

190.19 - Collagen Crosslinks, Any Method

Description

Collagen crosslinks, part of the matrix of bone upon which bone mineral is deposited, are biochemical markers the excretion of which provides a quantitative measurement of bone resorption. Elevated levels of urinary collagen crosslinks indicate elevated bone resorption. Elevated bone resorption contributes to age-related and postmenopausal loss of bone leading to osteoporosis and increased risk of fracture. The collagen crosslinks assay can be performed by immunoassay or by high performance liquid chromatography (HPLC). Collagen crosslink immunoassays measure the pyridinoline crosslinks and associated telopeptides in urine.

Bone is constantly undergoing a metabolic process called turnover or remodeling. This includes a degradation process, bone resorption, mediated by the action of osteoclasts, and a building process, bone formation, mediated by the action of osteoblasts. Remodeling is required for the maintenance and overall health of bone and is tightly coupled; that is, resorption and formation must be in balance. In abnormal states of bone remodeling, when resorption exceeds formation, it results in a net loss of bone. The measurement of specific, bone-derived resorption products provides analytical data about the rate of bone resorption.

Osteoporosis is a condition characterized by low bone mass and structural deterioration of bone tissue, leading to bone fragility and an increased susceptibility to fractures of the hip, spine, and wrist. The term primary osteoporosis is applied where the causal factor in the disease is menopause or aging. The term secondary osteoporosis is applied where the causal factor is something other than menopause or aging, such as long-term administration of glucocorticosteroids, endocrine-related disorders (other than loss of estrogen due to menopause), and certain bone diseases such as cancer of the bone.

With respect to quantifying bone resorption, collagen crosslink tests can provide adjunct diagnostic information in concert with bone mass measurements. Bone mass measurements and biochemical markers may have complementary roles to play in assessing effectiveness of osteoporosis treatment. Proper management of osteoporosis patients, who are on long-term therapeutic regimens, may include laboratory testing of biochemical markers of bone turnover, such as collagen crosslinks, that provide a profile of bone turnover responses within weeks of therapy. Changes in collagen crosslinks are determined following commencement of antiresorptive therapy. These can be measured over a shorter time interval when compared to bone mass density. If bone resorption is not elevated, repeat testing is not medically necessary.

HCPCS Codes (Alphanumeric, CPT® AMA)

Code	Description
82523	Collagen cross links, any method

ICD-10-CM Codes Covered by Medicare Program

The ICD-10-CM codes in the table below can be viewed on CMS' website as part of Downloads: Lab Code List, at <http://www.cms.gov/Medicare/Coverage/CoverageGenInfo/LabNCDsICD10.html>

Code	Description
E05.00	Thyrotoxicosis with diffuse goiter without thyrotoxic crisis or storm
E05.01	Thyrotoxicosis with diffuse goiter with thyrotoxic crisis or storm
E05.10	Thyrotoxicosis with toxic single thyroid nodule without thyrotoxic crisis or storm
E05.11	Thyrotoxicosis with toxic single thyroid nodule with thyrotoxic crisis or storm
E05.20	Thyrotoxicosis with toxic multinodular goiter without thyrotoxic crisis or storm
E05.21	Thyrotoxicosis with toxic multinodular goiter with thyrotoxic crisis or storm
E05.30	Thyrotoxicosis from ectopic thyroid tissue without thyrotoxic crisis or storm
E05.31	Thyrotoxicosis from ectopic thyroid tissue with thyrotoxic crisis or storm
E05.40	Thyrotoxicosis factitia without thyrotoxic crisis or storm
E05.41	Thyrotoxicosis factitia with thyrotoxic crisis or storm
E05.80	Other thyrotoxicosis without thyrotoxic crisis or storm
E05.81	Other thyrotoxicosis with thyrotoxic crisis or storm
E05.90	Thyrotoxicosis, unspecified without thyrotoxic crisis or storm
E05.91	Thyrotoxicosis, unspecified with thyrotoxic crisis or storm
E06.3	Autoimmune thyroiditis
E07.9	Disorder of thyroid, unspecified
E21.0	Primary hyperparathyroidism
E21.1	Secondary hyperparathyroidism, not elsewhere classified
E21.2	Other hyperparathyroidism
E21.3	Hyperparathyroidism, unspecified
E28.310	Symptomatic premature menopause
E28.319	Asymptomatic premature menopause
E28.39	Other primary ovarian failure
E28.8	Other ovarian dysfunction
E28.9	Ovarian dysfunction, unspecified
E55.9	Vitamin D deficiency, unspecified
E58	Dietary calcium deficiency
E59	Dietary selenium deficiency
E60	Dietary zinc deficiency

