Prior Authorization Review
Panel MCO Policy Submission

A separate copy of this form must accompany each policy submitted for review. Policies submitted without this form will not be considered for review.

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Type of Submission – Check all that apply:
- [ ] New Policy
- [x] Revised Policy*
- [ ] Annual Review – No Revisions

*All revisions to the policy must be highlighted using track changes throughout the document. Please provide any clarifying information for the policy below:

**CPB 0134 Bone Mass Measurements**

Revision History since last PARP submission:
07/12/2018 - This CPB has been revised to state that a portable pulse-echo ultrasound device (Bindex) is considered experimental and investigational for bone mass measurements.
01/24/2019 – Next tentative scheduled review date by Corporate.

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<th>Name of Authorized Individual (Please type or print):</th>
<th>Signature of Authorized Individual:</th>
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<tr>
<td>Dr. Bernard Lewin, M.D.</td>
<td>Bernard Lewin, M.D.</td>
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Bone Mass Measurements

*Please see amendment for Pennsylvania Medicaid at the end of this CPB.*

Policy

I. Aetna considers bone mass measurement using the established techniques listed below medically necessary for members who meet any of the following criteria:

   A. Individuals being monitored to assess the response to or efficacy of osteoporosis drug therapy (only dual-energy x-ray absorptiometry is considered medically necessary for this indication); or

   B. Individuals receiving (or expected to receive) glucocorticoid (steroid) therapy equivalent to 5 mg of prednisone or greater, per day, for more than 3 months; or

   C. Individuals on long-term anticonvulsant therapy (e.g., phenytoin, phenobarbital); or

   D. Individuals with celiac sprue; or

   E. Individuals with primary hyperparathyroidism; or

   F. Individuals with vertebral abnormalities as demonstrated by an x-ray to be indicative of osteoporosis, osteopenia, or vertebral fracture; or

   G. Men greater than 50 years of age with specific risk factors for osteoporosis (i.e., low body weight, weight loss, or physical inactivity) *(Note: covered for members with preventive services benefits only)*; or
H. Men with hypogonadism or receiving androgen deprivation treatment (e.g., leuprolide, histrelin, goserelin); or
I. Non-traumatic (fragility) fractures; or
J. Screening of men greater than 70 years of age (Note: covered for members with preventive services benefits only); or
K. Screening of women who have been determined to be estrogen-deficient (peri- or post-menopausal) (Note: covered for members with preventive services benefits only); or
L. Women on long-term (i.e., longer than 2 years) Depo-Provera Contraceptive Injection (CI) therapy; or
M. Women with hyperthyroidism
N. Women with Turner syndrome.

Aetna considers bone mass measurement experimental and investigational for all other indications (e.g., evaluation of osteoporosis/osteoporotic fractures in persons with schizophrenia who are on anti-psychotic medications) because its effectiveness for indications other than the ones listed above has not been established.

Repeat bone mass measurements are usually not indicated more frequently than once every 2 years. More frequent bone mass measurements may be considered medically necessary in any of the following circumstances:

A. For a confirmatory baseline bone mass measurement to permit monitoring of individuals in the future if the initial bone mass test was performed with a technique that is different from the proposed testing method; or
B. Monitoring of individuals on long-term glucocorticoid (steroid) therapy or anticonvulsant therapy of more than 3 months duration; or
C. Monitoring of individuals with uncorrected primary hyperparathyroidism.

Repeat bone mass measurement has no proven value for other indications.

II. Aetna considers simultaneous axial (central) and appendicular (peripheral) bone mass measurements medically necessary only in the following limited circumstances:
A. An axial scan is considered medically necessary to get a baseline measurement for monitoring if osteoporosis is identified with an appendicular scan; or
B. Appendicular measurements are considered medically necessary when artifacts obscure measurement at the axial skeleton; or
C. Member is diagnosed with uncorrected primary hyperparathyroidism.

Simultaneous axial and appendicular bone mass measurements have no proven value for other indications.

The following methods are established procedures of bone mass measurements of the axial or appendicular (peripheral) skeleton:

A. Dual energy X-ray absorptiometry (DEXA or DXA);
B. Quantitative computed tomography (QCT);
C. Radiographic absorptiometry (photodensitometry);
D. Single energy X-ray absorptiometry (SEXA);
E. Ultrasound bone mineral density studies (e.g., Achilles + Bone Sonometer, Sahara, SoundScan).

III. Aetna considers bone mass measurement by dual photon absorptiometry (DPA), dual X-ray and laser (DXL), single photon absorptiometry (SPA), or pulse-echo ultrasound (e.g., Bindex) experimental and investigational because their effectiveness for this indication has not been established.

IV. Aetna considers screening for vertebral fractures with dual energy x-ray absorptiometry (DEXA or DXA) (also known as morphometric x-ray absorptiometry) as an adjunct to bone mineral density measurement experimental and investigational. There is a lack of clinical trial evidence showing that individuals with vertebral fractures on DXA but with bone mineral density levels above treatment thresholds benefit from pharmacologic treatment (BCBSA, 2004; BCBSA, 2006). **Note:** Examples of vertebral fracture assessment application packages that have received 510(k) marketing clearance are the Instant Vertebral Assessment (IVA) (Hologic, Inc.) and Dual Energy Vertebral Assessment (DVA) (previously known as Lateral Vertebral Assessment (LVA) (GE Lunar Medical Systems).
V. Aetna considers tomosynthesis-based trabecular bone analysis for determination of bone strength in person with diabetes mellitus experimental and investigational because the effectiveness of this approach has not been established.

VI. Aetna considers cone beam computed tomography for evaluation of post-menopausal osteoporosis experimental and investigational because its effectiveness for this indication has not been established.

See also CPB 0039 - Weight Reduction Medications and Programs (../1_99/0039.html).

Background

This policy is adapted from guidelines for bone mineral density (BMD) screening from the Centers for Medicare and Medicaid Services, National Institutes of Health, the American Association of Clinical Endocrinologists, and the American Gastroenterological Association.

