ND

# Medical Policies

Print

**Policy Number:** L-5015
**Policy Name:** Bone Turnover Markers for Diagnosis and Management of Osteoporosis and Diseases Associated With High Bone Turnover
**Policy Type:** Medical **Policy Subtype:** Laboratory
**Effective Date:** 09-15-2025

## Description

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 proc esses 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.

## Policy Application

All claims submitted under this policy's section will be processed according to the policy effective date and associated revision effective dates in effect on the date of processing, regardless of service date.

## Criteria

Coverage is subject to the specific terms of the member's benefit plan.

Measurement of bone turnover markers is considered investigational to determine fracture risk in individuals with osteoporosis or with age-related risk factors for osteoporosis.

Measurement of bone turnover markers is considered investigational to determine response to therapy in individuals who are being treated for osteoporosis.

Measurement of bone turnover markers is considered investigational 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.

### Procedure Codes

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|---|---|---|
| 82523 | 83937 | 84080 |

### Summary of Evidence

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,

procollagen type 1 N-terminal propeptide and cross-linked C-telopeptide) 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 of 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 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 (e.g., 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 individual management or improve health outcomes. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

# Professional Statements and Societal Positions Guidelines

## Practice Guidelines and Position Statements

### The North American Menopause Society

In 2021, the North American Menopause Society (NAMS) issued a position statement on the management of osteoporosis in postmenopausal women. [19,] Per the NAMS:

- 'Bone turnover markers cannot diagnose osteoporosis and have varying ability to predict fracture risk in clinical trials. Bone turnover markers have been used primarily in clinical trials to demonstrate group responses to treatment. Although used by some osteoporosis specialists, the routine use of bone turnover markers in the evaluation of individuals with osteoporosis is not recommended.'
- 'Although changes in bone turnover markers are used by some specialists to assess adherence and effectiveness of therapy, routine use of bone markers is not recommended.'

### The Endocrine Society

The 2019 guidelines from the Endocrine Society recommend that in postmenopausal women with a low BMD and at high-risk of fractures who are being treated for osteoporosis, monitoring should be conducted by dual-energy X-ray absorptiometry at the spine and hip every one (1) to three (3) years. The Society considers measuring bone turnover markers (serum CTX for antiresorptive therapy or P1NP for bone anabolic therapy) as an alternative way of monitoring for poor response or non-adherence to therapy. The society notes that there is uncertainty over what constitutes an optimal response to treatment, but some experts suggest that a meaningful change is approximately 40 percent when compared from before to three (3) to six (6) months after starting treatment.

## The American Association of Clinical Endocrinologists and the American College of Endocrinology

The 2016 guidelines from the American Association of Clinical Endocrinologists and the American College of Endocrinology (AACE/ACE) gave a Grade B recommendation to consider using bone turnover markers for assessing individual compliance and therapy efficacy. AACE/ACE reviewed evidence that markers respond quickly to therapeutic intervention, and changes in markers have been associated with bone response to therapy and fracture risk reduction (level 1 RCT) supporting their use in clinical trials. However, the guidelines note that use in clinical practice is 'limited by high in vivo and assay variability, poor predictive ability in individual individuals, and lack of evidence-based thresholds for clinical decision-making.'

## National Osteoporosis Foundation

In 2014, the National Osteoporosis Foundation published its guidelines on the prevention and treatment of osteoporosis to prevent fractures. Regarding biochemical markers of bone turnover, the guidelines stated:

'Biochemical markers of bone turnover **can**

- aid in risk assessment and serve as an additional monitoring tool when treatment is initiated
- be repeated to determine if treatment is producing expected effect. '

'Biochemical markers of bone turnover **may**

- Predict rapidity of bone loss in untreated individuals
- Predict extent of fracture risk reduction when repeated after three to six (3 to 6) months of treatment with FDA [Food and Drug Administration]-approved therapies
- Predict magnitude of BMD [bone mineral density] increases with FDA-approved therapies
- Help determine adequacy of individual compliance and persistence with osteoporosis therapy
- Help determine duration of 'drug holiday' and when and if medication should be restarted (Data are quite limited to support this use, but studies are underway.)'

### North American Menopause Society

The North American Menopause Society (2010) provided a position statement on the management of osteoporosis in postmenopausal women. The statement included a recommendation that 'the routine use of biochemical markers of bone turnover in clinical practice is not generally recommended.'

