MASSACHUSETTS

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Medical Policy

Bone Turnover Markers for Diagnosis and Management of Osteoporosis and Diseases Associated with High Bone Turnover

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Policy Number: **549**

BCBSA Reference Number: 2.04.15
NCD/LCD: National Coverage Determination (NCD) for Collagen Crosslinks, any Method (190.19)

Related Policies

- Bone Mineral Density Studies, #450
- Vertebral Fracture Assessment with Densitometry, #449

Policy

Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity

Measurement of bone turnover markers in the diagnosis and management of osteoporosis is **INVESTIGATIONAL.**

Measurement of bone turnover markers in the management of patients with conditions associated with high rates of bone turnover, including but not limited to Paget's disease, primary hyperparathyroidism and renal osteodystrophy is **INVESTIGATIONAL.**

Medicare HMO Blue[SM] and Medicare PPO Blue[SM] Members

BCBSMA covers urine-based collagen cross-links testing for the following indications, for Medicare HMO Blue and Medicare PPO Blue members in accordance with CMS NCD:

- 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.

BCBSMA does not cover collagen cross-link assays in disorders where FDA restrictions indicate the test is not appropriate for Medicare HMO Blue and Medicare PPO Blue members in accordance with CMS NCD.

Medical necessity criteria and coding guidance can be found through the link(s) below.

National Coverage Determinations (NCDs)

National Coverage Determination (NCD) for Collagen Crosslinks, any Method (190.19)

Note: To review the specific NCD, please remember to click "accept" on the CMS licensing agreement at the bottom of the CMS webpage.

Prior Authorization Information

Inpatient

- For services described in this policy, precertification/preauthorization **IS REQUIRED** for all products if the procedure is performed **inpatient**.

Outpatient

- For services described in this policy, see below for products where prior authorization **might be required** if the procedure is performed **outpatient**.

	Outpatient
Commercial Managed Care (HMO and POS)	This is **not** a covered service.
Commercial PPO and Indemnity	This is **not** a covered service.
Medicare HMO Blue℠	Prior authorization is **not required**.
Medicare PPO Blue℠	Prior authorization is **not required**.

CPT Codes / HCPCS Codes / ICD Codes

Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage as it applies to an individual member.

Providers should report all services using the most up-to-date industry-standard procedure, revenue, and diagnosis codes, including modifiers where applicable.

The following codes are included below for informational purposes only; this is not an all-inclusive list.
The following CPT code is considered investigational for Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity:

CPT Codes

CPT codes:	Code Description
82523	Collagen cross-links, any method

The following CPT code is considered investigational for Commercial Members: Managed Care (HMO and POS), PPO, Indemnity, Medicare HMO Blue and Medicare PPO Blue:

CPT Codes

CPT codes:	Code Description
83937	Osteocalcin (bone g1a protein)

Description

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. Table 1 summarizes the various bone turnover markers.

Table 1. Bone Turnover Markers

Formation Markers	Resorption Markers
Serum osteocalcin	Serum and urinary hydroxyproline
Serum total alkaline phosphatase	Urinary total pyridinoline
Serum bone-specific alkaline phosphatase	Urinary total deoxypyridinoline
Serum procollagen I carboxyterminal propeptide	Urinary-free pyridinoline (also known as Pyrilinks)
Serum procollagen type 1 N-terminal propeptide	Urinary-free deoxypyridinoline (also known as Pyrilinks-D)
Bone sialoprotein	Serum and urinary collagen type I cross-linked N-telopeptide (also referred to as Osteomark)
	Serum and urinary collagen type I cross-linked C-telopeptide (also referred to as CrossLaps)
	Serum carboxyterminal telopeptide of type I collagen
	Tartrate-resistant acid phosphatase

Bone Density

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. Currently, fracture risk is primarily based on measurements of bone mineral density (BMD) in conjunction with other genetic and environmental factors, such as family history of osteoporosis, history of smoking, and weight. It is thought that the level of bone turnover markers may also predict fracture risk, possibly through a different mechanism than that associated with BMD. However, it must be emphasized that the presence of bone turnover markers in the serum or urine is not necessarily related to bone loss. For example, even if bone turnover is high, if resorption is balanced with formation, there will be no net bone loss. Bone loss will only occur if resorption exceeds formation. Therefore, bone turnover markers have been primarily studied as an adjunct, not an alternative, to measurements of BMD to estimate fracture risk and document the need for preventive or therapeutic strategies for osteoporosis.

In addition, bone turnover markers might provide a more immediate assessment of treatment response and predict change in BMD in response to treatment. Treatment-related changes in BMD occur very slowly. This fact, coupled with the precision of BMD technologies, has suggested that clinically significant changes in BMD could not be reliably detected until at least 2 years. In contrast, changes in bone turnover markers could be anticipated after 3 months of therapy.

Bone turnover markers have also been evaluated as markers of diseases associated with markedly high levels of bone turnover, such as Paget disease, primary hyperparathyroidism, and renal osteodystrophy.

Summary

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.

For individuals with osteoporosis or risk factors for age-related osteoporosis who receive measurement of bone turnover markers, 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. 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. In addition, controlled studies do not provide sufficient evidence that bone turnover marker measurement improves adherence to treatment, impacts management decisions, or improves health outcomes (eg, reduces fracture rates). The evidence is insufficient to determine the effects of the technology on health outcomes.

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 measurement of bone turnover markers, the evidence includes observational studies on the association between markers and disease activity, and systematic reviews 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 measurement of bone turnover markers can change patient management or improve health outcomes. The evidence is insufficient to determine the effects of the technology on health outcomes.

Policy History

Date	Action
2/2019	BCBSA National medical policy review. Description, summary and references updated. Policy statements unchanged.
3/2018	New references added from BCBSA National medical policy.
11/2015	New references added from BCBSA National medical policy.
7/2015	Clarified coding information.
6/2014	Updated Coding section with ICD10 procedure and diagnosis codes, effective 10/2015.
1/2014	New references added from BCBSA National medical policy.
11/2013	Added ICD-9 diagnosis code 256.9 to be in alignments with the NCD.
10/2013	Added ICD-9 diagnosis codes 252.00-252.02, 252.08 to be in alignment with the NCD.
6/2013	BCBSA National medical policy review. New investigational indications described. Effective 6/1/2013.
11/2011-4/2012	Medical policy ICD 10 remediation: Formatting, editing and coding updates.

	No changes to policy statements.
1/1/2011	New policy effective 1/1/2011 describing covered and non-covered indications.

Information Pertaining to All Blue Cross Blue Shield Medical Policies

Click on any of the following terms to access the relevant information:
Medical Policy Terms of Use
Managed Care Guidelines
Indemnity/PPO Guidelines
Clinical Exception Process
Medical Technology Assessment Guidelines

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