



Bisphosphonate Drug List Selection

Proven fracture risk reduction, long-term safety, and an internal analysis of actual fracture rates within our treated population were the measures used during our Pharmacy & Therapeutics Process to select bisphosphonates for the Drug List.

Provider information

Bisphosphonates are most commonly used for osteoporosis prevention and treatment. We feel it's important that our Drug List offers a range of bisphosphonate medications that have been selected for their proven ability to minimize the potential for painful, costly fractures. Although there are other treatment options for osteoporosis, the focus of this document is evaluation of bisphosphonate therapies.

Clinical review

Our clinical review, conducted during 1st quarter 2011, focused on efficacy and safety of bisphosphonates for secondary prevention of clinical fractures in postmenopausal osteoporosis (PMO). We reviewed data for all indications, revealing a lack of high quality evidence supporting use in primary prevention of PMO and for other FDA-approved indications, such as glucocorticoid-induced osteoporosis, male osteoporosis and Paget's disease.

The goal of osteoporosis therapy is clinical fracture prevention (symptomatic fractures resulting in pain and/or disability), particularly hip fracture due to high morbidity and mortality rates.¹ Studies evaluating intermediate markers like bone mineral density (BMD) that poorly correlate with fracture risk reduction were not included in the review; nor were low quality trials unless adequate supplementary data were provided.

Our review did not find quality head-to-head trials evaluating fracture risk reduction. Pivotal efficacy data for the bisphosphonates were confined to studies evaluating daily dosing regimens – not the weekly or monthly regimens more commonly used in clinical practice. Other trial limitations such as differing study designs and patient populations, and using mixed definitions of clinical measures, made bisphosphonate comparisons challenging.

Alendronate has the strongest data supporting efficacy, the most long-term safety information, a broad range of indications and convenient dosing.



Summary of evidence for bisphosphonates in PMO secondary fracture prevention

Endpoint	Alendronate/ Fosamax ^{2-3, 5, 7-8, 11-13}	Actonel/Atelvia ^{† 8, 10-11, 13}	Boniva ^{6, 8, 11, 13}	Reclast ^{4, 8-9, 11, 13}
Efficacy*				
Decreased vertebral fractures	✓	✓	✓	✓
Decreased hip and other fractures	✓	✓		✓
Safety				
Long-term safety data [†]	✓ (10 yrs; n=247)	✓ (7 yrs; n=164)	✓ (3 yrs; n=2,946)	✓ (2 yrs; n=2,127)
Risk of jaw osteonecrosis	✓	✓	✓	✓
Serious atrial fibrillation				✓
Clinical Attributes				
Dosage form	Oral	Oral	Oral and Injectable	Intravenous infusion
Dosing schedule	Weekly	Weekly or Monthly	Monthly	Yearly

✓ = Data available

* Fracture results generated from patient populations with confirmed osteoporosis; however, level of fracture risk varies across trials.

† The number of patients exposed for extended durations in clinical trials is limited.

‡ The efficacy of Atelvia (delayed-release risedronate) is based on the anti-fracture efficacy data of Actonel.

There has been increased concern about the possible association of atypical low-energy fractures and long-term bisphosphonate use.¹⁴ Currently there is insufficient evidence to determine if atypical fractures are a result of bisphosphonate use or advanced osteoporosis.¹⁵⁻²¹ Conservatively, in 2010 the Food and Drug Administration required a warning be added to product labeling discussing the potential risk for atypical fractures with bisphosphonate use.²²

Based on critical appraisal of the clinical data and input from the Endocrinology Advisory Panel, the Clinical Review Committee (CRC) determined that alendronate-containing products should be considered of highest clinical value. Within the bisphosphonate class, alendronate has the strongest data supporting efficacy, the most long-term safety information, a broad range of indications and convenient dosing. The committee also recognized the importance of compliance and adequate calcium and vitamin D intake to ensure the greatest benefit from therapy.

Value assessment

A published analysis of 45,939 oral bisphosphonate users with osteoporosis revealed the following:²³

- Alendronate/Fosamax use was associated with the lowest fracture rate over three years.
- Total health care costs were similar among the different bisphosphonate groups.
- Alendronate/Fosamax and Actonel users were the most adherent over 1 to 2 years. At three years, adherence was similar.
- Adherence was not significantly improved for once monthly versus once weekly regimens.

External pharmacoeconomic specialists, who are not company employees, agreed with the conclusions drawn from these analyses. Atelvia was not available at the time these analyses were conducted.

The least costly bisphosphonates for Anthem Blue Cross and Blue Shield include:

- Generic alendronate
- Actonel
- Actonel with Calcium
- Fosamax
- Fosamax Plus D



Tier placement

Final placement of the ten bisphosphonate products on our Drug List was determined based on the clinical review conclusions, followed by considerations from the value assessment, in order to make evidence-based, informed tier placement decisions. The lower, moderate and higher tiers of our bisphosphonate coverage are outlined below.

Bisphosphonate coverage on the Drug List

Lower member cost	Moderate member cost	Higher member cost
<ul style="list-style-type: none"> · Alendronate tablets 	<ul style="list-style-type: none"> · Actonel tablets · Actonel with calcium tablets · Fosamax oral solution · Fosamax Plus D tablets 	<ul style="list-style-type: none"> · Atelvia tablets · Boniva injection · Boniva tablets · Fosamax tablets · Reclast injection

To learn more about our Pharmacy & Therapeutics Process, visit anthem.com and select “Providers” on the bottom right. On the Provider landing page, under Formulary click “Rx Search.” Click the “Drug List Selection” tab, then scroll down and select the “How is our Drug List selection process unique?” link.

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