Osteoporosis is a cause of significant morbidity and mortality in men as well as post-menopausal women. It is a disease characterized by low bone density and increased bone fragility, which reduce bone strength. Post-menopausal osteoporosis is due to rapid bone loss that occurs with the decline in endogenous estrogen following menopause. However, in both men and women, increasing age and low BMD are 2 important independent risk factors for an initial vertebral or non-vertebral fracture. While the incidence of vertebral fracture increases with age, the increase is greater among women than men; however, mortality after fracture is higher among men. According to the literature, the diagnostic criteria for post-menopausal osteoporosis in women are well established; however, there is ongoing debate about the appropriate T-scores and BMD thresholds to diagnose osteoporosis in men (Bonnick, 2006).

Primary osteoporosis is an aged-related disease characterized by low bone mass, microarchitectural deterioration of bone tissue leading to enhanced bone fragility, and a consequent increase in fracture risk in the absence of other recognizable causes of bone loss. Present intervention efforts are directed largely at identifying
those peri-menopausal women who are the most likely to be at risk for future fracture, and providing preventive bisphosphonate therapy along with adequate calcium intake and weight bearing exercise. Secondary osteoporosis has an identifiable cause of bone loss. Many, but not all, patients receiving long-term therapy with glucocorticoids have rapid loss of bone; those who do, need to be identified for consideration of medication adjustments. Bone mass also is reduced in some patients with asymptomatic primary hyper-parathyroidism, that has been diagnosed as a result of multi-phasic screening tests. Whether these latter patients undergo parathyroidectomy may depend on there being a progressive loss of bone, presumed to be parathyroid hormone-dependent, and treatable by correction of the hyper-parathyroidism. Lastly, since not all patients with vertebral abnormalities have significant osteoporosis, identifying those who do, enables the costs and risks of follow-up and therapy to be directed and limited to those that require more extensive intervention.

Bone mass loss has also been associated with long-term (i.e., longer than 2 years) use of Depo-Provera Contraceptive Injection (CI) therapy. Depo-Provera CI therapy is indicated for the prevention of pregnancy. It reduces serum estrogen levels and is associated with significant loss of BMD as bone metabolism accommodates to a lower estrogen level. According to the prescribing information for Depo-Provera, BMD should be evaluated when a woman needs to continue to use Depo-Provera CI long-term (i.e., longer than 2 years). This loss of BMD is of particular concern during adolescence and early adulthood, a critical period of bone accretion. It is unknown if use of Depo-Provera CI by younger women will reduce peak bone mass and increase the risk for osteoporotic fracture in later life. In both adults and adolescents, the decrease in BMD appears to be at least partially reversible after Depo-Provera CI is discontinued and ovarian estrogen production increases (Pfizer, Inc., 2006).

The rationale for densitometry lies in the assumption that the strength or resistance of a bone to fracture is closely related to the mass of the mineral present in the bone; the lower the bone density, the greater the fracture risk. Although BMD can be measured by some multi-purpose imaging devices such as quantitative computed tomography (QCT) scanners, specific densitometry tests emit lower radiation and cost less. Single-photon absorptiometry (SPA), dual-photon absorptiometry (DPA), and dual-energy radiographic (x-ray) absorptiometry, (DEXA, DXA, DER, DRA) all calculate bone mass on the basis of tissue absorption of photons derived from either a radionuclide or an x-ray tube.
In the past, SPA and DPA were the most commonly used methods of measurement. These methods have largely been replaced by DEXA. Single-photon absorptiometry measures the distal third of the radius which is composed mainly of cortical bone whereas most non-traumatic fractures occur in the axial skeleton (spine) and proximal femur (hip), which have a significant amount of trabecular bone. Measuring trabecular bone mass in the ultradistal radius or calcaneus (heel) has been more difficult because of bone tapering and irregularities.

Dual photon absorptiometry measures trabecular bone but costs more, takes longer, and the patient must lie down; apparent changes in serial DPA results must be carefully interpreted because the aging of the Gd-153 source can result in an apparent increase in bone mineral content.

Dual-energy radiographic (x-ray) absorptiometry, available since 1987, is the current standard of care for bone mass measurement. It uses an x-ray tube, instead of an isotope to generate dual energy photons, resulting in higher image resolution and greater speed than DPA. DEXA has replaced DPA; previous DPA manufacturers have switched to producing DEXA scanners.

Some authorities have advocated annual bone mineral density screening. The International Society for Clinical Densitometry, an association of providers with an interest in bone density measurement, recommends annual testing to detect continued bone loss in patients receiving treatment. The position statement included a series of recommendations, but did not provide analysis to support these recommendations. In addition, the American College of Radiology has recommended annual testing in patients receiving treatment.

However, the clinical literature on the accuracy and precision of bone density measurement does not support a recommendation for annual screening. Erlichman and Holohan (1996) reviewed the literature on commonly used bone densitometry techniques, including DEXA. They found that, although reviews of recent studies report DEXA accuracy error from 3 to 6%, other data indicate that DEXA accuracy error of ashed bone specimens of 9%. (Measurements obtained by densitometers are compared with an independent standard measurement of bone mass, such as ashed bone sections. The accuracy error is determined by how much the measurement varies from this accepted or "true" value.)
Dual-energy radiographic (x-ray) absorptiometry scans of the femur have a precision error from 0.5 % to 3 %. Precision error is the variability in the measurements occurring with repeated measurements of the same object. A technique's precision is critical for serial measurements that correctly document bone loss over time. Factors such as patient positioning, calibration and standardization procedures, and differences in operator technique can result in large measurement variations. The precision of measurements is reduced outside of the controlled conditions of a clinical trial setting.

The requisite minimum intervals between measurements that are necessary to reliably detect a reduction in bone mass are related to the precision attainable with current instruments and the rate of bone mass loss, assuming that the accuracy of the instrument is invariable. If one assumed a 1 % precision error, an annual rate of bone loss of 3 % would be required to reliably detect bone mass loss after 1 year.

But Erlichman and Holohan (1996) explained that it is unlikely that yearly densitometry would be clinically indicated given the fact that 1 % precision error is rarely attained and that a 3 % annual loss in bone mass would be distinctly uncommon. Precision errors in the range of 2 to 3 % and annual bone mass losses of 1 to 2 % are parameters more representative of published data. In those instances, the minimum interval between densitometry measures necessary to document bone mass loss would be between 3.7 and 6 years.

