisone or greater per day;
- A patient on long-term (greater than one month) heparin therapy;
- A patient on long-term (greater than three months) phenytoin therapy. This is drug therapy of the treatment of seizures;
- A patient with known hyperparathyroidism when the test result is used to determine if the patient needs a parathyroidectomy;
- A patient with excessive doses of thyroid replacement (for this indication the test is covered only if the patient has a subnormal TSH level while on thyroid replacement);
- A woman with primary ovarian failure or post-ablative ovarian failure before the age of 40, who is suspected of having osteoporosis;
- A patient with known osteoporosis or osteopenia;
- A woman with documented estrogen deficiency and at clinical risk for osteoporosis;
- All postmenopausal women under age 65 who have one or more additional risk factors for osteoporosis, including personal history of fracture as an adult, current fracture or history of fracture in first-degree relative, current cigarette smoking, low body weight (<127 lb.);

- As part of the initial workup prior to the initiation of glucocorticoid therapy. The most commonly used glucocorticoids include prednisone, prednisolone, betamethasone, and dexamethasone (Decadron).

Repeat bone mineral density testing meets Blue Cross and Blue Shield of Alabama’s medical criteria for coverage when **performed every 24 or more months**.

Repeat bone mineral density testing performed more often than every 24 months in females who **do not develop new risk factors does not meet** Blue Cross and Blue Shield of Alabama’s medical criteria for coverage. This also applies to patients currently being treated with medications to increase bone density.

Repeat bone mineral density testing performed more often than every 24 months in females who **develop new risk factors meets** Blue Cross and Blue Shield of Alabama’s medical criteria for coverage.

❖ Males

Bone mineral density testing for osteoporosis in males meets Blue Cross and Blue Shield of Alabama’s medical criteria for coverage for men with **one of the following risk factors**:

- Age, >70;
- Low body weight (see Key Points);
- Weight loss (see Key Points);
- Physical inactivity (see Key Points);
- Previous osteoporotic fracture;
- Prolonged systemic corticosteroid therapy;
- Androgen deprivation therapy.

Repeat bone mineral density testing meets Blue Cross and Blue Shield of Alabama’s medical criteria for coverage when **performed every 24 or more months**.

Repeat bone mineral density testing performed more often than every 24 months in males who **do not develop new risk factors does not meet** Blue Cross and Blue Shield of Alabama’s medical criteria for coverage. This also applies to patients currently being treated with medications to increase bone density.

Repeat bone mineral density testing performed more often than every 24 months in males who **develop new risk factor meets** Blue Cross and Blue Shield of Alabama’s medical criteria for coverage

Blue Cross and Blue Shield of Alabama does not approve or deny procedures, services, testing, or equipment for our members. Our decisions concern coverage only. The decision of whether or not to have a certain test, treatment or procedure is one made between the physician and his/her patient. Blue Cross and Blue Shield of Alabama administers benefits based on the member's contract and corporate medical policies. Physicians should always exercise their best

medical judgment in providing the care they feel is most appropriate for their patients. Needed care should not be delayed or refused because of a coverage determination.

Key Points:

The most recent literature review was performed through January 25, 2017. Following is a summary of key literature to date.

Initial Measurement of Bone Mineral Density (BMD)

Early versions of this evidence review were based in part on 1998 guidelines from the National Osteoporosis Foundation (NOF) and TEC Assessments from 1999 and 2002. Because no data were available from randomized screening trials, the TEC Assessments focused on the evaluating the utility of bone mineral density (BMD) measurement in selecting patients for pharmacologic treatment to reduce risk of fracture. The TEC Assessments concluded that while both dual x-ray absorptiometry (DXA) and ultrasound densitometry were equivalent in predicting fracture risk, the two techniques appeared to identify different populations of at-risk patients. In addition, calcaneal ultrasound densitometry did not meet the TEC criteria as a technique to predict response to pharmacologic therapy.

A 2005 meta-analysis of data from 9891 men and 29,082 women (from 12 cohort studies in Europe and Canada) found that BMD measurement at the femoral neck with DXA was a strong predictor of hip fractures for both genders. At age 65 years, the risk ratio for osteoporotic fractures increased by 1.4 (95% confidence interval [CI], 1.3 to 1.5) in men and by 1.4 (95% CI, 1.3 to 1.5) in women for each standard deviation decrease in BMD. Data for measurement of BMD using ultrasound and peripheral DXA were available from 3 cohorts. The predictive ability of these devices was less than that of DXA measurements at the femoral neck.