Code	Description
E61.0	Copper deficiency
E61.1	Iron deficiency
E61.2	Magnesium deficiency
E61.3	Manganese deficiency
E61.4	Chromium deficiency
E61.5	Molybdenum deficiency
E61.6	Vanadium deficiency
E89.40	Asymptomatic postprocedural ovarian failure
E89.41	Symptomatic postprocedural ovarian failure
M48.50XA	Collapsed vertebra, not elsewhere classified, site unspecified, initial encounter for fracture
M48.51XA	Collapsed vertebra, not elsewhere classified, occipito-atlanto-axial region, initial encounter for fracture
M48.52XA	Collapsed vertebra, not elsewhere classified, cervical region, initial encounter for fracture
M48.53XA	Collapsed vertebra, not elsewhere classified, cervicothoracic region, initial encounter for fracture
M48.54XA	Collapsed vertebra, not elsewhere classified, thoracic region, initial encounter for fracture
M48.55XA	Collapsed vertebra, not elsewhere classified, thoracolumbar region, initial encounter for fracture
M48.56XA	Collapsed vertebra, not elsewhere classified, lumbar region, initial encounter for fracture
M48.57XA	Collapsed vertebra, not elsewhere classified, lumbosacral region, initial encounter for fracture
M48.58XA	Collapsed vertebra, not elsewhere classified, sacral and sacrococcygeal region, initial encounter for fracture
M80.00XA	Age-related osteoporosis with current pathological fracture, unspecified site, initial encounter for fracture
M80.011A	Age-related osteoporosis with current pathological fracture, right shoulder, initial encounter for fracture
M80.012A	Age-related osteoporosis with current pathological fracture, left shoulder, initial encounter for fracture
M80.019A	Age-related osteoporosis with current pathological fracture, unspecified shoulder, initial encounter for fracture
M80.021A	Age-related osteoporosis with current pathological fracture, right humerus, initial encounter for fracture
M80.022A	Age-related osteoporosis with current pathological fracture, left humerus, initial encounter for fracture
M80.029A	Age-related osteoporosis with current pathological fracture, unspecified humerus, initial encounter for fracture
M80.031A	Age-related osteoporosis with current pathological fracture, right forearm, initial encounter for fracture

Code	Description
M80.032A	Age-related osteoporosis with current pathological fracture, left forearm, initial encounter for fracture
M80.039A	Age-related osteoporosis with current pathological fracture, unspecified forearm, initial encounter for fracture
M80.041A	Age-related osteoporosis with current pathological fracture, right hand, initial encounter for fracture
M80.042A	Age-related osteoporosis with current pathological fracture, left hand, initial encounter for fracture
M80.049A	Age-related osteoporosis with current pathological fracture, unspecified hand, initial encounter for fracture
M80.051A	Age-related osteoporosis with current pathological fracture, right femur, initial encounter for fracture
M80.052A	Age-related osteoporosis with current pathological fracture, left femur, initial encounter for fracture
M80.059A	Age-related osteoporosis with current pathological fracture, unspecified femur, initial encounter for fracture
M80.061A	Age-related osteoporosis with current pathological fracture, right lower leg, initial encounter for fracture
M80.062A	Age-related osteoporosis with current pathological fracture, left lower leg, initial encounter for fracture
M80.069A	Age-related osteoporosis with current pathological fracture, unspecified lower leg, initial encounter for fracture
M80.071A	Age-related osteoporosis with current pathological fracture, right ankle and foot, initial encounter for fracture
M80.072A	Age-related osteoporosis with current pathological fracture, left ankle and foot, initial encounter for fracture
M80.079A	Age-related osteoporosis with current pathological fracture, unspecified ankle and foot, initial encounter for fracture
M80.08XA	Age-related osteoporosis with current pathological fracture, vertebra(e), initial encounter for fracture
M80.80XA	Other osteoporosis with current pathological fracture, unspecified site, initial encounter for fracture
M80.811A	Other osteoporosis with current pathological fracture, right shoulder, initial encounter for fracture
M80.812A	Other osteoporosis with current pathological fracture, left shoulder, initial encounter for fracture
M80.819A	Other osteoporosis with current pathological fracture, unspecified shoulder, initial encounter for fracture
M80.821A	Other osteoporosis with current pathological fracture, right humerus, initial encounter for fracture
M80.822A	Other osteoporosis with current pathological fracture, left humerus, initial encounter for fracture