Furthermore, there are no clinical data that demonstrate improved outcomes in osteoporosis patients who are screened annually. Clinical trials of the bisphosphonate alendronates for the treatment of osteoporosis have found that failure to respond to therapy is a rare event.

A clinical practice guideline on osteoporosis in men issued by the American College of Physicians (ACP) (Qaseem et al, 2008) recommended that physicians periodically assess elderly men for risk factors for osteoporosis. Although osteoporosis is often viewed as a disease of women, studies show that osteoporotic fractures in men are associated with significant morbidity and mortality, resulting in substantial disease burden, death, and healthcare costs. The prevalence of osteoporosis is estimated to be 7 % in white men, 5 % in black men, and 3 % in Hispanic men. Data on prevalence of osteoporosis in Asian-American men and other ethnic groups are lacking. The guideline recommended
clinicians assess risk factors for osteoporosis in older men and obtain a DXA scan for men at increased risk for osteoporosis who are candidates for drug therapy. Risk factors for osteoporosis in men include age greater than 70 years, low body weight (body mass index [BMI] less than 20 to 25 kg/m² or lower), weight loss (greater than 10 %), lack of regular physical activity, such as walking, climbing stairs, carrying weights, housework, or gardening, use of oral corticosteroids, previous osteoporotic fracture, and androgen deprivation therapy. The ACP also recommended further research to evaluate osteoporosis screening tests in men and that, presently, non-DXA tests are either "too insensitive or have insufficient data to reach conclusions."

Metabolic bone diseases that fall under the generic term "renal osteodystrophy" represent abnormal development of bone and major long-term complications in end-stage renal disease. Chronic kidney disease (CKD) is associated with an increased risk of fracture. Decreased bone mass and disruption of micro-architecture occur early in the course of CKD and worsens with the progressive decline in renal function so that at the time of initiation of dialysis at least 50 % of patients have had a fracture. Despite the excess fracture risk, and the associated increases in morbidity and mortality, little is known about the factors that are associated with an increase in fracture risk; and the utility of bone mass measurements in patients with CKD is unclear. Jamal (2010) reviewed the epidemiology and etiology of fractures in patients with CKD; and summarized published data that described the association between bone mass measurements and fracture in patients with CKD. Patients with CKD suffer from fractures due to impairments in bone quantity, bone quality, as well as abnormalities of neuromuscular function. The complex etiology of fractures combined with the technical limitations of BMD testing, both by DEXA and by peripheral QCT, limits the clinical utility of bone mass measurements for fracture prediction in CKD; this is particularly true among patients with stages 4 and 5 CKD. As such, clinicians should not routinely order BMD testing in patients with CKD. The author concluded that further research, to ascertain if BMD together with other non-invasive measures to assess bone strength can predict fracture, is needed.

The conclusions of this assessment are consistent with those of an earlier assessment of BMD testing for renal disease prepared by the Agency for Health Care Policy and Research (Ehrlichman and Holohan, 1996), which concluded that BMD measurements are not able to differentiate uremic bone diseases or predict
fracture risk in patients with renal osteodystrophy. As a result, BMD measurements currently do not provide useful information that could support therapeutic decisions in the management of these patients.

The U.S. Preventive Services Task Force updated its 2002 recommendation on screening for osteoporosis (USPSTF, 2011). The USPSTF evaluated evidence on the diagnostic accuracy of risk assessment instruments for osteoporosis and fractures, the performance of DEXA and peripheral bone measurement tests in predicting fractures, the harms of screening for osteoporosis, and the benefits and harms of drug therapy for osteoporosis in women and men. The USPSTF recommends screening for osteoporosis in women aged 65 years or older and in younger women whose fracture risk is equal to or greater than that of a 65-year old white woman who has no additional risk factors (Grade B recommendation). The USPSTF concluded that the current evidence is insufficient to assess the balance of benefits and harms of screening for osteoporosis in men.

The European Association of Urology’s guidelines on “Male hypogonadism” (Dohle et al, 2012) states that “In men with an abnormal BMD, BMD measurements should be repeated 6 and 12 months after the start of TRT [testosterone replacement therapy] and thereafter annually”. (Level of evidence: 4 [Evidence obtained from expert committee reports or opinions or clinical experience of respected authorities]; Grade of recommendation: C [Made despite the absence of directly applicable clinical studies of good quality]).

The Clinical Practice Guidelines for the Care of Girls and Women with Turner Syndrome (Gravholt, et al., 2017) recommends a DEXA scan every 5 years due to the increased risk of osteoporosis in these patients.

Dual X-ray and laser (DXL) is a technique that is currently being examined as a means for bone mass measurement. This approach employs 2 X-ray beams in conjunction with a laser. This technique supposedly has the advantage of filtering out any influence that adipose tissue inside and outside the bone may have on the accuracy of DXA measurements; DXL has been studied mainly on the heel.

Kullenberg and Falch (2003) compared the prevalence of osteoporosis (using a T-score threshold of -2.5 for heel measurements) by DXL technology with that obtained by DXA measurements at the femoral neck, spine and forearm. The prevalence of osteoporosis for women aged 50 years or older was 28 % for DXL
measurements of the heel bone and 30, 22 and 32 % for DXA measurements of the lumbar spine, femoral neck and forearm, respectively. Bone mineral density was also measured by DXL in the heel bone and by DXA in spine and femoral neck in 251 women (mean age of 62 +/- 14.5 years) when attending an osteoporosis clinic. The sensitivity and specificity for osteoporosis and osteopenia for the DXL measurements were calculated assuming a low T-score at the spine or femoral neck as the criterion for a correct diagnosis. The sensitivity was found to be 80 % for osteoporosis and 82 % for osteopenia and the specificity was 82 % for osteoporosis and 89 % for osteopenia. The authors concluded that DXL measurement at the heel bone, using a T-score threshold of -2.5 for classification of osteoporosis, is in concordance with the World Health Organization (WHO) definition of osteoporosis.

