

Corporate Medical Policy

Bone Turnover Markers for the Diagnosis and Management of Osteoporosis

File Name: bone_turnover_markers_for_the_diagnosis_and_management_of_osteoporosis
Origination: 12/2000
Last CAP Review: 3/2012
Next CAP Review: 3/2013
Last Review: 3/2012

Description of Procedure or Service

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

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 osteoblasts and osteoclasts 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. Bone-turnover markers have been extensively researched in diseases associated with markedly high levels of bone turnover, such as Paget's disease, primary hyperparathyroidism, glucocorticoid-induced osteoporosis, or renal osteodystrophy. There has been recent interest in the use of bone-turnover markers to evaluate age-related osteoporosis, a disease characterized by slow, prolonged bone loss, resulting in an increased risk of fractures at the hip, spine, or wrist. Currently, fracture risk is based primarily 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. (Refer to separate policy entitled "Bone Mineral Density Studies".)

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.

Collagen cross-links are generally reliable markers of bone resorption because they are stable in serum and urine. These marker links bind 3 molecules of collagen in the bone and are released from the bone matrix after resorption, either free or bound to the N- or C- telopeptide of collagen.

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Collagen cross-links may be detected using either HPLC (Pyr and D-Pyr) or immunoassays (Pyr, D-Pyr, CTx, NTx). In addition to collagen cross-links, alkaline phosphatase (ALP) is a commonly used marker due to its ease of measurement; however, it lacks sensitivity and specificity for detecting osteoporosis since only about half of the ALP activity is derived from bone. Bone-specific alkaline phosphatase (B-ALP) is a better marker of bone formation than ALP. Serum osteocalcin is a small noncollagenous protein that is a product of osteoblasts and thus increased levels reflect bone formation. Tartrate-resistant acid phosphatase (TRAP) is produced by osteoclasts; it is thought to be active in bone matrix degradation.

Several tests for bone turnover markers have been cleared by the U.S. Food and Drug Administration (FDA) using the 510(k) process.

Collagen cross-links tests:

1995: Pyrilinks test (Metra Biosystems) measures collagen Type 1 crosslink, pyridinium
1996: Osteomark test (Ostex International) measures crosslinked N-telopeptides of type 1 collagen (NTx)
1999: Serum Crosslaps One Step Elisa test measures hydroxyproline

Other bone turnover tests:

2000: Ostase (Beckman Coulter) measures bone-specific alkaline phosphatase (B-ALP)
2001: N-MID Osteocalcin One Step ELISA (Osteometer Bio Tech) measures osteocalcin (OC)

Related Guideline:

Screening for Vertebral Fracture with Dual X-ray Absorptiometry (DEXA)

Related Policy:

Bone Mineral Density Studies

This policy does not address the use of bone turnover markers with conditions such as hyperparathyroidism and renal osteodystrophy.

****Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.*

Policy

Bone turnover markers for diagnosis and management of osteoporosis are considered investigational. BCBSNC does not provide coverage for investigational services or procedures.

Benefits Application

This medical policy relates only to the services or supplies described herein, Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

When Measurement of Bone Turnover Markers is covered

Not applicable.

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When Measurement of Bone Turnover Markers is not covered

Measurement of bone turnover markers is considered investigational in the diagnosis and management of osteoporosis. BCBSNC does not cover investigational services.

Policy Guidelines

The literature suggests that bone turnover marker levels may be independently associated with osteoporosis and fracture risk in groups of individuals. However, there is insufficient evidence that current methods for measuring 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 or improves health outcomes such as reducing fracture rates.

Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable code: 82523, 83937, 84080

There is no specific CPT code for bone-specific alkaline phosphatase (ALK), but several laboratory websites identify CPT 84080 for the Ostase test.

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources

From policy entitled: Collagen Cross Links as Markers of Bone Turnover

BCBSA Medical Policy Reference Manual, 7/16/99

National Institutes of Health, Consensus Statement 111. www.odp.od.nih.gov/consensus/cons/111/111_statement.htm

Specialty Matched Consultant Advisory Panel - 9/2001

BCBSA Medical Policy Reference Manual, 10/8/2002; 2.04.15

Specialty Matched Consultant Advisory Panel - 8/2003

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.04.15, 11/9/04

Specialty Matched Consultant Advisory Panel - 8/25/05

Bone Turnover Markers for the Diagnosis and Management of Osteoporosis

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.04.15, 8/17/05.