Code	Description
M80.829A	Other osteoporosis with current pathological fracture, unspecified humerus, initial encounter for fracture
M80.831A	Other osteoporosis with current pathological fracture, right forearm, initial encounter for fracture
M80.832A	Other osteoporosis with current pathological fracture, left forearm, initial encounter for fracture
M80.839A	Other osteoporosis with current pathological fracture, unspecified forearm, initial encounter for fracture
M80.841A	Other osteoporosis with current pathological fracture, right hand, initial encounter for fracture
M80.842A	Other osteoporosis with current pathological fracture, left hand, initial encounter for fracture
M80.849A	Other osteoporosis with current pathological fracture, unspecified hand, initial encounter for fracture
M80.851A	Other osteoporosis with current pathological fracture, right femur, initial encounter for fracture
M80.852A	Other osteoporosis with current pathological fracture, left femur, initial encounter for fracture
M80.859A	Other osteoporosis with current pathological fracture, unspecified femur, initial encounter for fracture
M80.861A	Other osteoporosis with current pathological fracture, right lower leg, initial encounter for fracture
M80.862A	Other osteoporosis with current pathological fracture, left lower leg, initial encounter for fracture
M80.869A	Other osteoporosis with current pathological fracture, unspecified lower leg, initial encounter for fracture
M80.871A	Other osteoporosis with current pathological fracture, right ankle and foot, initial encounter for fracture
M80.872A	Other osteoporosis with current pathological fracture, left ankle and foot, initial encounter for fracture
M80.879A	Other osteoporosis with current pathological fracture, unspecified ankle and foot, initial encounter for fracture
M80.88XA	Other osteoporosis with current pathological fracture, vertebra(e), initial encounter for fracture
M81.0	Age-related osteoporosis without current pathological fracture
M81.6	Localized osteoporosis [Lequesne]
M81.8	Other osteoporosis without current pathological fracture
M84.40XA	Pathological fracture, unspecified site, initial encounter for fracture
M84.411A	Pathological fracture, right shoulder, initial encounter for fracture
M84.412A	Pathological fracture, left shoulder, initial encounter for fracture
M84.419A	Pathological fracture, unspecified shoulder, initial encounter for fracture

Code	Description
M84.421A	Pathological fracture, right humerus, initial encounter for fracture
M84.422A	Pathological fracture, left humerus, initial encounter for fracture
M84.429A	Pathological fracture, unspecified humerus, initial encounter for fracture
M84.431A	Pathological fracture, right ulna, initial encounter for fracture
M84.432A	Pathological fracture, left ulna, initial encounter for fracture
M84.433A	Pathological fracture, right radius, initial encounter for fracture
M84.434A	Pathological fracture, left radius, initial encounter for fracture
M84.439A	Pathological fracture, unspecified ulna and radius, initial encounter for fracture
M84.441A	Pathological fracture, right hand, initial encounter for fracture
M84.442A	Pathological fracture, left hand, initial encounter for fracture
M84.443A	Pathological fracture, unspecified hand, initial encounter for fracture
M84.444A	Pathological fracture, right finger(s), initial encounter for fracture
M84.445A	Pathological fracture, left finger(s), initial encounter for fracture
M84.446A	Pathological fracture, unspecified finger(s), initial encounter for fracture
M84.451A	Pathological fracture, right femur, initial encounter for fracture
M84.452A	Pathological fracture, left femur, initial encounter for fracture
M84.453A	Pathological fracture, unspecified femur, initial encounter for fracture
M84.454A	Pathological fracture, pelvis, initial encounter for fracture
M84.459A	Pathological fracture, hip, unspecified, initial encounter for fracture
M84.461A	Pathological fracture, right tibia, initial encounter for fracture
M84.462A	Pathological fracture, left tibia, initial encounter for fracture
M84.463A	Pathological fracture, right fibula, initial encounter for fracture
M84.464A	Pathological fracture, left fibula, initial encounter for fracture
M84.469A	Pathological fracture, unspecified tibia and fibula, initial encounter for fracture
M84.471A	Pathological fracture, right ankle, initial encounter for fracture
M84.472A	Pathological fracture, left ankle, initial encounter for fracture
M84.473A	Pathological fracture, unspecified ankle, initial encounter for fracture
M84.474A	Pathological fracture, right foot, initial encounter for fracture
M84.475A	Pathological fracture, left foot, initial encounter for fracture
M84.476A	Pathological fracture, unspecified foot, initial encounter for fracture
M84.477A	Pathological fracture, right toe(s), initial encounter for fracture
M84.478A	Pathological fracture, left toe(s), initial encounter for fracture
M84.479A	Pathological fracture, unspecified toe(s), initial encounter for fracture
M84.48XA	Pathological fracture, other site, initial encounter for fracture
M84.50XA	Pathological fracture in neoplastic disease, unspecified site, initial encounter for fracture

