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

EFFECTIVE DATE: 11|01|2019
POLICY LAST UPDATED: 02|06|2020

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 (BMD) 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 BMD can be observed.

MEDICAL CRITERIA

Not applicable

PRIOR AUTHORIZATION

Prior authorization review is not required.

POLICY STATEMENT

BlueCHiP for Medicare

Measurement of bone turnover markers are covered

Commercial Products

Measurement of bone turnover markers is considered not medically necessary for the following indications:

- to determine fracture risk in patients with osteoporosis or with age-related risk factors for osteoporosis.
- to determine response to therapy in patients who are being treated for osteoporosis.
- the management of patients with conditions associated with high rates of bone turnover, including but not limited to Paget disease, primary perparathyroidism, and renal osteodystrophy.

COVERAGE

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

BACKGROUND

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. Currently, fracture risk is primarily based on measurements of 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, 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 researched as markers of diseases associated with markedly high levels of bone turnover, such as Paget disease, primary hyperparathyroidism, and renal osteodystrophy.

The literature suggests that bone turnover marker levels may be independently associated with osteoporosis and fracture risk in some groups, but there is insufficient evidence reporting an association for any specific marker. Questions remain about whether bone turnover markers are sufficiently sensitive to reliably determine individual treatment responses. In addition, there is insufficient evidence from controlled studies that bone turnover marker measurement improves adherence to treatment, impacts management decisions, and/or improves health outcomes such as reducing fracture rates. Thus, the use of bone turnover markers for the diagnosis and management of osteoporosis is considered not medically necessary.

There is insufficient evidence that measurement of bone turnover markers improves patient management or health outcomes in patients with conditions associated with high bone turnover including Paget disease, primary hyperparathyroidism, and renal osteodystrophy. Thus, bone turnover marker testing for these other conditions is considered not medically necessary.

CODING

BlueCHiP for Medicare
The following CPT codes are medically necessary
82523 Collagen cross links, any method
83937 Osteocalcin (bone g1a protein)

Commercial Products
The following codes are not medically necessary when filed with a diagnosis below.
82523 Collagen cross links, any method
83937 Osteocalcin (bone g1a protein)

Not medically necessary diagnosis:
M81.0-M81.8
Z13.820
Z82.62

RELATED POLICIES

None

PUBLISHED

Provider Update, April 2020
Provider Update, August 2018
Provider Update, February 2017
Provider Update, August 2015

