

Medical Coverage Policy | Bone Turnover Markers for the Diagnosis and Management of Osteoporosis and Diseases Associated with High Bone Turnover



EFFECTIVE DATE: 07|01|2014

POLICY LAST REVIEWED: 02|04|2026

OVERVIEW

Bone turnover markers are biochemical markers of either bone formation or bone resorption. Commercially available tests are available to assess some of these markers in urine and/or serum by high-performance liquid chromatography or immunoassay. Assessment of bone turnover markers is proposed to supplement bone mineral density measurement in the diagnosis of osteoporosis and to aid in treatment decisions. Bone turnover markers could also potentially be used to evaluate treatment effectiveness before changes in bone mineral density can be observed.

MEDICAL CRITERIA

Not applicable

PRIOR AUTHORIZATION

Not applicable

Note: Laboratories are not allowed to obtain clinical authorization or participate in the authorization process on behalf of the ordering physician. Only the ordering physician shall be involved in the authorization, appeal or other administrative processes related to prior authorization/medical necessity.

In no circumstance shall a laboratory or a physician/provider use a representative of a laboratory or anyone with a relationship to a laboratory and/or a third party to obtain authorization on behalf of the ordering physician, to facilitate any portion of the authorization process or any subsequent appeal of a claim where the authorization process was not followed and/or a denial for clinical appropriateness was issued, including any element of the preparation of necessary documentation of clinical appropriateness. If a laboratory or a third party is found to be supporting any portion of the authorization process, BCBSRI will deem the action a violation of this policy and severe action will be taken up to and including termination from the BCBSRI provider network. If a laboratory provides a laboratory service that has not been authorized, the service will be denied as the financial liability of the participating laboratory and may not be billed to the member.

POLICY STATEMENT

Medicare Advantage Plans and Commercial Products

Measurement of bone turnover markers using Collagen Crosslinks testing for the following indications may be considered medically necessary when filed with a covered diagnosis code. Refer to Coding section for details.

- 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; and
- 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.

Measurement of all other bone turnover markers (i.e. Osteocalcin test) are considered not covered for Medicare Advantage Plans and not medically necessary for Commercial Products the following indications:

- to determine fracture risk in individuals with osteoporosis or with age-related risk factors for osteoporosis

- to determine response to therapy in individuals who are being treated for osteoporosis
- in the management of individuals with conditions associated with high rates of bone turnover, including but not limited to Paget disease, primary hyperparathyroidism, and renal osteodystrophy.

Commercial Products

Some genetic testing services are not covered and a contract exclusion for any self-funded group that has excluded the expanded coverage of biomarker testing related to the state mandate, R.I.G.L. §27-19-81 described in the Biomarker Testing Mandate policy. For these groups, a list of which genetic testing services are covered with prior authorization, are not medically necessary or are not covered because they are a contract exclusion can be found in the Coding section of the Genetic Testing Services or Proprietary Laboratory Analyses policies. Please refer to the appropriate Benefit Booklet to determine whether the member's plan has customized benefit coverage. Please refer to the list of Related Policies for more information.

COVERAGE

Benefits may vary between groups and contracts. Please refer to the appropriate Evidence of Coverage or Subscriber Agreement for laboratory tests and applicable not covered/not medically necessary benefits/coverage.

BACKGROUND

Bone Turnover

After cessation of growth, bone is in a constant state of remodeling (or turnover), with initial absorption of bone by osteoclasts followed by deposition of new bone matrix by osteoblasts. This constant bone turnover is critical to the overall health of the bone, by repairing microfractures and remodeling the bony architecture in response to stress. Normally, the action of osteoclasts and osteoblasts is balanced, but bone loss occurs if the 2 processes become uncoupled. Bone turnover markers can be categorized as bone formation markers or bone resorption markers and can be identified in serum and/or urine. There is interest in the use of bone turnover markers to evaluate age-related osteoporosis, a condition characterized by slow, prolonged bone loss, resulting in an increased risk of fractures at the hip, spine, or wrist. Measurement of bone turnover markers may aid in the diagnosis (by determining fracture risk) and therapeutic monitoring (by determining response to treatment) of osteoporosis. Bone turnover markers may also be used for the management of other diseases associated with high bone turnover (eg, primary hyperparathyroidism, Paget disease, renal osteodystrophy).

Collagen Crosslinks

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:

1. Identify individuals with elevated bone resorption, who have osteoporosis in whom response to treatment is being monitored;
2. Predict response (as assessed by bone mass measurements) to FDA approved antiresorptive therapy in postmenopausal women; and
3. 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.

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 three months after starting anti-resorptive therapy; followed by a repeat assay in 12 months after the three-month assay; and thereafter not more than annually, unless there is a change in therapy in which circumstance an additional test may be indicated three 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.

Measurement of All Other Bone Turnover Markers (i.e. Osteocalcin Test)

For individuals with osteoporosis or risk factors for age-related osteoporosis who receive a measurement of bone turnover markers to determine fracture risk, the evidence includes observational studies on the association between markers and osteoporosis and fracture risk, and systematic reviews of those studies. Relevant outcomes are test validity and morbid events. Few studies have directly addressed whether any bone turnover markers beyond bone mineral density (BMD) measurements are independent predictors of fracture risk. One meta-analysis investigated the independent role of bone turnover markers in fracture risk prediction and found a statistically significant but modest association between bone turnover markers (specifically, PINP and CTX) and future fracture risk after adjusting for BMD and clinical risk factors. Other studies have suggested that bone turnover marker levels may be independently associated with osteoporosis and fracture risk in some groups, but there is insufficient evidence reporting on an association with any specific marker. Questions remain whether bone turnover markers are sufficiently sensitive to determine reliably individual treatment responses. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who are being treated for osteoporosis who receive a measurement of bone turnover markers to determine response to therapy, the evidence includes an observational study, randomized controlled trials (RCTs), and a systematic review these RCTs. Relevant outcomes are test validity and morbid events. There is limited evidence on the impact of bone turnover markers on the management of osteoporosis. Individual RCTs and a systematic review of these RCTs have not found that feedback on bone turnover markers improves treatment adherence rates. No studies were identified that evaluated whether the use of bone turnover markers leads to management changes that are expected to improve outcomes. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with conditions associated with high rates of bone turnover other than age-related osteoporosis (eg, primary hyperparathyroidism, Paget disease, renal osteodystrophy) who receive a measurement of bone turnover markers, the evidence includes observational studies on the association between markers and disease activity and a systematic review of those studies. Relevant outcomes are test validity and morbid events. The largest amount of evidence has been published on Paget disease; a systematic review found correlations between several bone turnover markers and disease activity prior to and/or after bisphosphonate treatment. There is a lack of evidence on how the measurement of bone turnover markers can change patient management or improve health outcomes. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

CODING

Medicare Advantage Plans and Commercial Products

The following CPT code(s) are covered when filed with one of the diagnosis codes in the attachments below:
82523 Collagen cross links, any method

[Covered ICD-10 Codes for CPT Code 82523](#)

The following CPT code(s) are not covered for Medicare Advantage Plans and not medically necessary for Commercial Products when filed with an ICD-10 Diagnosis Code* listed below;
83937 Osteocalcin (bone g1a protein)

***Not medically necessary ICD-10 Diagnosis Codes:**

M81.0-M81.8
Z13.820

RELATED POLICIES

Biomarker Testing Mandate
Genetic Testing Services

PUBLISHED

Provider Update, April 2026
Provider Update, April 2025
Provider Update, May 2024
Provider Update, April 2023
Provider Update, April 2022

REFERENCES

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