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 (For Plan internal use only)

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 is considered **INVESTIGATIONAL** to determine fracture risk in patients with osteoporosis or with age-related risk factors for osteoporosis.

Measurement of bone turnover markers is considered **INVESTIGATIONAL** 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.

Measurement of bone turnover markers is considered **INVESTIGATIONAL** to determine response to therapy in patients who are being treated for osteoporosis.

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.

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 two 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. 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 carboxy-terminal telopeptide of type I collagen
	Tartrate-resistant acid phosphatase

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 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 BMD measurements are independent predictors of fracture risk. 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. Overall, the evidence does not suggest that any bone turnover marker is an independent predictor of fracture risk, beyond BMD. 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 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. There is a limited amount of evidence on the impact of bone turnover markers on the management of osteoporosis. Individual RCTs and a meta-analysis of these RCTs have not found that feedback on bone turnover marker 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 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 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.

Policy History

Date	Action
2/2022	Annual policy review. Policy statements unchanged.
3/2021	Annual policy review. Description, summary, and references updated. Policy statements unchanged.
1/2021	Medicare information removed. See MP #132 Medicare Advantage Management for local coverage determination and national coverage determination reference.
6/2020	Annual policy review. New investigational indications described. Effective 6/1/2020.
2/2019	Annual policy review. Description, summary, and references updated. Policy statements unchanged.
3/2018	Annual policy review. New references added.
11/2015	Annual policy review. New references added.
7/2015	Clarified coding information.

6/2014	Updated Coding section with ICD10 procedure and diagnosis codes, effective 10/2015.
1/2014	Annual policy review. New references added.
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	Annual 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

References

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