A systematic review of the evidence to update U.S. Preventive Services Task Force (USPSTF) recommendations on screening for osteoporosis was published in 2010. The authors state that most DXA testing includes central DXA (i.e., measurements at the hip and lumbar spine) and that most randomized controlled trials (RCTs) of osteoporosis medications have had study inclusion criteria based on the findings of central DXA. The authors found that calcaneal quantitative ultrasound (QUS) measurement can also predict fracture but has a low correlation with DXA. Consequently, the clinical relevance of calcaneal QUS findings is unclear because medication studies have not selected patients based on QUS findings. In addition, the investigators reviewed large population-based cohorts on DXA screening and concluded that the predictive performance of DXA is similar for women and men.

In 2013, Gadam et al performed a cross-sectional analysis of data to evaluate the incremental predictive ability of BMD measured using DXA when added to the FRAX model. The study included 151 subjects (145 women, six men) older than 50 years of age without a prior osteoporosis diagnosis and who were not being treated with U.S. Food and Drug Administration (FDA)-approved medications for treating osteoporosis. Of the 151 individuals, predictions of ten year fracture risk were identical for 127 patients (84%) when BMD was added to the FRAX model compared with the FRAX model without BMD. Of the subjects who had different risk estimates, the difference in risk prediction resulted in an additional two patients meeting the

NOF threshold for treatment when BMD was added to the FRAX model. Age was the only risk factor that differed significantly between participants with identical versus different recommendations ($p < 0.001$). Subjects who were younger (mean age, 64 years) were more likely to receive identical predictions than older subjects (mean age, 76 years). The study had a relatively small sample size and lacked longitudinal data on fracture. It provides some initial evidence that BMD may not add substantially to the predictive ability of the FRAX models, but these findings need to be corroborated in prospective studies with larger sample sizes.

Crandall et al (2015) reported results from 11,392 participants in the Women's Health Initiative (WHI) BMD Cohort, a prospective observational study of postmenopausal women with a mean follow-up of 8.5 years. Each standard deviation decline in lower BMD measured with central DXA was associated with higher wrist fracture risk, the adjusted hazard ratio (HR) being 1.7 (95% CI, 1.4 to 1.9) for femoral neck BMD and 1.5 (95% CI, 1.3 to 1.6) for lumbar spine BMD.

Cauley et al (2016) reported risk factors for hip fractures in 5994 men with a mean of 8.6 years of follow-up from the Osteoporotic Fractures in Men Study. Femoral neck BMD was measured using DXA. The incidence rate of hip fracture 33.4 per 1000 person-years in men with BMD T scores less than -2.5 who also had 4 or more risk factors, 14.5 per 1000 person-years in men age 80 years and older with 3 or more major comorbidities, and 0.88 per 1000 person-years in men age less than 70 years with zero comorbidities. Low BMD by World Health Organization classification (T score < -2.5) was highly associated with hip fracture (hazard ratio [HR], 3.3; 95% CI, 2.7 to 3.9) in a competing risk model after adjusting for several other fracture risk factors (e.g., age, previous fracture).

Section Summary: Initial Measurement of Bone Mineral Density

Central DXA is the most widely used method for measuring BMD. Several large studies have demonstrated a relation between fracture risk and BMD as measured by DXA in women and men. Most RCTs of the osteoporosis medications have had study inclusion criteria based on central DXA. These RCTs have shown that several osteoporosis medications are effective at reducing fracture risk in postmenopausal women with BMD in the osteoporotic range identified by central DXA and/or preexisting hip or vertebral fracture. This chain of evidence establishes that measuring BMD with central DXA improves health outcomes. There is less evidence for other methods of measuring BMD. BMD measured with other techniques may also be associated with fracture risk but has not been used to select participants for trials of osteoporosis medications.

Repeat Measurement of BMD for Individuals without Osteoporosis on the Initial Screen

In the analysis from the WHI BMD cohort (2015) previously described, changes in central DXA were examined over a 3-year period. A total of 9172 women had baseline and year 3 measures of femoral neck BMD and 9216 women had baseline and year 3 measures of lumbar spine. Decrease in femoral neck BMD between baseline and year 3 was associated with increased risk of subsequent wrist fracture (HR=1.2; 95% CI, 1.0 to 1.3; $p=0.03$). Change in lumbar spine BMD was not associated with wrist fracture by year 3 (HR=1.1; 95% CI, 0.95 to 1.2; $p=0.22$).

Leslie et al (2016) reported on repeat BMD measurements in clinical practice for fracture risk assessment from a large clinical BMD database for Manitoba, Canada, of women and men ages 50 years and older from 1990 to 2009. BMD was measured in the hip, lumbar spine, and femoral neck using DXA. A total of 50,215 participants had 1 BMD measurement, 14,619 had a second measurement, 4722 had a third measurement, and 1500 had a fourth measurement. The mean time between measurements was 4.2 years. Total hip BMD was predictive of major osteoporotic fracture at each time point. The association between BMD and major osteoporotic fracture was similar for the first and second BMD measurements: adjusted hazard ratios per standard deviation were 1.5 (95% CI, 1.3 to 1.6) and 1.6 (95% CI, 1.5 to 1.8), respectively. The hazard ratio for the second measurement was similar when stratified by preceding change in BMD or osteoporosis therapy.

