

**Regence BlueCross BlueShield of Oregon • Regence BlueShield  
Regence BlueCross BlueShield of Utah • Regence BlueShield of Idaho  
Independent licensees of the Blue Cross and Blue Shield Association**

**Medication Policy Manual**

**Policy No:** dru155

**Topic:** Actonel<sup>®</sup>, risedronate-Containing  
Medications (Actonel, Actonel with Calcium)

**Date of Origin:** July 18, 2008

**Revised/Effective Date:** July 17, 2009

**Next Review Date:** July, 2010

**IMPORTANT REMINDER**

This Medical Policy has been developed through consideration of medical necessity, generally accepted standards of medical practice, and review of medical literature and government approval status.

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

The purpose of medical policy is to provide a guide to coverage. Medical Policy is not intended to dictate to providers how to practice medicine. Providers are expected to exercise their medical judgment in providing the most appropriate care.

**Description**

Risedronate (Actonel<sup>®</sup>) is a bisphosphonate, a medication used to treat or prevent osteoporosis (bone loss).

## **Policy/Criteria**

- I.** Most contracts require prior authorization approval of risedronate prior to coverage. Risedronate may be considered medically necessary when a generic oral bisphosphonate (such as alendronate) has not been tolerated or is contraindicated.
  
- II.** Administration and Authorization Period
  - A.** Regence considers risedronate to be a self-administered medication.
  
  - B.** Authorization may be reviewed at least annually to confirm that current medical necessity criteria are met.

## **Position Statement**

### *Summary*

- Osteoporosis is characterized by low bone mass and structural deterioration, leading to bone fragility and an increased risk of fractures of the hip, spine and wrist. <sup>[7]</sup> The objective of treatment of osteoporosis is to reduce the incidence of fractures.
  
- Generic alendronate provides the best value for the prevention and treatment of osteoporosis.
  
- There is no reliable evidence that any one bisphosphonate is more effective than another for fracture prevention.
  
- There is no reliable evidence that any one bisphosphonate is safer or better tolerated than another.
  
- There is no reliable comparative evidence to differentiate harms.
  
- All oral bisphosphonates carry some degree of risk of gastric irritation (oral formulations more so than injectables).

### *Clinical Efficacy*

- There is evidence that alendronate (Fosamax<sup>®</sup>), ibandronate (Boniva<sup>®</sup>), risedronate (Actonel), and zoledronic acid (Reclast<sup>®</sup>) decrease the risk of fracture.

- There are clinical trials of at least three years that show that alendronate (Fosamax), risedronate (Actonel), ibandronate (Boniva), and zoledronic acid (Reclast) each reduce the risk of fracture in patients with osteoporosis. Fourteen to 23 patients need to be treated for 3 years to prevent one vertebral fracture. This is similar between the bisphosphonate medications.
- All fracture data for oral bisphosphonates are based on the daily dosage form only. There are no fracture data for the weekly or monthly products or other modified dosing regimens.
- Bisphosphonates increase bone mineral density (BMD). Increased BMD correlates to a decrease in the risk of fractures.
- There is no evidence demonstrating superiority of any drug over another for the prevention of fractures. None of the head-to-head comparisons between agents had large enough sample sizes to detect differences. <sup>[4]</sup>

### *Safety*

- Side effects are similar for all oral bisphosphonate medications and include gastrointestinal problems such as difficulty swallowing, gastric ulcer and inflammation of the esophagus. <sup>[4,17]</sup>
- Based on the FDA safety review regarding the possibility of an association between atrial fibrillation and bisphosphonate therapy the FDA states that healthcare professionals should not alter their prescribing patterns for bisphosphonates and patients should not stop taking their bisphosphonate medication. <sup>[18]</sup>
- All of the bisphosphonates have extremely long presence in bone - years for oral, decades for IV zoledronic acid. The long term toxicity is unknown.
- Injectable products are options for patients with contraindications to the oral formulations, and are associated with fewer GI adverse events.
- There have been reports of osteonecrosis of the jaw (particularly following intravenous bisphosphonate treatment for patients with cancer). The level of risk for osteonecrosis in patients being treated for osteoporosis with bisphosphonates is not known, but appears extremely small for at least up to 5 years. <sup>[17]</sup>