Code	Description
M84.511A	Pathological fracture in neoplastic disease, right shoulder, initial encounter for fracture
M84.512A	Pathological fracture in neoplastic disease, left shoulder, initial encounter for fracture
M84.519A	Pathological fracture in neoplastic disease, unspecified shoulder, initial encounter for fracture
M84.521A	Pathological fracture in neoplastic disease, right humerus, initial encounter for fracture
M84.522A	Pathological fracture in neoplastic disease, left humerus, initial encounter for fracture
M84.529A	Pathological fracture in neoplastic disease, unspecified humerus, initial encounter for fracture
M84.531A	Pathological fracture in neoplastic disease, right ulna, initial encounter for fracture
M84.532A	Pathological fracture in neoplastic disease, left ulna, initial encounter for fracture
M84.533A	Pathological fracture in neoplastic disease, right radius, initial encounter for fracture
M84.534A	Pathological fracture in neoplastic disease, left radius, initial encounter for fracture
M84.539A	Pathological fracture in neoplastic disease, unspecified ulna and radius, initial encounter for fracture
M84.541A	Pathological fracture in neoplastic disease, right hand, initial encounter for fracture
M84.542A	Pathological fracture in neoplastic disease, left hand, initial encounter for fracture
M84.549A	Pathological fracture in neoplastic disease, unspecified hand, initial encounter for fracture
M84.550A	Pathological fracture in neoplastic disease, pelvis, initial encounter for fracture
M84.551A	Pathological fracture in neoplastic disease, right femur, initial encounter for fracture
M84.552A	Pathological fracture in neoplastic disease, left femur, initial encounter for fracture
M84.553A	Pathological fracture in neoplastic disease, unspecified femur, initial encounter for fracture
M84.559A	Pathological fracture in neoplastic disease, hip, unspecified, initial encounter for fracture
M84.561A	Pathological fracture in neoplastic disease, right tibia, initial encounter for fracture
M84.562A	Pathological fracture in neoplastic disease, left tibia, initial encounter for fracture
M84.563A	Pathological fracture in neoplastic disease, right fibula, initial encounter for fracture
M84.564A	Pathological fracture in neoplastic disease, left fibula, initial encounter for fracture
M84.569A	Pathological fracture in neoplastic disease, unspecified tibia and fibula, initial encounter for fracture
M84.571A	Pathological fracture in neoplastic disease, right ankle, initial encounter for fracture
M84.572A	Pathological fracture in neoplastic disease, left ankle, initial encounter for fracture
M84.573A	Pathological fracture in neoplastic disease, unspecified ankle, initial encounter for fracture
M84.574A	Pathological fracture in neoplastic disease, right foot, initial encounter for fracture
M84.575A	Pathological fracture in neoplastic disease, left foot, initial encounter for fracture
M84.576A	Pathological fracture in neoplastic disease, unspecified foot, initial encounter for fracture