A 2013 study by Berry et al did not find that changes in BMD 4 years after initial measurement added substantially to the prediction of fracture risk in untreated subjects. The authors included 210 women and 492 men (mean age, 75 years) from the Framingham Osteoporosis Study, a population-based cohort study, who had 2 BMD measurements (mean, 3.7 years apart) and did not have a hip fracture before the second test. BMD of the femoral neck was measured using a dual-photon absorptiometer from 1987 through 1991 and DXA from 1992 through 1999. Median follow-up was 9.6 years after the second BMD test. During this time, 76 individuals experienced a hip fracture and 113 had a major osteoporotic fracture (fracture of the hip, spine, forearm, or shoulder). In receiver operating curve analyses, adding repeat BMD to a model containing baseline BMD did not meaningfully improve the model's ability to predict hip fracture (area under the curve [AUC], 0.72; 95% CI, 0.66 to 0.79). When percent change in BMD was used, the AUC was 0.71 (95% CI, 0.65 to 0.78) in a model including only baseline BMD and 0.68 (95% CI, 0.62 to 0.75) in a model including percent change in BMD.

A 2012 multicenter prospective study by Gourlay et al provided data on the optimal bone density screening interval in a large cohort of women with normal BMD measured by DXA or osteopenia at an initial screen. The investigators included a total of 4,957 women age 67 years or older that had BMD data at two or more examinations or at one examination before a competing risk event (hip or clinical vertebral fracture). More than 99% of the sample reported they were white. The study only included women who were candidates for osteoporosis screening. Other women, such as those with osteoporosis at baseline or with a history of a hip or clinical vertebral fracture were excluded, as they would already be candidates for pharmacological treatment. The primary outcome was the estimated time interval for 10% of participants to make the transition from normal BMD or osteopenia at baseline to osteoporosis before a hip or clinical vertebral fracture occurred and before starting osteoporosis treatment. For women with normal BMD at baseline, the estimated BMD testing interval was 16.8 years (95% confidence interval [CI]: 11.5 to 24.6). The study also found that the estimated BMD testing interval was 17.3 years (95% CI: 13.9 to 21.5) for women with mild osteopenia at baseline, 4.7 years (95% CI: 4.2 to 5.2) with moderate osteopenia, and 1.1 years (95% CI: 1.0 to 1.3) for women with advanced osteopenia.

Longitudinal changes in BMD measured by DXA, as a function of age and antiresorptive agents, were reported in 2008 by the Canadian Multicentre Osteoporosis Study Research Group. Among a random selection of 9423 men and women from nine major Canadian cities, 4433 women and

1935 men (70%) were included for analysis. The subjects were 25 years of age or older with BMD measurements repeated three or five years apart; they tended to have better health than the 30% who did not have longitudinal data and who were excluded from analysis. Results showed that annual rates of bone loss, measured at the hip or femoral neck, increased between 25 and 85 years of age in women who were not on antiresorptive therapy, with accelerated periods of bone loss around menopausal transition (age range, 40-54 years) and after 70 years of age. Antiresorptive therapy, which primarily consisted of hormone replacement when the study began in 1995, was associated with attenuated bone loss across all age ranges. In women 50 to 79 years of age, the average loss in BMD over a five-year period was 3.2% in nonusers of antiresorptive therapy and 0.2% in women who used antiresorptive therapy. The pattern in men was generally similar to that of women with two exceptions, BMD loss began earlier in men, and the rate of change remained relatively constant between 40 and 70 years of age. Notably, BMD at the lumbar spine did not parallel measurements at the hip and femoral neck, suggesting that vertebral bone density assessment may be obscured by degenerative changes in the spine or other artifact. The report concluded that “although current guidelines recommend that measurements of bone density be repeated once every two to three years, our data suggest that, at this rate of testing, the average person would exhibit change well below the margin of error, especially since only 25% of women experienced a loss of bone density that exceeded 5% over five years.”

In 2009, Frost and colleagues developed a prognostic model to determine the optimal screening interval for an individual without osteoporosis (defined as T-score more than -2.5). They used prospective population-based data collected from 1,008 women and 750 men who were non-osteoporotic at baseline; participants received BMD screening every two years and received a median follow-up of 7.1 years. The prognostic model included the variables of age and initial BMD score; results were presented in complex tables stratified by these two variables. In the table of estimated time to reach 20% risk of sustaining a fracture or osteoporosis, most of the time estimates were three years or longer. The shortest time to reach a 20% risk was estimated at 2.4 years; this was for women 80 years and older with a baseline T-score of -2.2. For a typical screening candidate, a 65-year-old woman with a baseline T-score of -1.0, the estimated time to reach a 10% risk of fracture was 3.8 years and to reach a 20% risk of fracture was 6.5 years. Overall, the study suggests that the three- to five-year time interval included in the policy for repeat measurement of BMD in people who tested normal is reasonable, but that an individualized model could result in longer or shorter recommended re-testing intervals.