Martini et al (2004) evaluated the reproducibility and the diagnostic accuracy of a new device for the assessment of BMD of the heel (DXL Calscan). This technique associates X-ray absorptiometry to the measure of heel thickness with a laser beam. The calcaneus BMD, calcaneus quantitative sonography (QUS), and lumbar spine and total-body BMD, were evaluated in 40 post-menopausal women. On the basis of the BMD T-score measured by DXA of L2 to L4, 20 women were classified as osteoporotic and 20 women were considered non-osteoporotic according to the WHO classification. The short-term coefficient of variation of the DXL was 2.4 % and 1.7 % in osteoporotic and non-osteoporotic women, respectively. The calcaneus BMD was lower in osteoporotic than in non-osteoporotic women. Among osteoporotic patients, 14 patients had a T-score lower than -2.5 at Calscan, whereas only 4 patients classified as non-osteoporotic based on the lumbar spine BMD were mis-classified by Calscan. In these patients, the sensitivity and specificity of heel ultrasound measurements were 70 % and 85 %, respectively. The DXL BMD was highly correlated with the total-body BMD, Stiffness at the calcaneus, and the L2 to L4 BMD. The authors concluded that the Calscan DXL appeared easy to use; the time of examination was relatively short; the reproducibility was sufficiently good; and the diagnostic accuracy and relationships with other devices were good.

Salminen and colleagues (2005) examined the relationship between calcaneal and axial BMD in an elderly female population. These researchers also investigated the influence of changing the reference populations on T-score values. Bone mineral density was determined in 388 women (mean age of 73 years) participating in a cross-sectional study. BMD values were determined at the left hip and the lumbar
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spine, L1 to L4, using Hologic QDR 4500 equipment for DXA. The calcaneal measurements were made with DEXA-T, a device using a DXL technique that combines DXA measurement with measurement of the heel thickness using a laser reflection technique. DEXA-T is an older version of the Calscan DXL device now commercially available. T-score values were calculated for hip measurements with both the original reference population of the Hologic device and the NHANES III reference population. T-scores for heel measurements were calculated with the original reference population of the peripheral device and the Calscan database, a new calcaneal reference population. Changing the reference populations had a great influence on both the heel and the hip T scores, especially those of the femoral neck where the percentage of subjects identified as osteoporotic decreased from 53 % to 23 %. The authors concluded that, with the NHANES III and the larger Calscan database, using the cut-off point of -2.5 SD, the heel measurements had optimal accuracy for detecting osteoporosis at either the combination of the lumbar spine and the femoral neck or the combination of the lumbar spine, the femoral neck, the total hip and the trochanter. BMD measurements of the calcaneus with DXL correlated fairly well with measurements at axial sites at the group level, while in individual subjects large deviations were observed between all the measured sites. They also stated that the influence of the reference populations on the T-scores is substantial when different DXA methods are being compared; the total number of subjects classified as osteoporotic varied from 7 % to 53 % between the sites and with different reference populations.

de Klerk et al (2009) compared BMD expressed in T-scores measured by DXA and DXL (Calscan). The aim of this study was to define threshold T-scores on the Calscan that could exclude or predict osteoporosis correctly in comparison with DXA. Patients 50 years of age or older attending the emergency department with a fracture were offered osteoporosis screening and enrolled in this study. BMD was measured at the hip and spine using DXA and at the calcaneus using Calscan. A T-score measured by DXA less than or equal to -2 SD below the reference population was defined as manifest osteoporosis and was the treatment threshold. During a 10-month study period, 182 patients were screened with both devices. The mean DXA-T-score was -1.63 SD (range of -4.9 to 2.1) and Calscan T-score -1.91 SD (range of -5.3 to 1.4). There was a significant correlation between both devices (r = 0.47, p < 0.01). Using an upper threshold for the Calscan T-score of -1.3 SD, 47 patients could be classified as non-osteoporotic with 89.3 % sensitivity (95 % CI: 80.0 to 95.3 %). Using a lower threshold for the Calscan T-score of -2.9 SD, 34 patients could be classified by the Calscan as osteoporotic with 90.7 %
specificity (95% CI: 83.5 to 95.4). The remaining 101 patients could only be correctly classified by DXA-T-scores. The authors concluded that although DXA is the established modality worldwide in measuring BMD it is restricted to specialized centers. Peripheral bone densitometers like the Calscan are widely available. When BMD measurements with DXA were compared to Calscan measurements it was possible to correctly classify 81 of 182 patients based on the Calscan T-score. Of these 81 patients 34 could be classified as manifest osteoporotic and 47 as non-osteoporotic. Thus, the authors concluded that Calscan seems to be a promising technique that might be used as a screening device, especially when DXA is not easily available.

Yumru et al (2009) compared DXL heel measurements of BMD and DEXA total hip and lumbar spine BMD measurements for their ability to detect osteoporosis and osteopenia according to WHO criteria. The study included 164 women aged 40 to 83 years. DXL heel measurements were recorded for all patients and 89 of the women underwent DEXA. For DXL heel measurements/DEXA lumbar spine measurements, the relative sensitivity was 50%, relative specificity was 97% and relative reliability (Kappa score) was 0.55 for osteoporosis detection. For detecting osteoporosis or osteopenia, the relative sensitivity increased to 86% but the relative specificity reduced to 38% and the relative reliability was considerably lower (Kappa score 0.21). The authors concluded that although previous studies have shown DXL heel measurement to be a good technique in the diagnosis and assessment of osteoporosis based on BMD, particularly for fast, cost-effective bone scanning, they suggested that there are currently insufficient data to prove its use as a standard measurement technique for BMD.