Code	Description
M84.58XA	Pathological fracture in neoplastic disease, other specified site, initial encounter for fracture
M84.60XA	Pathological fracture in other disease, unspecified site, initial encounter for fracture
M84.611A	Pathological fracture in other disease, right shoulder, initial encounter for fracture
M84.612A	Pathological fracture in other disease, left shoulder, initial encounter for fracture
M84.619A	Pathological fracture in other disease, unspecified shoulder, initial encounter for fracture
M84.621A	Pathological fracture in other disease, right humerus, initial encounter for fracture
M84.622A	Pathological fracture in other disease, left humerus, initial encounter for fracture
M84.629A	Pathological fracture in other disease, unspecified humerus, initial encounter for fracture
M84.631A	Pathological fracture in other disease, right ulna, initial encounter for fracture
M84.632A	Pathological fracture in other disease, left ulna, initial encounter for fracture
M84.633A	Pathological fracture in other disease, right radius, initial encounter for fracture
M84.634A	Pathological fracture in other disease, left radius, initial encounter for fracture
M84.639A	Pathological fracture in other disease, unspecified ulna and radius, initial encounter for fracture
M84.641A	Pathological fracture in other disease, right hand, initial encounter for fracture
M84.642A	Pathological fracture in other disease, left hand, initial encounter for fracture
M84.649A	Pathological fracture in other disease, unspecified hand, initial encounter for fracture
M84.650A	Pathological fracture in other disease, pelvis, initial encounter for fracture
M84.651A	Pathological fracture in other disease, right femur, initial encounter for fracture
M84.652A	Pathological fracture in other disease, left femur, initial encounter for fracture
M84.653A	Pathological fracture in other disease, unspecified femur, initial encounter for fracture
M84.659A	Pathological fracture in other disease, hip, unspecified, initial encounter for fracture
M84.661A	Pathological fracture in other disease, right tibia, initial encounter for fracture
M84.662A	Pathological fracture in other disease, left tibia, initial encounter for fracture
M84.663A	Pathological fracture in other disease, right fibula, initial encounter for fracture
M84.664A	Pathological fracture in other disease, left fibula, initial encounter for fracture
M84.669A	Pathological fracture in other disease, unspecified tibia and fibula, initial encounter for fracture
M84.671A	Pathological fracture in other disease, right ankle, initial encounter for fracture
M84.672A	Pathological fracture in other disease, left ankle, initial encounter for fracture
M84.673A	Pathological fracture in other disease, unspecified ankle, initial encounter for fracture
M84.674A	Pathological fracture in other disease, right foot, initial encounter for fracture
M84.675A	Pathological fracture in other disease, left foot, initial encounter for fracture
M84.676A	Pathological fracture in other disease, unspecified foot, initial encounter for fracture
M84.68XA	Pathological fracture in other disease, other site, initial encounter for fracture

Code	Description
M85.9	Disorder of bone density and structure, unspecified
M88.0	Osteitis deformans of skull
M88.1	Osteitis deformans of vertebrae
M88.811	Osteitis deformans of right shoulder
M88.812	Osteitis deformans of left shoulder
M88.819	Osteitis deformans of unspecified shoulder
M88.821	Osteitis deformans of right upper arm
M88.822	Osteitis deformans of left upper arm
M88.829	Osteitis deformans of unspecified upper arm
M88.831	Osteitis deformans of right forearm
M88.832	Osteitis deformans of left forearm
M88.839	Osteitis deformans of unspecified forearm
M88.841	Osteitis deformans of right hand
M88.842	Osteitis deformans of left hand
M88.849	Osteitis deformans of unspecified hand
M88.851	Osteitis deformans of right thigh
M88.852	Osteitis deformans of left thigh
M88.859	Osteitis deformans of unspecified thigh
M88.861	Osteitis deformans of right lower leg
M88.862	Osteitis deformans of left lower leg
M88.869	Osteitis deformans of unspecified lower leg
M88.871	Osteitis deformans of right ankle and foot
M88.872	Osteitis deformans of left ankle and foot
M88.879	Osteitis deformans of unspecified ankle and foot
M88.88	Osteitis deformans of other bones
M88.89	Osteitis deformans of multiple sites
M88.9	Osteitis deformans of unspecified bone
M89.9	Disorder of bone, unspecified
M94.9	Disorder of cartilage, unspecified
N92.4	Excessive bleeding in the premenopausal period
N95.0	Postmenopausal bleeding
N95.1	Menopausal and female climacteric states
N95.8	Other specified menopausal and perimenopausal disorders
N95.9	Unspecified menopausal and perimenopausal disorder
S12.9XXA	Fracture of neck, unspecified, initial encounter