A 2007 study by Hillier and colleagues did not find that follow-up central DXA BMD measurements eight years after a baseline screen provided substantial value in terms of predicting risk of fracture. The study included 4,124 women age 65 years and older and assessed total hip BMD at initial and follow-up screening examinations. In analyses adjusted for age and weight change, the initial and repeat BMD measurements had similar associations with fracture risk; this included risk of vertebral fractures, non-vertebral fractures and hip fractures. Stratifying the analysis by initial BMD T scores (i.e., normal, osteopenic or osteoporotic) did not alter findings.

Section Summary: Repeat Measurement of BMD for Individuals Without Osteoporosis on Initial Screen

Scant research has been done on the frequency of BMD monitoring for osteoporosis. The available research has evaluated repeat measurement with central DXA. Evidence on whether repeat measurements add to risk prediction compared with a single measurement is mixed. A longitudinal study suggests that a 3- to 5-year interval for repeat measurement of BMD in people who tested normal at baseline is reasonable, although the optimal interval may differ depending on risk factors.

Serial Measurement of Central BMD to Monitor Treatment Response

In 2009, Bell et al conducted a secondary analysis of data from the Fracture Intervention Trial (FIT), which randomized 6,459 post-menopausal women with low BMD to receive treatment with bisphosphonates or placebo; women underwent annual bone density scans. In their analysis, the investigators estimated between-person (treatment-related) variation and within-person (measurement-related) variation in hip and spine BMD measured by central DXA over time to assess the value of repeat bone mineral density scans for monitoring response to treatment. After three years, the mean cumulative increase in hip bone mineral density was 0.30 g/cm² in the alendronate group compared to a mean decrease of 0.012 g/cm² in the placebo group. Moreover, 97.5% of patients treated with alendronate had increases in hip bone mineral density of at least 0.019g/cm² suggesting a clinically significant response. However, the study also found large within-person variability in year-to-year bone density measurements. The average within-person variation in BMD measurement was 0.013 g/cm², which was substantially higher than the average annual increase in BMD in the alendronate group, 0.085 g/cm². Additional studies are needed to determine the optimal time interval for re-screening after starting bisphosphonate treatment.

Serial Measurement of Central BMD to Monitor Discontinuation of Treatment

In 2014, Bauer et al reported fracture risk prediction among women who discontinued alendronate after four to five years of treatment in the FLEX (Fracture Intervention Trial Long-term Extension) study. Women aged 61 to 86 years who had previously been treated with alendronate were randomized to five more years of alendronate or to placebo. A prior report of this study found that although hip BMD decreased in the placebo group, rates of fracture were similar between the group randomized to placebo and the group that continued on bisphosphonate therapy. It should be noted that alendronate has a half-life in humans that is estimated to exceed ten years. During the five years of placebo, 94 of 437 women (22%) experienced one or more symptomatic fractures; most of these (87%) occurred after one year. Post-hoc analysis found that older age and lower hip (but not spine) DXA at time of discontinuation were significantly related to increased fracture risk; however, changes in BMD between the beginning of discontinuation to years one and three were not.

Children and Adolescents

The Children's Oncology Group (COG) published a review in 2008 that summarized the existing literature that has defined characteristics of cancer survivors at risk for bone mineral deficits and contributed to the surveillance and counseling recommendations outlined in the COG long-term follow-up guidelines. Children and adolescents may experience bone problems and endocrine problems during and after therapy for oncologic problems. Reduced bone mineral density