In a systematic review for an American College of Physicians (ACP)’s guideline on “Screening for osteoporosis in men” (Liu et al, 2008) evaluated: (i) risk factors for osteoporotic fracture in men that may be mediated through low BMD, and (ii) the performance of non-DXA tests in identifying men with low BMD. Studies identified through the MEDLINE database (1990 to July 2007) were included for analysis. Articles that assessed risk factors for osteoporotic fracture in men or evaluated a non-DXA screening test against a gold standard of DXA were selected. Researchers performed independent dual abstractions for each article, determined performance characteristics of screening tests, and assessed the quality of included articles. A published meta-analysis of 167 studies evaluating risk factors for low BMD-related fracture in men and women found high-risk factors to be increased age (greater than 70 years), low body weight (BMI less than 20 to
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25 kg/m²), weight loss (greater than 10%), physical inactivity, prolonged corticosteroid use, and previous osteoporotic fracture. An additional 102 studies assessing 15 other proposed risk factors were reviewed; most had insufficient evidence in men to draw conclusions. Twenty diagnostic study articles were reviewed. At a T-score threshold of -1.0, calcaneal ultrasonography had a sensitivity of 75% and specificity of 66% for identifying DXA-determined osteoporosis (DXA T-score, -2.5). At a risk score threshold of -1, the Osteoporosis Self-Assessment Screening Tool had a sensitivity of 81% and specificity of 68% to identify DXA-determined osteoporosis. The authors concluded that key risk factors for low BMD-mediated fracture include increased age, low body weight, weight loss, physical inactivity, prolonged corticosteroid use, previous osteoporotic fracture, and androgen deprivation therapy. Moreover, they stated that non-DXA tests either are too insensitive or have insufficient data to reach conclusions.

Indeed, the AAP’s clinical practice guideline on “Screening for osteoporosis in men” (Qaseem et al, 2008) recommended that clinicians obtain dual-energy x-ray absorptiometry for men who are at increased risk for osteoporosis and are candidates for drug therapy. Furthermore, UpToDate reviews on “Screening for osteoporosis” (Kleerekoper, 2012) and “Osteoporotic fracture risk assessment” (Lewiecki, 2012) mentioned the use of dual energy x-ray absorptiometry, but not DXL.

Wren et al (2014) noted that early assessment of bone mass may be useful for predicting future osteoporosis risk if bone measures “track” during growth. This prospective, longitudinal, multi-center study examined tracking of bone measures in children and adolescents over 6 years to sexual and skeletal maturity. A total of 240 healthy male and 293 healthy female patients, aged 6 to 17 years, underwent yearly evaluations of height, weight, BMI, skeletal age, Tanner stage, and DEXA bone measurements of the whole body, spine, hip, and forearm for 6 years. All subjects were sexually and skeletally mature at final follow-up. Correlation was performed between baseline and 6-year follow-up measures, and change in DEXA Z-scores was examined for subjects who had baseline Z less than -1.5. DEXA Z-scores (r = 0.66 to 0.87) had similar tracking to anthropometric measures (r = 0.6 to -0.74). Tracking was stronger for BMD compared with bone mineral content and for girls compared with boys. Tracking was weakest during mid- to late-puberty but improved when Z-scores were adjusted for height. Almost all subjects with baseline Z less than -1.5 had final Z-scores below average, with the majority remaining less than -1.0. The authors concluded that bone status during childhood
is a strong predictor of bone status in young adulthood, when peak bone mass is achieved. They stated that these findings suggested that bone mass measurements in children and adolescents may be useful for early identification of individuals at risk for osteoporosis later in life.

In a pilot study, Aubry-Rozier et al (2014) compared vertebral fracture assessments (VFA) and lateral X-rays in terms of inter- and intra-observer reliability and degree of correlation for the detection of syndesmophytes in ankylosing spondylitis (AS). These researchers recruited 19 patients with AS and recent lumbar or cervical lateral X-rays with at least 1 syndesmophyte. Each patient underwent DEXA with measurement of BMD and dorso-lumbar VFA. Intra- and inter-reader reliability for VFA and X-rays were measured using 2 independent, blinded observers and Cohen's kappa values. An adapted modified Stoke Ankylosing Spondylitis Spinal Score (amSASSS) was generated with each method, and these 2 values correlated. For X-rays, intra-observer and inter-observer agreement were 94.3 % (κ = 0.83) and 98.6 % (κ = 0.96), respectively; for VFA, corresponding values were 92.8 % (κ = 0.79) and 93.8 % (κ = 0.82). Overall agreement between the 2 techniques was 88.6 % (κ = 0.72). The Pearson correlation coefficient for the 2 methods was 0.95 for the modified Stoke Ankylosing Spondylitis Spinal Score. Per DEXA-generated BMD, greater than 50 % of patients were osteopenic and 10 % osteoporotic. The authors concluded that in terms of reproducibility and correlation with X-rays, performing a VFA appeared to be a candidate for assessing radiographic damage in AS, thought further research is needed to justify this indication.

In January 2018, the American Medical Association (AMA) issued a new Category III CPT code for Bindex measurement. Bindex is a hand-held, portable pulse-echo ultrasound device that can be used to help diagnose osteoporosis. Unlike other quantitative ultrasound that measures sound speed and attenuation in the heel, Bindex measures the cortical bone thickness of the tibia and the algorithm calculates the Density Index, a parameter which estimates bone mineral density at the hip as measured with DXA. Bindex detects osteoporosis with 90% sensitivity and specificity compared with axial dual-energy X-ray absorptiometry (DXA). Bindex can be connected to and used with any laptop or desktop computer's USB socket.

Bindex is intended to be used alongside current algorithmic fracture risk assessment tools (FRAX or QFracture). If these suggest an intermediate or high
risk of osteoporosis fracture, Bindex could be used to determine whether referral for DXA scan is needed (in the case of confirmed intermediate risk) or not (if low risk). Treatment could be considered for those at high fracture risk or high risk for osteoporosis as measured with Bindex.

The evidence comes from two studies including 1,127 participants recruited in the USA and Finland. The studies show reasonable agreement for osteoporosis risk when determined in women with intermediate risk using FRAX and Bindex compared with FRAX and DXA. One study (Karjalainen et al. 2016) examined the association between dual-energy X-ray absorptiometry (DXA) measurements at the proximal femur and Bindex (measured at the tibia), using a diagnostic threshold for the density index based on International Society for Clinical Densitometry (ISCD) and National Osteoporosis Society guidelines. The study by Schousboe et al. (2017) estimated the diagnostic accuracy of Bindex using the threshold density index from the Karjalainen et al. (2016) study.