Code	Description
Z79.3	Long term (current) use of hormonal contraceptives
Z79.51	Long term (current) use of inhaled steroids
Z79.52	Long term (current) use of systemic steroids
Z79.891	Long term (current) use of opiate analgesic
Z79.899	Other long term (current) drug therapy

Indications

Generally speaking, collagen crosslink testing is useful mostly in “fast losers” of bone. The age when these bone markers can help direct therapy is often pre-Medicare. By the time a fast loser of bone reaches age 65, she will most likely have been stabilized by appropriate therapy or have lost so much bone mass that further testing is useless. Coverage for bone marker assays may be established, however, for younger Medicare beneficiaries and for those men and women who might become fast losers because of some other therapy such as glucocorticoids. Safeguards should be incorporated to prevent excessive use of tests in patients for whom they have no clinical relevance.

Collagen crosslinks testing is used to:

- Identify individuals with elevated bone resorption, who have osteoporosis in whom response to treatment is being monitored.
- Predict response (as assessed by bone mass measurements) to FDA approved antiresorptive therapy in postmenopausal women.
- Assess response to treatment of patients with osteoporosis, Paget’s disease of the bone, or risk for osteoporosis where treatment may include FDA approved antiresorptive agents, anti-estrogens or selective estrogen receptor moderators.

Limitations

Because of significant specimen to specimen collagen crosslink physiologic variability (15-20%), current recommendations for appropriate utilization include: one or two base-line assays from specified urine collections on separate days; followed by a repeat assay about 3 months after starting anti-resorptive therapy; followed by a repeat assay in 12 months after the 3-month assay; and thereafter not more than annually, unless there is a change in therapy in which circumstance an additional test may be indicated 3 months after the initiation of new therapy.

Some collagen crosslink assays may not be appropriate for use in some disorders, according to FDA labeling restrictions.

ICD-10-CM Codes That Do Not Support Medical Necessity

Any ICD-10-CM code not listed in either of the ICD-10-CM covered or non-covered sections.

Sources of Information

Arnaud CD. Osteoporosis: Using ‘bone markers’ for diagnosis and monitoring. *Geriatrics* 1996; 51:24-30.

Chesnut CH, III, Bell NH, Clark G, et al. Hormone replacement therapy in postmenopausal women: urinary N-telopeptide of type I collagen monitors therapeutic effect and predicts response of bone mineral density. *Am. J. Med.* 1997;102:29-37.

Garnero P, Delmas PD. Clinical usefulness of markers of bone remodelling in osteoporosis. In: Meunier PJ. (ed). *Osteoporosis: diagnosis and management*. London: Martin Dunitz Ltd 1998:79-101.

Garnero P, Shih WJ, Gineyts E, et al. Comparison of new biochemical markers of bone turnover in late postmenopausal osteoporotic women in response to alendronate treatment. *J. Clin. Endocrinol. Metab.* 1994;79:1693-700.

Harper KD, Weber TJ. Secondary osteoporosis - Diagnostic considerations. *Endocrinol. Metab. Clin. North Am.* 1998;27:325-48.

Hesley RP, Shepard KA, Jenkins DK, Riggs BL. Monitoring estrogen replacement therapy and identifying rapid bone losers with an immunoassay for deoxypyridinoline. *Osteoporos. Int.* 1998;8:159-64.

Melton LJ, III, Khosla S, Atkinson EJ, et al. Relationship of bone turnover to bone density and fractures. *J. Bone Miner. Res.* 1997;12:1083-91.

Millard PS. Prevention of osteoporosis: making sense of the published evidence. In: Rosen CJ (ed). *Osteoporosis: diagnostic & therapeutic principles*. Totowa: Humana Press. 1996:275-85.

Rosen CJ. Biochemical markers of bone turnover. In: Rosen CJ(ed). *Osteoporosis: diagnostic and therapeutic principles*. Totowa: Humana Press Inc. 1996:129-41.

Schneider DL, Barrett-Connor EL. Urinary N-Telopeptide levels discriminate normal, osteopenic, and osteoporotic bone mineral density. *Arch. Intern. Med.* 1997;157:1241-5.