(BMD) is particularly common among survivors of hematologic malignancies and brain tumors. Some of the risk seems to be related to the underlying cancer: bone mineral is already decreased, compared to normal for age, at the time of diagnosis of ALL. Chemotherapy and/or radiation therapy further increases these risks. Reduced BMD is often clinically invisible and unrecognized until a fracture occurs. Symptoms of fractures associated with osteoporosis may include bone pain, abnormal gait, vertebral collapse, back pain, or low-impact fractures. Most survivors of childhood cancer will regain bone mass with increasing time after therapy. However, BMD may be permanently reduced if the cancer or its treatment reduces peak bone mass, so children treated during puberty are particularly at risk. In addition, there may be progressive effects on BMD if the individual has a treatment related endocrinopathy (e.g., growth hormone deficiency or hypogonadism), or nephropathy causing chronic renal phosphate loss (e.g., Fanconi syndrome associated with ifosfamide). Glucocorticoids are an important component of chemotherapy for many childhood cancers. They contribute to bone loss through a variety of mechanisms, including direct inhibitory effects on osteoblasts and by inhibiting production of growth hormone, insulin-like growth factor (IGF-1), androgens, and estrogens. Current guidelines from the Children's Oncology Group recommend that all patients treated with agents that predispose to reduced BMD, including glucocorticoids, cranial radiation, methotrexate, or HCT, have a quantitative measure of BMD at the time of entry into long-term follow up, which typically occurs two years after completion of cancer chemotherapy. BMD should be measured with either dual energy x-ray absorptiometry (DXA) or quantitative computed tomography (QCT). The methodology employed may influence the results, and the optimal approach has not been established. The DXA results must be interpreted using age- and gender-specific standards (Z-scores) and not adult standards (T-scores). Results from the baseline evaluation and other clinical factors should determine the need for follow-up. In general, patients with normal BMD study results (e.g., Z-score -1) do not require follow-up examinations. Patients with significant BMD deficits (e.g., Z-scores < -2), recurrent fractures, or medical risk factors for decreasing BMD such as GHD or hypogonadism, require endocrine evaluation and treatment, counseling to optimize lifestyle factors affecting bone health, and long-term follow up of BMD.

Women and Breast Cancer

Women who have had breast cancer treatment may be at increased risk for osteoporosis for several reasons. Certain chemotherapy drugs can cause ovaries to stop making estrogen, bringing on early menopause. Also, if the ovaries are removed or irradiated, early menopause may result. These reduced levels of estrogen can cause bone loss. Aromatase inhibitors are a new type of hormonal therapy used to treat postmenopausal women with breast cancer. Some studies suggest that these drugs may lead to a loss of bone density, but the long-term results are not yet known.

Men

Osteoporosis in men is underdiagnosed and undertreated worldwide and in the United States. A 60-year-old white man has a 25% lifetime risk for an osteoporotic fracture, and the consequences of the fracture can be severe. The one-year mortality rate in men after hip fracture is twice that of females.

A meta-analysis showed that the most important risk factors for osteoporosis in men are age (>70 years), low body weight (body mass index <20 to 25 kg/m² or lower), weight loss (>10% [compared with the usual young or adult weight or weight loss in recent years]), physical inactivity (participates in no physical activity on a regular basis [walking, climbing stairs, carrying weights, housework, or gardening]), use of oral corticosteroids, androgen deprivation therapy, and previous fragility fracture.

Gastric Bypass

Recently, there has been interest in gastric bypass surgery as a potential risk factor for osteoporosis. Several case series have found a significant decrease in BMD at one or more sites following gastric bypass surgery. For example, Carrasco and colleagues reported on a series of 42 women, mean age 38 years, who underwent gastric bypass surgery. A year after surgery there was a significant reduction of 3% in total BMD, reduction of 10.5% in hip BMD and reduction of 7.4% in spine BMD. Another case series by Fleischer and colleagues included 23 individuals, aged 20–64 years, who had gastric bypass surgery. After one year of follow-up, there was a significant decrease in hip BMD, a mean loss of 9.2% at the femoral neck and 8.0% of the total hip. There was not a significant difference in lumbar spine BMD. Decline in BMD was strongly associated with the extent of weight loss and the authors speculated that this change might, in part, be due to unloading of the skeleton. Moreover, the authors comment that the study had a small sample size and larger longer-term studies are needed to answer the question of how bone density loss accompanying weight loss affects bone quality and fracture risk. The one comparative study that was identified had a different finding as regards hip BMD. This was a retrospective cohort study by Valderas et al. It included 26 post-menopausal women (mean age 58 years) who underwent Roux-en-Y gastric bypass and 26 women non-operated women matched for age and body mass index. After a mean of 3.1 years after surgery, the mean decrease in femoral neck BMD was 0.892 g/cm² in the gastric bypass group and 0.934 cm² in the comparison group; this difference was not statistically significant. Differences in lumbar spine BMD also did not differ significantly. Two clinical guidelines, the National Osteoporosis Foundation (NOF) and the American Association of Clinical Endocrinologists (AACE) list gastric surgery as one of many factors linked to an increased risk of osteoporosis or fracture.

