

**FAST FACTS AND CONCEPTS #113**  
**BISPHOSPHONATES FOR BONE PAIN****Elizabeth Weinstein and Robert Arnold MD****Background**

Bisphosphonates are used for the treatment or prophylaxis of cancer-related bone complications, including pain. The mechanism of action is thought to be related to inhibition of bone resorption. All bisphosphonates inhibit osteoclast activity and some also inhibit the maturation of mononuclear precursors into active osteoclasts. In the United States, two preparations are used: zoledronic acid and pamidronate.

**Analgesic Therapy**

Breast cancer and multiple myeloma have been found to be the most responsive tumors to bisphosphonates. Pain relief has been shown to a lesser degree in lung, GI and prostate carcinomas. Standard starting doses include: zoledronic acid 4 mg IV over 15 minutes and pamidronate 90mg IV administered over 2 hours. 50-70% of patients achieve a 30% reduction in pain within a week. The average duration of pain relief is 12 weeks after a single 90 mg infusion of pamidronate. If analgesia is not achieved within a week, the patient can be retreated. Analgesic effect is related both to the dose per week and the total dose per infusion for pamidronate. Typically patients are treated every 3-4 weeks to achieve maximal effect. If the pain is well controlled the dosing interval can be extended to a longer period without change in effect.

**Prophylaxis**

In patients with breast cancer or multiple myeloma, and asymptomatic bone metastases, monthly bisphosphonates decrease skeletal-related events (SRE) (pathologic fractures, spinal cord compression, surgery to bone, or radiation therapy to bone) by 30%. Bisphosphonates may also reduce the risk of SRE in prostate cancer with bone metastases. The dosages of pamidronate and zoledronic acid are the same as used in analgesic therapy. There is no evidence that these medications prevent SRE in patients without known bone involvement, however a number of clinical trials are in process.

**Toxicity**

Pamidronate and zoledronic acid have the same safety profiles. Both cause an injection site reaction and a flu-like syndrome that responds well to acetaminophen. Less common side effects include hypocalcemia and scleritis. Renal dysfunction is a side effect of long-term, high dose or short interval/frequency use of bisphosphonates; this is typically reversible with discontinuation of the drug. Bisphosphonates are contraindicated in renal failure and with patients who experience an increase in creatinine (>0.5 mg/dl over baseline or >1.0 in patients with pre-existing renal insufficiency). In moderate renal dysfunction (Cr > 3.0 mg/dl) the dose of both agents should either be reduced and/or the infusion time increased. *Fast Fact* #196 discusses bisphosphonate induced osteonecrosis of the jaw.

**Cost**

The average wholesale price for zoledronic acid 4mg is \$856; the AWP of pamidronate 90 mg is \$88. In considering the cost difference between these two drugs it is important to acknowledge the added costs to patients, physicians and medical facilities for the infusion time of pamidronate (average appointment time 2h 52 min vs. 1h 6min for zoledronic acid).

**References**

1. Hillner B, Ingle J, Chlebowski RT, et al. ASCO 2003 update on the role of bisphosphonates and bone health issues in women with breast cancer. *J Clin Oncol.* 2003; 21(21):4042-4057.
2. Pereira J. Management of Bone Pain. In: Portenoy RK, Bruera E, eds. *Topics in Palliative Care, Volume 3.* New York, NY: Oxford University Press: 1998.
3. Body JJ, Mancini I. Bisphosphonates for cancer patients: why, how and when? *Support Care Cancer.* 2002; 10(5):399-407.

4. Body JJ. Dosing regimens and main adverse events of bisphosphonates. *Semin Oncol.* 2001; 28(4, Suppl 11):49-53.
5. Strang P. Analgesic effect of bisphosphonates on bone pain in breast cancer patients: a review article. *Acta Oncol.* 1996; 35(Suppl 5):50-54.
6. Berenson JR, Rosen LS, Howell A, et al: Zoledronic acid reduces skeletal-related events in patients with osteolytic metastases. *Cancer.* 2001; 91:1191-1200.
7. DesHarnais CL, Bajwa K, Markle JP, et al. A microcosting analysis of zoledronic acid and pamidronate therapy in patients with metastatic bone disease. *Support Cancer Care.* 2001; 9:545-551.
8. Palmieri C, Fullarton J, Brown J. Comparative efficacy of bisphosphonates in metastatic breast and prostate cancer and multiple myeloma: A mixed-treatment meta-analysis. *Cancer Res* 2013; 19(24): 6863-72.
9. Wong MHF, Stockler MR, Pavlakis N. Bisphosphonates and other bone agents for breast cancer (Review). *Cochrane Database of Systematic Reviews.* 2012, Issue 2. Art. No.: CD003474.DOI: 10.1002/14651858.CD003474.pube.

**Version History:** This *Fast Fact* was originally edited by David E Weissman MD and published in April 2004. Re-copy-edited in April 2009; then copy-edited again by Dr. Sam Maiser June 2015 in which references #8 and #9 were added and incorporated into the text..

**Fast Facts and Concepts** are edited by Sean Marks MD (Medical College of Wisconsin) and associate editor Drew A Rosielle MD (University of Minnesota Medical School), with the generous support of a volunteer peer-review editorial board, and are made available online by the [Palliative Care Network of Wisconsin](#) (PCNOW); the authors of each individual *Fast Fact* are solely responsible for that *Fast Fact's* content. The full set of *Fast Facts* are available at [Palliative Care Network of Wisconsin](#) with contact information, and how to reference *Fast Facts*.

**Copyright:** All *Fast Facts and Concepts* are published under a Creative Commons Attribution-NonCommercial 4.0 International Copyright (<http://creativecommons.org/licenses/by-nc/4.0/>). *Fast Facts* can only be copied and distributed for non-commercial, educational purposes. If you adapt or distribute a *Fast Fact*, let us know!

**Disclaimer:** *Fast Facts and Concepts* provide educational information for health care professionals. This information is not medical advice. *Fast Facts* are not continually updated, and new safety information may emerge after a *Fast Fact* is published. Health care providers should always exercise their own independent clinical judgment and consult other relevant and up-to-date experts and resources. Some *Fast Facts* cite the use of a product in a dosage, for an indication, or in a manner other than that recommended in the product labeling. Accordingly, the official prescribing information should be consulted before any such product is used.