

# Collagen Crosslinks (Any Method)

CPT: 82523

---

## CMS National Coverage Policy

### Coverage Indications, Limitations, and/or Medical Necessity

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.

### 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.

---

Visit [QuestDiagnostics.com/MLCP](https://www.questdiagnostics.com/MLCP) to view current limited coverage tests, reference guides, and policy information.

To view the complete policy and the full list of codes, please refer to the CMS website reference

[www.cms.gov](https://www.cms.gov) ►

# Collagen Crosslinks (Any Method)

CPT: 82523

The ICD10 codes listed below are the top diagnosis codes currently utilized by ordering physicians for the limited coverage test highlighted above that are also listed as medically supportive under Medicare's limited coverage policy. **If you are ordering this test for diagnostic reasons that are not covered under Medicare policy, an Advance Beneficiary Notice form is required.**

Please refer to the [Limitations or Utilization Guidelines](#) section on previous page(s) for frequency information.

Code	Description
E05.90	Thyrotoxicosis, unsp without thyrotoxic crisis or storm
E06.3	Autoimmune thyroiditis
E21.0	Primary hyperparathyroidism
E21.3	Hyperparathyroidism, unspecified
E55.9	Vitamin D deficiency, unspecified
E61.1	Iron deficiency
M80.00XA	Age-rel osteopor w current path fracture, unsp site, init
M81.0	Age-related osteoporosis w/o current pathological fracture
M81.6	Localized osteoporosis [Lequesne]
M81.8	Other osteoporosis without current pathological fracture
M85.80	Oth disrd of bone density and structure, unspecified site
M85.88	Oth disrd of bone density and structure, other site
M85.89	Oth disrd of bone density and structure, multiple sites
M85.9	Disorder of bone density and structure, unspecified
M88.9	Osteitis deformans of unspecified bone
M89.9	Disorder of bone, unspecified
N95.1	Menopausal and female climacteric states
N95.9	Unspecified menopausal and perimenopausal disorder
Z79.52	Long term (current) use of systemic steroids
Z79.899	Other long term (current) drug therapy

Visit [QuestDiagnostics.com/MLCP](https://www.questdiagnostics.com/MLCP) to view current limited coverage tests, reference guides, and policy information.

To view the complete policy and the full list of codes, please refer to the CMS website reference

[www.cms.gov](https://www.cms.gov) ►

Last updated: 10/01/24

#### Disclaimer:

This diagnosis code reference guide is provided as an aid to physicians and office staff in determining when an ABN (Advance Beneficiary Notice) is necessary. Diagnosis codes must be applicable to the patient's symptoms or conditions and must be consistent with documentation in the patient's medical record. Quest Diagnostics does not recommend any diagnosis codes and will only submit diagnosis information provided to us by the ordering physician or his/her designated staff. The CPT codes provided are based on AMA guidelines and are for informational purposes only. CPT coding is the sole responsibility of the billing party. Please direct any questions regarding coding to the payer being billed.

#### QuestDiagnostics.com

Quest, Quest Diagnostics, any associated logos, and all associated Quest Diagnostics registered or unregistered trademarks are the property of Quest Diagnostics. All third-party marks—® and ™—are the property of their respective owners. © 2016 Quest Diagnostics Incorporated. All rights reserved.