Summary of Evidence

For individuals who are eligible for screening of bone mineral density (BMD) based on risk factor assessment who receive dual x-ray absorptiometry (DXA) analysis of central sites (hip or spine), the evidence includes large cohort studies, observational studies, and systematic reviews. Relevant outcomes are disease-specific survival, morbid events, functional outcomes, health status measures, quality of life, hospitalizations, medication use, and resource utilization. BMD measurements with central DXA identify individuals at increased risk of fracture. There is sufficient evidence that osteoporosis medications are effective at reducing fracture risk in postmenopausal women with BMD in the osteoporotic range identified by central DXA. Therefore, a chain of evidence establishes that screening BMD with central DXA is likely to improve health outcomes. Evidence to support serial or repeat measurement of BMD is less compelling; nonetheless, the available evidence and the consensus of clinical evidence-based guidelines support at least a 2-year interval in BMD measurement to monitor response to pharmacologic therapy. Finally, available evidence suggests that at least a 3- to 5-year timeframe is reasonable for repeat measurement of BMD in individuals who initially tested normal and to

monitor pharmacologic therapy. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

Practice Guidelines and Position Statements

In 2012, the American College of Obstetricians and Gynecologists (ACOG) issued updated guidelines on managing osteoporosis in women. The guidelines recommend that BMD screening should begin for all women at age 65 years. In addition, they recommend screening for women younger than 65 years in whom the Fracture Risk Assessment (FRAX) Tool indicates a ten-year risk of osteoporotic fracture of at least 9.3%. Alternatively, they recommend BMD screening women in younger than 65 or with any of the following risk factors (these are similar, but not identical to risk factors in FRAX):

- Personal medical history of a fragility fracture
- Parental medical history of hip fracture
- Weight less than 127 lb
- Medical causes of bone loss (i.e., medications or disease)
- Current smoker
- Alcoholism
- Rheumatoid arthritis
- For women who begin medication treatment for osteoporosis, a repeat BMD is recommended one to two years later to assess effectiveness. If BMD is improved or stable, additional BMD testing (in the absence of new risk factors) is not recommended. The guideline notes that it generally takes 18 to 24 months to document a clinically meaningful change in BMD and thus a two-year interval after treatment initiation is preferred to one year.
- The guidelines do not specifically discuss repeat BMD screening for women who have a normal finding on the initial test.
- Routine BMD screening is not recommended for newly menopausal women as a “baseline” screen.

National Osteoporosis Foundation

The National Osteoporosis Foundation (NOF) updated its practice guidelines in 2014. NOF guidelines recommend that all postmenopausal women and men age 50 and older should be evaluated clinically for osteoporosis risk to determine the need for BMD testing.

BMD assessment is indicated in:

- Women age 65 and older and men age 70 and older, regardless of other risk factors
- Younger postmenopausal women and men aged 50–69 with clinical risk factors for fracture
- Adults who have a fracture after age 50
- Adults with a condition or taking a medication associated with low bone mass or bone loss

NOF states that measurements for monitoring patients should be performed in accordance with medical necessity, expected response and in consideration of local regulatory requirements. NOF recommends that repeat BMD assessments generally agree with Medicare guidelines of every

two years, but recognizes that testing more frequently may be warranted in certain clinical situations.

NOF also indicates that “Central DXA assessment of the hip or lumbar spine is the “gold standard” for serial assessment of BMD. Biological changes in bone density are small compared to the inherent error in the test itself, and interpretation of serial bone density studies depends on appreciation of the smallest change in BMD that is beyond the range of error of the test. This least significant change (LSC) varies with the specific instrument used, patient population being assessed, measurement site, technologist’s skill with patient positioning and test analysis, and the confidence intervals used. Changes in the BMD of less than three to six percent at the hip and two to four percent at the spine from test to test may be due to the precision error of the testing itself.”

American College of Physicians

The American College of Physicians 2008 guidelines recommends that clinicians:

- Periodically perform individualized assessment of risk factors for osteoporosis in men older than 50 years;
 - Grade: strong recommendation; moderate-quality evidence
 - Factors that increase the risk for osteoporosis in men include age (>70 years), low BMI, weight loss, physical inactivity, corticosteroid use, androgen deprivation therapy, and previous fragility fracture.
- Obtain dual energy x-ray absorptiometry for men who are at increased risk of osteoporosis and are candidates for drug therapy.
 - Grade: strong recommendation; moderate-quality evidence
 - The guidelines indicate that bone density measurement with DXA is the accepted reference standard for diagnosing osteoporosis in men; because treatment trials have not measured the effectiveness of therapy for osteoporosis diagnosed by ultrasound densitometry rather than DXA, the role of ultrasound in diagnosis remains uncertain. This evidence review found no studies that evaluated the optimal intervals for repeated screening by using BMD measurement with DXA in men.

American College of Radiology

Practice guidelines from the American College of Radiology (ACR), last amended in 2014, state that BMD measurement is indicated whenever a clinical decision is likely to be directly influenced by the result of the test. Indications for DXA include but are not limited to the following patient populations:

- All women age 65 years and older and men age 70 years and older (asymptomatic screening).
- Women younger than age 65 years who have additional risk for osteoporosis, based on medical history and other findings. Additional risk factors for osteoporosis include:
 - a. Estrogen deficiency
 - b. A history of maternal hip fracture that occurred after the age of 50 years.
 - c. Low body mass (less than 127 lbs or 57.6 kg).
 - d. History of amenorrhea (more than 1 year before age 42 years).