### International Society for Clinical Densitometry

In 2011, a joint statement by the International Society for Clinical Densitometry and the International Osteoporosis Foundation on the Fracture Risk Assessment Model (FRAX) fracture risk prediction algorithms indicated that the 'Evidence that bone turnover markers predict fracture risk independent of BMD [bone mineral density] is inconclusive. Therefore, bone turnover markers are not included as risk factors in FRAX.'

### National Bone Health Alliance

Recommendations from the National Bone Health Alliance (2017) considered N-terminal propeptide of type I procollagen (PINP) and C-terminal telopeptide of type I collagen (CTX-I) as 'international reference standards' for bone formation and resorption, respectively. Among the conditions associated with increased bone turnover were primary hyperparathyroidism, vitamin D deficiency, immobility, fracture, and Paget disease; the guidelines also considered diseases associated with low or disassociated bone turnover. The National Bone Health Alliance advised that caregivers control for factors such as food intake, time of sample collection, and handling procedure (i.e., CTX-I assays should be conducted in a fasting state); and that those interpreting the results of bone turnover marker tests be familiar with how uncontrollable factors (i.e. age, comorbidities, medications) may interact with an individual's CTX-I or PINP levels.

### U.S. Preventive Services Task Force Recommendations

The U.S. Preventive Services Task Force (2018) recommended screening for osteoporosis with bone measurement testing to prevent osteoporotic fractures in women 65 years and older. The Task Force recommended screening for osteoporosis with bone measurement testing to prevent osteoporotic fractures in postmenopausal women younger than 65 years who are at increased risk of osteoporosis, as determined by a formal clinical risk assessment tool. The recommendations on osteoporosis screening addressed dual-energy x-ray absorptiometry testing but did not mention bone turnover markers.

## Diagnosis Codes

### Osteoporosis

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|---|---|---|---|---|---|---|
| M80.00XA | M80.00XD | M80.00XG | M80.00XK | M80.00XP | M80.00XS | M80.0AXD |
| M80.0AXG | M80.0AXK | M80.0AXP | M80.0AXS | M80.011A | M80.011G | M80.011K |

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|---|---|---|---|---|---|---|
| M80.011P | M80.011S | M80.012A | M80.012D | M80.012K | M80.012P | M80.012S |
| M80.019A | M80.019D | M80.019G | M80.019P | M80.019S | M80.021A | M80.021D |
| M80.021G | M80.021K | M80.021S | M80.022A | M80.022D | M80.022G | M80.022K |
| M80.022P | M80.029A | M80.029D | M80.029G | M80.029K | M80.029P | M80.029S |
| M80.031D | M80.031G | M80.031K | M80.031P | M80.031S | M80.032A | M80.032G |
| M80.032K | M80.032P | M80.032S | M80.039A | M80.039D | M80.039K | M80.039P |
| M80.039S | M80.041A | M80.041D | M80.041G | M80.041P | M80.041S | M80.042A |
| M80.042D | M80.042G | M80.042K | M80.042S | M80.049A | M80.049D | M80.049G |
| M80.049K | M80.049P | M80.051A | M80.051D | M80.051G | M80.051K | M80.051P |
| M80.051S | M80.052D | M80.052G | M80.052P | M80.052S | M80.059A | M80.059G |
| M80.059K | M80.059P | M80.059S | M80.061A | M80.061D | M80.061K | M80.061P |
| M80.061S | M80.062A | M80.062D | M80.062G | M80.062P | M80.062S | M80.069A |
| M80.069D | M80.069G | M80.069K | M80.069S | M80.071A | M80.071D | M80.071G |
| M80.071K | M80.071P | M80.072A | M80.072D | M80.072G | M80.072K | M80.072P |
| M80.072S | M80.079D | M80.079G | M80.079K | M80.079P | M80.079S | M80.08XA |
| M80.08XG | M80.08XK | M80.08XP | M80.08XS | M80.1052K | M80.80XA | M80.80XD |
| M80.80XK | M80.80XP | M80.80XS | M80.811A | M80.811D | M80.811G | M80.811P |
| M80.811S | M80.812A | M80.812D | M80.812G | M80.812K | M80.812S | M80.819A |
| M80.819D | M80.819G | M80.819K | M80.819P | M80.821A | M80.821D | M80.821G |
| M80.821K | M80.821P | M80.821S | M80.822D | M80.822G | M80.822K | M80.822P |
| M80.822S | M80.829A | M80.829G | M80.829K | M80.829P | M80.829S | M80.831A |
| M80.831D | M80.831K | M80.831P | M80.831S | M80.832A | M80.832D | M80.832G |
| M80.832P | M80.832S | M80.839A | M80.839D | M80.839G | M80.839K | M80.839S |
| M80.841A | M80.841D | M80.841G | M80.841K | M80.841P | M80.842A | M80.842D |
| M80.842G | M80.842K | M80.842P | M80.842S | M80.849D | M80.849G | M80.849K |
| M80.849P | M80.849S | M80.851A | M80.851G | M80.851K | M80.851P | M80.851S |
| M80.852A | M80.852D | M80.852K | M80.852P | M80.852S | M80.859A | M80.859D |
| M80.859G | M80.859P | M80.859S | M80.861A | M80.861D | M80.861G | M80.861K |