Karjalainen et al (2016) stated that due to the lack of diagnostics in primary health care, over 75% of osteoporotic patients are not diagnosed. A new ultrasound method for primary health care is proposed. Results suggest applicability of ultrasound method for osteoporosis diagnostics at primary health care. There is a lack of effective screening and diagnostics of osteoporosis at primary health care. In this study, a new ultrasound (US) method is proposed for osteoporosis diagnostics. A total of 572 Caucasian women (age 20 to 91 years) were examined using pulse-echo US measurements in the tibia and radius. This method provides an estimate of bone mineral density (BMD), i.e. density index (DI). Areal BMD measurements at the femoral neck (BMD(neck)) and total hip (BMD(total)) were determined by using axial dual-energy X-ray absorptiometry (DXA) for women older than 50 years of age (n = 445, age = 68.8 ± 8.5 years). The osteoporosis thresholds for the DI were determined according to the International Society for Clinical Densitometry (ISCD). Finally, the FRAX questionnaire was completed by 425 participants. Osteoporosis was diagnosed in individuals with a T-score -2.5 or less in the total hip or femoral neck (n = 75). By using the ISCD approach for the DI, only 28.7% of the subjects were found to require an additional DXA measurement. These results suggest that combination of US measurement and FRAX in osteoporosis management pathways would decrease the number of DXA measurements to 16% and the same treatment decisions would be reached at 85.4% sensitivity and 78.5% specificity levels. The authors concluded that the present results demonstrate a significant correlation between the ultrasound and
DXA measurements at the proximal femur. The thresholds presented here with the application to current osteoporosis management pathways show promise for the technique to significantly decrease the amount of DXA referrals and increase diagnostic coverage; however, these results need to be confirmed in future studies.

Schousboe et al (2017) stated pulse-echo ultrasonometry can be used as a pre-screen for hip osteoporosis before dual-energy x-ray absorptiometry (DXA), potentially allowing DXA to be avoided for the majority of post-menopausal women. Pulse-echo ultrasound measures of tibia cortical thickness are also associated with radiographically confirmed prior fractures, independent of femoral neck bone mineral density. The aim of this trial was to estimate how well a pulse-echo ultrasound device discriminates those who have from those who do not have hip osteoporosis (femoral neck bone mineral density [BMD] or total hip BMD T-score ≤ -2.5), and to estimate the association of pulse-echo ultrasound measures with prevalent (radiographically confirmed) clinical fractures. Five hundred fifty-five post-menopausal women age 50 to 89 had femoral neck and total hip BMD measured by dual-energy x-ray absorptiometry (DXA), and pulse-echo ultrasound measures of distal radius, proximal tibia, distal tibia cortical thickness, and multi- and single-site density indices (DI). Using previously published threshold ultrasound values, the authors estimated the proportion of women who would avoid a follow-up DXA after pulse-echo ultrasonometry, and the sensitivity and specificity of this for the detection of hip osteoporosis. Logistic regression models were used to estimate the associations of pulse-echo ultrasound measures with radiographically confirmed clinical fractures within the prior 5 years. Using multi-site and single-site DI measures, follow-up DXA could be avoided for 73 and 69 % of individuals, respectively, while detecting hip osteoporosis with 80-82 % sensitivity and 81 % specificity. Radiographically confirmed prior fracture was associated with ultrasound measures of single-site DI (odds ratio (OR) 1.55, 95 % confidence interval (CI), 1.06 to 2.26) and proximal tibia cortical thickness (OR 1.47, 95 % CI 1.10 to 1.96), adjusted for age, body mass index, and femoral neck BMD. The authors concluded that pulse-echo ultrasonometry can be used as an initial screening test for hip osteoporosis. Prospective studies of how well pulse-echo ultrasound measures predict subsequent clinical fractures are warranted.

A medical technology innovation briefing by the National Institute for Health and Clinical Excellence (NICE, 2017) noted that there are no prospective studies showing the effect of Bindex on the need for DXA scans, and limited data on the correlation between tibial bone thickness and femoral bone mineral density (citing
Karjalainen et al (2016) and Schousboe et al (2017)). Also, the Bindex density index threshold values are only validated in women of white European family origin, which may limit the generalizability of the results. There are no nationally recognized or U.S. governmental position statements or practice guidelines that address the use of pulse-echo ultrasound to determine osteoporosis risk or for screening.

**Bone Mineral Density and Anti-psychotic Medications:**

Wang and associates (2014) examined the effects of conventional and atypical anti-psychotics on BMD and serum prolactin levels (PRL) in patients with schizophrenia. A total of 163 first-episode inpatients with schizophrenia were recruited, to whom 1 of 3 conventional anti-psychotics (perphenazine, sulpiride, and chlorpromazine) or 1 of 3 atypical anti-psychotics (clozapine, quetiapine, and aripiprazole) was prescribed for 12 months as appropriate; BMD and PRL were tested before and after treatment. Same measures were conducted in 90 matched healthy controls. Baseline BMD of postero-anterior L1 to L4 ranged from 1.04 ± 0.17 to 1.42 ± 1.23, and there was no significant difference between the patients group and healthy control group. However, post-treatment BMD values in patients (ranging from 1.02 ± 0.15 to 1.23 ± 0.10) were significantly lower than that in healthy controls (ranging from 1.15 ± 0.12 to 1.42 ± 1.36). The BMD values after conventional anti-psychotics were significantly lower than that after atypical anti-psychotics. The PRL level after conventional anti-psychotics (53.05 ± 30.25 ng/ml) was significantly higher than that after atypical anti-psychotics (32.81 ± 17.42 ng/ml). Conditioned relevance analysis revealed significant negative correlations between the PRL level and the BMD values after conventional anti-psychotics. The authors concluded that the increase of PRL might be an important risk factor leading to a high prevalence of osteoporosis in patients with schizophrenia on long-term conventional anti-psychotic medication.