## References

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10. Fosamax<sup>®</sup> (alendronate sodium) Prescribing Information. February 2008. Merck & Co., Inc. Whitehouse Station, NJ.
11. Boniva<sup>®</sup> (ibandronate sodium) Tablets Prescribing Information. November 2008. Roche Laboratories Inc., Nutley, NJ.
12. Forteo<sup>®</sup> teriparatide (rDNA origin) injection Prescribing Information. June 2008. Eli Lilly and Company - Indianapolis, IN
13. Evista<sup>®</sup> (raloxifene hydrochloride) Tablets Prescribing Information. October 2008. Eli Lilly and Company - Indianapolis, IN.
14. Reclast<sup>®</sup> (zoledronic acid) Injection Prescribing Information. May 2009. Novartis Pharmaceuticals Corporation, East Hanover, NJ.
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18. U.S. Food and Drug Administration [page on the internet] 2008. November 12, 2008 [Update to the October 1, 2007 Early Communication about the Ongoing Safety Review of Bisphosphonates](#). Available at:  
<http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm079352.htm> accessed June 22, 2009

<b>Cross References</b>
Boniva <sup>®</sup> , ibandronate injectable dru156
Boniva <sup>®</sup> , ibandronate oral dru157
Forteo <sup>®</sup> , teriparatide dru085
Reclast <sup>®</sup> , zoledronic acid dru158

<b>Codes</b>	<b>Number</b>	<b>Description</b>
HCPCS	J1740	Injection, ibandronate sodium, 1 mg (Boniva 3 MG/3ML KIT)
HCPCS	J3488	Injection, zoledronic acid (Reclast), 1 mg (Reclast 5 MG/100ML SOLN)

**Appendix 1:** Indications for specified osteoporosis therapy

	<b>Alendronate</b>	<b>Risedronate</b>	<b>Ibandronate</b>	<b>Zoledronic acid</b>
Postmenopausal Osteoporosis: Prevention	✓	✓	✓	✓
Postmenopausal Osteoporosis: Treatment	✓	✓	✓	✓
Glucocorticoid-Induced Osteoporosis: Prevention	—	✓	—	✓
Glucocorticoid-Induced Osteoporosis: Treatment	✓	✓	—	✓
Osteoporosis in Men	✓	✓	—	✓
Paget's disease	✓	✓	—	✓

## Appendix 2: Dosing regimens of bisphosphonate therapy

Drug Products	Usual Dose/Route	Administration Considerations
alendronate (Fosamax <sup>®</sup> ) <sup>[10]</sup>	<ul style="list-style-type: none"> <li>• 5 mg p.o. daily</li> <li>• 10 mg p.o. daily</li> <li>• 35 mg p.o. weekly</li> <li>• 70 mg p.o. weekly</li> <li>• 40mg p.o. daily x 6mo</li> </ul>	<ul style="list-style-type: none"> <li>• Taken 30 minutes before first food, beverage, or medication</li> <li>• Swallowed with a full glass of water (180 to 240 mL).</li> <li>• Followed by at least 60 mL (one-fourth cup) of water</li> <li>• Do not lie down for at least 30 minutes and until after their first food of the day</li> </ul>
ibandronate (Boniva <sup>®</sup> ) <sup>[11]</sup>	<ul style="list-style-type: none"> <li>• 2.5 mg p.o. daily</li> <li>• 150 mg p.o. monthly</li> <li>• 3 mg IV every 3 months</li> </ul>	<ul style="list-style-type: none"> <li>• Taken 60 minutes before the first food or drink (other than water)</li> <li>• Swallowed whole with a full glass of plain water (180 to 240 mL; 6 to 8 oz)</li> <li>• Do not lie down for 60 minutes</li> </ul>
risedronate (Actonel <sup>®</sup> ) <sup>[9]</sup>	<ul style="list-style-type: none"> <li>• 5 mg p.o. daily</li> <li>• 35 mg p.o. weekly</li> <li>• 30 mg p.o. daily x 2mo (Paget's)</li> <li>• 75 mg p.o. two consecutive days/month</li> <li>• 150mg p.o. monthly</li> </ul>	<ul style="list-style-type: none"> <li>• Taken 30 minutes before the first food or drink of the day other than water</li> <li>• Full glass of plain water (6 to 8 oz).</li> <li>• Do not lie down for 30 minutes</li> </ul>
zoledronic acid injectable (Reclast <sup>®</sup> ) <sup>[14]</sup>	5 mg IV once annually	Given over no less than 15 minutes