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| M80.861S | M80.862A | M80.862D | M80.862G | M80.862K | M80.862P | M80.869A |
| M80.869D | M80.869G | M80.869K | M80.869P | M80.869S | M80.871D | M80.871G |
| M80.871K | M80.871P | M80.871S | M80.872A | M80.872G | M80.872K | M80.872P |
| M80.872S | M80.879A | M80.879D | M80.879K | M80.879P | M80.879S | M80.88XA |
| M80.88XD | M80.88XG | M80.88XP | M80.88XS | M80.8AXA | M80.8AXD | M80.8AXG |
| M80.8AXK | M80.8AXS | M81.0 | M81.6 | M81.8 | Z13.820 | Z82.62 |

### Paget's Disease

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|---|---|---|---|---|---|---|
| M88.0 | M88.1 | M88.811 | M88.812 | M88.819 | M88.821 | M88.822 |
| M88.829 | M88.831 | M88.832 | M88.839 | M88.841 | M88.842 | M88.849 |
| M88.851 | M88.852 | M88.859 | M88.861 | M88.862 | M88.869 | M88.871 |
| M88.872 | M88.879 | M88.88 | M88.89 | M88.9 | | |

### Primary Hyperparathyroid & Renal Osteodystrophy

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|---|---|
| E21.0 | N25.0 |

### CURRENT CODING

#### CPT:

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| 82523 | COLLAGEN CROSS LINKS ANY METHOD | Commercial |
| 83937 | ASSAY OF OSTEOCALCIN | Commercial |
| 84080 | ASSAY OF PHOSPHATASE ALKALINE ISOENZYMES | Commercial |
| 82523 | COLLAGEN CROSS LINKS ANY METHOD | Medicaid Expansion |
| 83937 | ASSAY OF OSTEOCALCIN | Medicaid Expansion |
| 84080 | ASSAY OF PHOSPHATASE ALKALINE ISOENZYMES | Medicaid Expansion |

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## L-5015


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## ND Committee Review

Internal Medical Policy Committee 7-22-2020 Adopted policy

Internal Medical Policy Committee 7-22-2021 Annual Review

Internal Medical Policy Committee 7-21-2022 Annual Review - no changes in criteria

Internal Medical Policy Committee 7-26-2023 Annual Review - no changes in criteria

Internal Medical Policy Committee 9-12-2023 Revision - Effective November 06, 2023

- *Added* diagnosis codes M80.0AXA; M80.0AXD; M80.0AXG; M80.0AXK; M80.0AXP; M80.0AXS; M80.8AXA; M80.8AXD; M80.8AXG; M80.8AXK; M80.8AXP; and M80.8AXS; and
- *Added* Summary of Evidence; and
- *Added* statement regarding The North American Menopause Society under Professional Statements and Societal Positions Guidelines.

Internal Medical Policy Committee 9-17-2024 Coding update - Effective November 04, 2024

- *Removed* diagnosis codes M80.052K and M8.81; and
- *Added* M80.1052K and M88.1

## Disclaimer

*Current medical policy is to be used in determining a Member's contract benefits on the date that services are rendered. Contract language, including definitions and specific inclusions/exclusions, as well as state and federal law, must be considered in determining eligibility for coverage. Members must consult their applicable benefit plans or contact a Member Services representative for specific coverage information. Likewise, medical policy, which addresses the issue(s) in any specific case, should be considered before utilizing medical opinion in adjudication. Medical technology is constantly evolving, and the Company reserves the right to review and update medical policy periodically.*