De Hert and colleagues (2016) noted that the use of anti-psychotic medications can increase PRL levels, causing hyperprolactinemia (HPRL). Although the occurrence of osteoporosis within the population of patients with schizophrenia has been recognized, the precise nature of the association between anti-psychotic treatment, PRL, osteoporosis, and the disease itself appeared to be elusive. These investigators reviewed the literature regarding the association between osteoporosis and PRL and summarized the available evidence with respect to the impact of PRL-elevating anti-psychotics on BMD and fractures in non-elderly
patients with schizophrenia. The authors concluded that although long-standing HPRL can have an impact on the rate of bone metabolism and, when associated with hypogonadism, may lead to decreased bone density in both female and male subjects, the relative contribution of anti-psychotic-induced HPRL in bone mineral loss in patients with schizophrenia remains unclear. They stated that methodological shortcomings of existing studies, including the lack of prospective data and the focus on measurements of BMD instead of bone turnover markers, precluded definitive conclusions regarding the relationship between PRL-raising anti-psychotics and BMD loss in patients with schizophrenia. They stated that more well-designed prospective studies of these biomarkers are needed to establish the precise relationship between anti-psychotics, PRL levels and osteoporosis/osteoporotic risk.

Tomosynthesis-Based Trabecular Bone Analysis and Diabetes Mellitus:

Fujii and colleagues (2016) determined femoral neck strength in patients with diabetes mellitus by using trabecular bone analysis values and tomosynthesis images and compared its parameters between vertebral compression fracture and non-fracture groups. A total of 49 patients with diabetes mellitus were included. Within 1 week, patients underwent DXA, tomosynthesis, and CT covering the T10 vertebral body to the hip joints. The trabecular patterns of tomosynthesis images were extracted, and the total strut length, bone volume per tissue volume, and 5 textural features (homogeneity, entropy, correlation, contrast, and variance) were obtained as the indices of tomosynthesis images. Failure load of the femoral neck, which was determined with the CT-based finite-element method (FEM), was used as the reference standard for bone strength. A forward step-wise multiple regression analysis for evaluating the availability of the tomosynthesis image indices was performed. The BMD at DXA and tomosynthesis image indices were compared between the vertebral compression fracture (n = 16) and non-fracture groups (n = 33) according to Genant semi-quantitative morphometric methods by using 1-way analysis of variance. The combination of BMD with the bone volume per tissue volume at the principal tensile group and the correlation at the principal compressive group showed the highest correlation to the failure load at CT FEM, and the correlation ($r^2 = 0.83$) was higher than that between the failure load and the BMD alone ($r^2 = 0.76; p < 0.001$). The averages of the bone volume per tissue volume and entropy at the principal tensile group in the vertebral compression fracture group were lower than those in the non-fracture group ($p = 0.017$ and $p = 0.029$, respectively), but there was no difference in BMD. The authors concluded
that tomosynthesis-based trabecular bone analysis is technically feasible and, in combination with BMD measurements, can potentially be used to determine bone strength in patients with diabetes mellitus.

Cone Beam Computed Tomography for Evaluation of Post-Menopausal Osteoporosis:

Mostafa and colleagues (2016) examined the feasibility of using mandibular cone beam computed tomography (CBCT) radiomorphometric indices and box-counting fractal dimension (FD) to (i) detect osteoporosis in post-menopausal women, (ii) compare them with the healthy control group, and (iii) correlate the findings with the BMD measured by DXA. This study consisted of 50 post-menopausal women, with age ranging from 55 to 70 years. Based on their DXA results, they were classified into osteoporotic and control groups. Mandibular CBCT radiomorphometric indices and FD analysis were measured. Significant differences were found for the CT cortical index scores (CTCI), CT mental index (CTMI) and CT mandibular index (CTI) between the control and osteoporotic groups. The control group showed higher mean values than the osteoporotic group. For FD values, no significant differences were found between the 2 groups. The authors concluded that these findings suggested that radiomorphometric indices that were assessed using CBCT could be used as a useful adjuvant tool to refer patients at risk of osteoporosis for further densitometric analysis. Regarding FD, further research must be conducted to evaluate the usefulness of using this tool in CBCT images to diagnose osteoporosis. Moreover, they stated that further research should contain a larger sample size of female populations of different age groups and menstruation conditions. Also, further research should include patients with osteopenia, as this may give further information about the mandibular osseous changes at the initial stages of the disease.

Brasileiro and associates (2017) correlated radiometric indices from CBCT images and BMD in post-menopausal women. A total of 60 post-menopausal women with indications for dental implants and CBCT evaluation were selected; DXA was performed, and patients were divided into (i) normal, (ii) osteopenia, and (iii) osteoporosis groups, according to the WHO criteria.

Cross-sectional images were used to evaluate the CTMI, the computed tomography index (inferior) (CTI (I)) and computed tomography index (superior) (CTI (S)). Student's t test was used to compare the differences between the indices of the
groups’ intraclass correlation coefficient (ICC). Statistical analysis showed a high degree of inter-observer and intra-observer agreement for all measurements (ICC > 0.80). The mean values of CTMI, CTI (S), and CTI (I) were lower in the osteoporosis group than in osteopenia and normal patients (p < 0.05). In comparing normal patients and women with osteopenia, there was no statistically significant difference in the mean value of CTI (I) (p = 0.075). The authors concluded that quantitative CBCT indices may help dentists to screen for women with low spinal and femoral BMD so that they can refer post-menopausal women for bone densitometry.

Guerra and co-workers (2017) systematically reviewed the literature about the capability of CBCT images to identify individuals with low BMD. As the literature is scarce regarding this topic, the purpose of this systematic review was also to guide future research in this area. A detailed search was performed in 5 databases without restrictions of time or languages. Additionally, a grey literature search was conducted. The Quality Assessment Tool for Diagnostic Accuracy Studies-2 was applied to evaluate the methodological design of selected studies. With the inclusion of only 6 studies, the evidence was limited to endorse the use of CBCT assertively as a diagnostic tool for low BMD. All of the 3 studies that analyzed radiomorphometric indices found that the linear measurements of the mandibular inferior cortex were lower in osteoporotic individuals; CBCT-derived radiographic density vertebral and mandibular measurements were also capable for differentiating individuals with osteoporosis from individuals with normal BMD. The analysis of the cervical vertebrae showed high accuracy measurements. The authors concluded that this systematic review indicated a scarcity of studies regarding the potential of CBCT for screening individuals with low BMD. However, the studies indicated that radiomorphometric indices and CBCT-derived radiographic density should be promising tools for differentiating individuals with osteoporosis from individuals with normal BMD.