- Women younger than age 65 years or men younger than age 70 years who have additional risk factors, including:
 - a. Current use of cigarettes
 - b. Loss of height, thoracic kyphosis.
- Individuals of any age with bone mass osteopenia, or fragility fractures on imaging studies such as radiographs, computed tomography (CT, or magnetic resonance imaging [MRI])
- Individuals age 50 years and older who develop a wrist, hip, spine, or proximal humerus fracture with minimal or no trauma, excluding pathologic fractures.
- Individuals of any age who develop 1 or more insufficiency fractures.
- Individuals receiving (or expected to receive) glucocorticoid therapy for more than three (3) months.
- Individuals beginning or receiving long-term therapy with medications known to adversely affect BMD (e.g., anticonvulsant drugs, androgen deprivation therapy, aromatase inhibitor therapy, or chronic heparin.
- Individuals with an endocrine disorder known to adversely affect BMD (e.g., hyperparathyroidism, hyperthyroidism, or Cushing's syndrome).
- Hypogonadal men older than 18 years and men with surgically or chemotherapeutically induced castration.
- Women younger than age 65 years who have additional risk for osteoporosis, based on individuals with medical conditions that could alter BMD, such as:
 - a. Chronic renal failure.
 - b. Rheumatoid arthritis and other inflammatory arthritis.
 - c. Eating disorders, including anorexia nervosa and bulimia.
 - d. Organ transplantation.
 - e. Prolonged immobilization.
 - f. Conditions associated with secondary osteoporosis, such as gastrointestinal malabsorption or malnutrition, sprue, osteomalacia, vitamin D deficiency, acromegaly, chronic alcoholism or established cirrhosis, and multiple myeloma
 - g. Individuals who have had gastric bypass for obesity. The accuracy of DXA in these patients might be affected by obesity.
- Individuals being considered for pharmacologic therapy for osteoporosis.
- Individuals being monitored to:
 - a. Assess the effectiveness of osteoporosis drug therapy.
 - b. Follow-up medical conditions associated with abnormal BMD.

International Society for Clinical Densitometry

The 2013 update of the International Society for Clinical Densitometry guidelines recommend bone density testing in the following patients:

- Women age 65 and older;
- Postmenopausal women under age 65 with risk factors for fracture such as;
 - Low body weight
 - Prior fracture
 - High risk medication use

- Disease or condition associated with bone loss.
- Women during the menopausal transition with clinical risk factors for fracture, such as low bone weight, prior fracture or high-risk medication use;
- Men age 70 and older;
- Men under age 70 if they have risk factors for low bone mass such as;
 - Low body weight
 - Prior fracture
 - High risk medication use
 - Disease or condition associated with bone loss
- Adults with a fragility fracture;
- Adults with a disease or condition associated with low bone mass or bone loss;
- Anyone being considered for pharmacologic therapy;
- Anyone being treated, to monitor treatment effect
- Anyone not receiving therapy in who evidence of bone loss would lead to treatment.

In 2010, the American Association of Clinical Endocrinologists issued guidelines for the diagnosis and treatment of postmenopausal osteoporosis. The guidelines list the potential uses for BMD measurements in postmenopausal women as:

- Screening for osteoporosis
- Establishing the severity of osteoporosis or bone loss
- Determining fracture risk
- Identifying candidates for pharmacologic intervention
- Assessing changes in bone mass over time
- Enhancing acceptance of and perhaps adherence with treatment
- Assessing skeletal consequences of diseases, conditions, or medications known to cause bone loss

The North American Menopause Society issued a 2010 position statement, which states that fracture is the most significant risk of low bone density. The statement also concludes that BMD is an important determinant of fracture risk, especially in women 65 years and older.

U.S. Preventive Services Task Force Recommendations

In January 2011, the U.S. Preventative Services Task Force (USPSTF) issued updated recommendations on screening for osteoporosis with bone density measurements. The USPSTF recommends routine osteoporosis screening in women age 65 years or older and in younger women whose risk of fracture is at least equal to that of a 65-year-old average-risk white woman. This represents a change from the previous (2002) version in which there was no specific recommendation regarding screening in women younger than 65 years-old. The supporting document notes that there are multiple instruments to predict risk for low BMD and that the USPSTF used the WHO Fracture Risk Assessment Tool (i.e., FRAX). The updated USPSTF recommendations state that the scientific evidence is insufficient to recommend for or against routine osteoporosis screening in men. The Task Force did not recommend specific screening tests but said that the most commonly used tests are DXA of the hip and lumbar spine and quantitative ultrasound of the calcaneus.