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.04.15, 4/25/06.

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.04.15, 10/10/06.

North American Menopause Society. Management of osteoporosis in postmenopausal women: 2006 position statement of The North American Menopause Society. *Menopause*. 2006;13(3):340-367.

American College of Obstetricians and Gynecologists. (2004, January) ACOG Practice Bulletin Number 50, Clinical Management Guidelines for Obstetrician-Gynecologists "Osteoporosis".

Specialty Matched Consultant Advisory Panel - 8/29/07

Policy retitled: Bone Turnover Markers for Diagnosis and Management of Osteoporosis

National Osteoporosis Foundation. Clinician's guide to prevention and treatment of osteoporosis. Retrieved on October 29, 2009 from http://www.nof.org/professionals/NOF_Clinicians_Guide.pdf

Bergmann P, Body JJ, Boonen S et al. Evidence-based guidelines for the use of biochemical markers of bone turnover in the selection and monitoring of bisphosphonate treatment in osteoporosis: a consensus document of the Belgian Bone Club. *Int J Clin Pract* 2008; 63(1):19-26.

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.04.15, 5/8/08.

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.04.15, 9/10/09.

Specialty Matched Consultant Advisory Panel – 2/2010

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.04.15, 9/16/10.

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.04.15, 9/1/11

Specialty Matched Consultant Advisory Panel – 3/21/12

Policy Implementation/Update Information

From policy entitled: Collagen Cross Links as Markers of Bone Turnover

12/00	Original policy issued.
4/01	Typo corrected above. Changed date of origination from 12/2002 to 12/2000.
9/01	Specialty Matched Consultant Advisory Panel review. No change in criteria.
8/03	Specialty Matched Consultant Advisory Panel review 8/4/03. Benefits Application section revised. Statement added to Billing/Coding section indicating that medical records may be ordered.
3/04	Billing/Coding section updated for consistency.
9/1/05	Added information to "Policy Guidelines" regarding investigational rationale. Policy key words and reference sources added. Specialty Matched Consultant Advisory Panel review - 8/25/05.
9/24/07	Reference sources added. Specialty Matched Consultant Advisory Panel review - 8/29/07. No change in criteria. (pmo)

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Policy retitled: Bone Turnover Markers for Diagnosis and Management of Osteoporosis

- 4/27/10 Policy retitled to Bone Turnover Markers for Diagnosis and Management of Osteoporosis from Collagen Cross Links as Markers of Bone Turnover. Specialty Matched Consultant Advisory Panel review 2/11/2010. Policy revisions include bone turnover markers other than collagen cross links. Bone turnover markers remain investigational in the diagnosis and management of osteoporosis. Reference sources added. Notice given 4/27/2010. Policy effective date 8/3/2010. (btw)
- 3/29/11 The following statement was added to the Billing/Coding section: *There is no specific CPT code for bone-specific alkaline phosphatase (ALK), but several laboratory websites identify CPT 84080 for the Ostase test.* (adn)
- 4/17/12 Related policy and related guideline added. Added “bone turnover marker levels may be independently associated with osteoporosis and fracture risk in groups of individuals” and added revision “In addition, there is insufficient evidence from controlled studies that bone turnover marker measurement improves adherence to treatment or improves health outcomes such as reducing fracture rates” in Policy Guidelines section. No change to policy intent. Specialty Matched Consultant Advisory Panel review 3/21/12 (sk)

Medical policy is not an authorization, certification, explanation of benefits or a contract. Benefits and eligibility are determined before medical guidelines and payment guidelines are applied. Benefits are determined by the group contract and subscriber certificate that is in effect at the time services are rendered. This document is solely provided for informational purposes only and is based on research of current medical literature and review of common medical practices in the treatment and diagnosis of disease. Medical practices and knowledge are constantly changing and BCBSNC reserves the right to review and revise its medical policies periodically.