Furthermore, an UpToDate review on “Clinical manifestations, diagnosis, and evaluation of osteoporosis in postmenopausal women” (Rosen and Drezner, 2017) states “Several different methods are available to measure bone density. DXA gives an accurate and precise estimate of BMD. Thus, in clinical practice, DXA is the technology used for diagnostic classification”. It does not mention cone beam computed tomography as a diagnostic tool.
Information in the [brackets] below has been added for clarification purposes. Codes requiring a 7th character are represented by "+":

<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
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<tbody>
<tr>
<td>CPT codes covered if selection criteria are met:</td>
<td></td>
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<tr>
<td>76977</td>
<td>Ultrasound bone density measurement and interpretation, peripheral site(s), any method [not covered for monitoring osteoporosis drug therapy]</td>
</tr>
<tr>
<td>77078</td>
<td>Computerized tomography, bone mineral density study, 1 or more sites [not covered for monitoring osteoporosis drug therapy]</td>
</tr>
<tr>
<td>77080 - 77081</td>
<td>Dual energy x-ray absorptiometry (DXA), bone density study, 1 or more sites</td>
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<tr>
<td>CPT codes not covered for indications listed in the CPB:</td>
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<tr>
<td>70486</td>
<td>Computed tomography, maxillofacial area; without contrast material [not covered for osteoporosis screening]</td>
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<tr>
<td>77085</td>
<td>Dual-energy X-ray absorptiometry (DXA), bone density study, 1 or more sites; axial skeleton (eg, hips, pelvis, spine), including vertebral fracture assessment</td>
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<tr>
<td>77086</td>
<td>Vertebral fracture assessment via dual-energy X-ray absorptiometry (DXA)</td>
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<tr>
<td>78350</td>
<td>Bone density (bone mineral content) study, one or more sites; single photon absorptiometry</td>
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<tr>
<td>78351</td>
<td>Bone density (bone mineral content) study, one or more sites; dual photon absorptiometry, one or more sites</td>
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HCPCS codes covered if selection criteria are met:

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<tr>
<td>G0130</td>
<td>Single energy x-ray absorptiometry (SEXA) bone density study, one or more sites; appendicular skeleton (peripheral) (e.g., radius, wrist, heel) [not covered for monitoring osteoporosis drug therapy]</td>
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Other HCPCS codes related to the CPB:

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<th>Code</th>
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<tr>
<td>J1050</td>
<td>Injection, medroxyprogesterone acetate, 1 mg</td>
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<tr>
<td>J1950</td>
<td>Injection, leuprolide acetate (for depot suspension), per 3.75 mg</td>
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<tr>
<td>J9202</td>
<td>Goserelin acetate implant, per 3.6 mg</td>
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<tr>
<td>J9217</td>
<td>Leuprolide acetate (for depot suspension), 7.5 mg</td>
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<tr>
<td>J9218</td>
<td>Leuprolide acetate, per 1 mg</td>
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<tr>
<td>J9219</td>
<td>Leuprolide acetate implant, 65 mg</td>
</tr>
<tr>
<td>Code</td>
<td>Code Description</td>
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<td>----------------------------------------------------------------------------------</td>
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<tr>
<td>E05.00 - E05.91</td>
<td>Thyrotoxicosis [hyperthyroidism]</td>
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<td>E20.0 - E20.9</td>
<td>Hypoparathyroidism</td>
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<td>E28.39</td>
<td>Other primary ovarian failure</td>
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<td>E29.1</td>
<td>Testicular hypofunction</td>
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<td>E34.50 - E34.52</td>
<td>Androgen insensitivity syndrome</td>
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<td>G40.001 - G40.919</td>
<td>Epilepsy and recurrent seizures</td>
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<td>K90.0</td>
<td>Celiac disease</td>
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<td>M80.011+ - M80.88X+</td>
<td>Osteoporosis with current pathological fracture</td>
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<td>M81.0 - M81.8</td>
<td>Osteoporosis without current pathological fracture [not covered for post-</td>
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<td></td>
<td>menopausal osteoporosis]</td>
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<td>M84.411+ - M84.48X+</td>
<td>Pathologic fracture, not elsewhere classified</td>
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<td>M85.80 - M85.9</td>
<td>Other specified disorders of bone density and structure [osteopenia]</td>
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<td>N92.4</td>
<td>Excessive bleeding in the premenopausal period</td>
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<td>N95.0 - N95.9</td>
<td>Menopausal and other perimenopausal disorders</td>
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<td>R56.1</td>
<td>Posttraumatic seizures</td>
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<td>R56.9</td>
<td>Unspecified convulsions</td>
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<td>S12.000+ - S12.9XX+</td>
<td>Fracture of cervical vertebra and other parts of the neck</td>
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<td>S22.000+ - S22.089+</td>
<td>Fracture of thoracic vertebra</td>
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<td>Fracture of lumbar vertebra</td>
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<tr>
<td>S32.10X+ - S32.19X+</td>
<td>Fracture of sacrum</td>
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<tr>
<td>S32.2XX+</td>
<td>Fracture of coccyx</td>
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<td>Z78.0</td>
<td>Asymptomatic postmenopausal state</td>
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<tr>
<td>Z79.51 - Z79.52</td>
<td>Long term (current) use of steroids [glucocorticoid therapy]</td>
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</table>
The above policy is based on the following references:


15. Miller PD, Njeh CF, Jankowski LG, et al. What are the standards by which bone mass measurement at peripheral skeletal sites should be used in the diagnosis of osteoporosis. J Clin Densitom. 2002;5 Suppl:S39-S45.


67. Kleerekoper M. Screening for osteoporosis. UpToDate [online serial]. Waltham, MA: UpToDate; updated September 2012.

68. Lewiecki EM. Osteoporotic fracture risk assessment. UpToDate [online serial]. Waltham, MA: UpToDate; updated December 2012.


79. Rosen HN, Drezner MK. Clinical manifestations, diagnosis, and evaluation of osteoporosis in postmenopausal women. UpToDate Inc., Waltham, MA. Last reviewed December 2017.


AETNA BETTER HEALTH® OF PENNSYLVANIA

Amendment to
Aetna Clinical Policy Bulletin Number:
0134 Bone Mass Measurements

There are no amendments for Medicaid.

www.aetnabetterhealth.com/pennsylvania  Revised 07/12/2018