The USPSTF recommendations state the following on BMD screening intervals: "...A lack of evidence exists about the optimal intervals for repeat screening and whether repeated screening is necessary in a woman with normal BMD. Because of limitations in the precision of testing, a minimum of two years may be needed to reliably measure a change in BMD; however, longer intervals may be necessary to improve fracture risk prediction."

Key Words:

Bone mineral density testing, BMD, bone mineral density studies, bone mineral studies, Dual X-ray Absorptiometry, DXA, Dual-energy x-ray absorptiometry, DEXA, Quantitative Computed Tomography QCT, Ultrasound Densitometry, dual photon absorptiometry, radiographic absorptiometry, single photon absorptiometry, Lunar iDXA

Approved by Governing Bodies:

Several devices that measure bone density have been cleared for marketing by the U.S. Food and Drug Administration (FDA) through the 510(k) process. Some examples include:

- QCT-Bone Mineral Phantom (Image Analysis) in 1985
- Quantitative Digital Radiography (QDR™; Hologic) x-ray bone densitometer using dual x-ray absorptiometry in 1987
- Lunar DPX bone densitometer (now GE Lunar DPX NT®; GE Healthcare) in 1988
- Accudxa2® Bone Mineral Density Assessment System (Lone Oak Medical Technologies, Doylestown, PA) in 2012.

In addition, some ultrasound bone sonometers have been approved by FDA through the premarket approval (PMA) process. One example is the Sahara® Clinical Bone Sonometer (Hologic), which received approval in March 1998. Its intended use is for quantitative ultrasound measurement of the calcaneus (heel bone), the results of which can be used in conjunction with other clinical risk factors as an aid in the diagnosis of osteoporosis and medical conditions leading to reduced bone density, and ultimately in the determination of fracture risk.

Benefit Application:

Coverage is subject to member's specific benefits. Group specific policy will supersede this policy when applicable.

ITS: Home Policy provisions apply

FEP contracts: Special benefit consideration may apply. Refer to member's benefit plan. FEP does not consider investigational if FDA approved and will be reviewed for medical necessity.

Current Coding:

CPT codes:

76977	Ultrasound bone density measurement and interpretation, peripheral site(s), any method
77078	Computed tomography, bone mineral density study, 1 or more sites; axial skeleton (e.g., hips, pelvis, spine)
77080	Dual-energy x-ray absorptiometry (DXA), bone density study, 1 or more sites; axial skeleton (e.g., hips, pelvis, spine)
77081	Dual-energy x-ray absorptiometry (DXA), bone density study, 1 or more sites; appendicular skeleton (peripheral) (e.g., radius, wrist, heel)

As stated earlier in the policy, single and dual photon absorptiometry are now rarely used and may be considered obsolete. The CPT codes for these techniques are:

78350	Bone density (bone mineral content) study, 1 or more sites; single photon absorptiometry
78351	Bone density (bone mineral content) study, 1 or more sites; dual photon absorptiometry

Pulse echo ultrasound:

0508T	Pulse-echo ultrasound bone density measurement resulting in indicator of axial bone mineral density, tibia (Effective 07/01/2018)
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HCPCS code:

G0130	Single energy x-ray absorptiometry (SEXA) bone density study, one or more sites; appendicular skeleton peripheral) (e.g., radius, wrist, heel)
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 Medical Policy Panel, March 2013
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 Medical Policy Panel, March 2014
 Medical Policy Group, January 2015**(4)**: Removed Policy section with Effective dates of service on or after February 1, 2012 and prior to February 12, 2013. No other policy change. Updates to Key Points and References
 Medical Policy Panel, March 2015
 Medical Policy Group, March 2015 **(4)**: Updates to Key Points and References. No change in policy statement.
 Medical Policy Panel, September 2015

Medical Policy Group, October 2015 **(2)**: Updates to Description, Key Points, Current Coding, and References; no change in policy statement.

Medical Policy Panel, March 2017

Medical Policy Group, April 2017 **(7)**: 2017 Updates to Description, Key Points, Approved by Governing Bodies, and References; deleted Previous Coding section. No change in policy statement.

Medical Policy Group, June 2018: Quarterly Coding Update, July 2018. Added new CPT code 0508T to Current Coding.

This medical policy is not an authorization, certification, explanation of benefits, or a contract. Eligibility and benefits are determined on a case-by-case basis according to the terms of the member's plan in effect as of the date services are rendered. All medical policies are based on (i) research of current medical literature and (ii) review of common medical practices in the treatment and diagnosis of disease as of the date hereof. Physicians and other providers are solely responsible for all aspects of medical care and treatment, including the type, quality, and levels of care and treatment.

This policy is intended to be used for adjudication of claims (including pre-admission certification, pre-determinations, and pre-procedure review) in Blue Cross and Blue Shield's administration of plan contracts.