REFERENCES

1. Tamaki J, Iki M, Kadowaki E, et al. Biochemical markers for bone turnover predict risk of vertebral fractures in postmenopausal women over 10 years: the Japanese Population-based Osteoporosis (JPOS) Cohort Study. *Osteoporos Int.* Mar 2013;24(3):887-897. PMID 22885773
2. Bauer DC, Garnero P, Harrison SL, et al. Biochemical markers of bone turnover, hip bone loss, and fracture in older men: the MrOS study. *J Bone Miner Res.* Dec 2009;24(12):2032-2038. PMID 19453262
3. Johansson H, Oden A, Kanis JA, et al. A meta-analysis of reference markers of bone turnover for prediction of fracture. *Calcif Tissue Int.* May 2014;94(5):560-567. PMID 24590144
4. Biver E, Chopin F, Coiffier G, et al. Bone turnover markers for osteoporotic status assessment? A systematic review of their diagnosis value at baseline in osteoporosis. *Joint Bone Spine.* Jan 2012;79(1):20-25. PMID 21724445
5. Bauer DC, Garnero P, Hochberg MC, et al. Pretreatment levels of bone turnover and the antifracture efficacy of alendronate: the fracture intervention trial. *J Bone Miner Res.* Feb 2006;21(2):292-299. PMID 16418785
6. Abe Y, Ishikawa H, Fukao A. Higher efficacy of urinary bone resorption marker measurements in assessing response to treatment for osteoporosis in postmenopausal women. *Tohoku J Exp Med.* Jan 2008;214(1):51-59. PMID 18212487
7. Shiraki M, Itabashi A. Short-term menatetrenone therapy increases gamma-carboxylation of osteocalcin with a moderate increase of bone turnover in postmenopausal osteoporosis: a randomized prospective study. *J Bone Miner Metab.* 2009;27(3):333-340. PMID 19172219
8. Funck-Brentano T, Biver E, Chopin F, et al. Clinical utility of serum bone turnover markers in postmenopausal osteoporosis therapy monitoring: a systematic review. *Semin Arthritis Rheum.* Oct 2011;41(2):157-169. PMID 21507464
9. Baxter I, Rogers A, Eastell R, et al. Evaluation of urinary N-telopeptide of type I collagen measurements in the management of osteoporosis in clinical practice. *Osteoporos Int.* Mar 2013;24(3):941-947. PMID 22872068
10. Cosman F, de Beur SJ, LeBoff MS, et al. Clinician's guide to prevention and treatment of osteoporosis. *Osteoporos Int.* Oct 2014;25(10):2359-2381. PMID 25182228
11. Burch J, Rice S, Yang H, et al. Systematic review of the use of bone turnover markers for monitoring the response to osteoporosis treatment: the secondary prevention of fractures, and primary prevention of fractures in high-risk groups. *Health Technol Assess.* Feb 2014;18(11):1-180. PMID 24534414
12. Roux C, Giraudeau B, Rouanet S, et al. Monitoring of bone turnover markers does not improve persistence with ibandronate treatment. *Joint Bone Spine.* Jul 2012;79(4):389-392. PMID 21703900
13. Rianon N, Alex G, Callender G, et al. Preoperative serum osteocalcin may predict postoperative elevated parathyroid hormone in patients with primary hyperparathyroidism. *World J Surg.* Jun 2012;36(6):1320-1326. PMID 22278606
14. Al Nofal AA, Altayar O, BenKhadra K, et al. Bone turnover markers in Paget's disease of the bone: a systematic review and meta-analysis. *Osteoporos Int.* Jul 2015;26(7):1875-1891. PMID 26037791
15. Cosman F, de Beur SJ, LeBoff MS, et al. Clinician's guide to prevention and treatment of osteoporosis. *Osteoporos Int.* Oct 2014;25(10):2359-2381. PMID 25182228
16. North American Menopause Society. Management of osteoporosis in postmenopausal women: 2010 position statement of The North American Menopause Society. *Menopause.* Jan-Feb 2010;17(1):25-54; quiz 55-26. PMID 20061894
17. Vasikaran S, Cooper C, Eastell R, et al. International Osteoporosis Foundation and International Federation of Clinical Chemistry and Laboratory Medicine position on bone marker standards in osteoporosis. *Clin Chem Lab Med.* Aug 2011;49(8):1271-1274. PMID 21605012
18. McCloskey EV, Vasikaran S, Cooper C. Official Positions for FRAX(R) clinical regarding biochemical markers from Joint Official Positions Development Conference of the International Society for Clinical Densitometry and International Osteoporosis Foundation on FRAX(R). *J Clin Densitom.* Jul-Sep 2011;14(3):220-222. PMID 21810528
19. Szulc P, Naylor K, Hoyle NR, et al. Use of CTX-I and PINP as bone turnover markers: National Bone Health Alliance recommendations to standardize sample handling and patient preparation to reduce pre-analytical variability. *Osteoporos Int.* Jun 19 2017. PMID 28631236
20. U.S. Preventive Services Task Force (USPSTF). Osteoporosis: Screening 2011;

http://www.uspreventiveservicestaskforce.org/uspstf10/osteoporosis/osteosum.htm. Accessed November 20, 2017.
21. Centers for Medicare & Medicaid Services. National Coverage Determination (NCD) for Collagen Crosslinks, any
Method (190.19). 2002; https://www.cms.gov/medicare-coverage-database/details/ncddetails.aspx?NCDId=96&ncdver=1&DocID=190.19&SearchType=Advanced&bc=IAAAABAAAAAA&. Accessed
November 30, 2017.
22. Rules and Regulations: Medicare National Coverage Decision for Collagen Crosslinks, Any Method Other Names/Abbreviations. *Federal Register.* 2001;66(226):58843-58844.