

Phase 3 / Head-to-Head Trial / 1,718 Patients Newly Diagnosed with Multiple Myeloma<sup>1</sup>

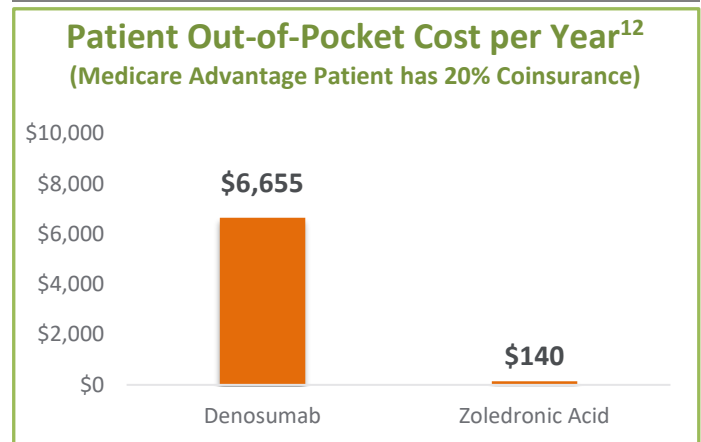
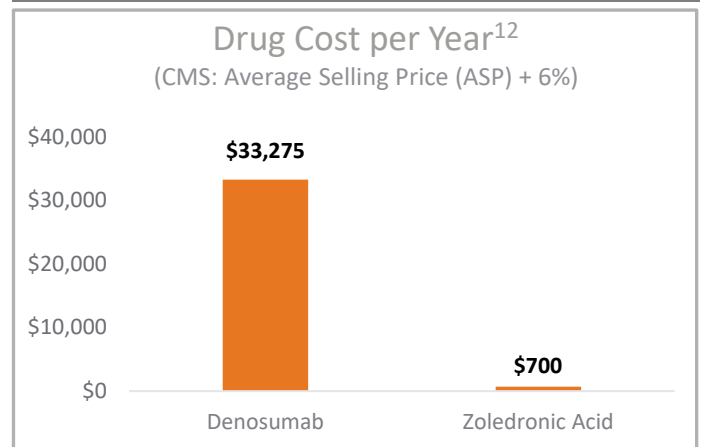
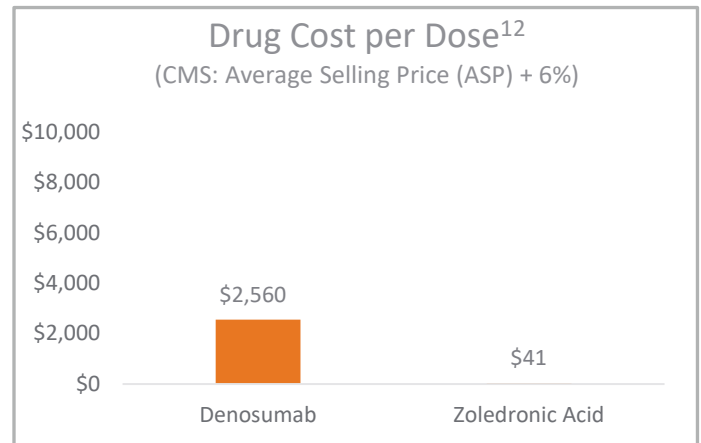
- Zoledronic acid and denosumab were clinically comparable in preventing skeletal-related events (spinal cord compression, pathological fracture, or surgery or radiotherapy to affected bone). [p-value (non-inferiority)=0.010]<sup>1</sup>
- Both zoledronic acid and denosumab had similar rates of grade 3 adverse events. Most common were, febrile neutropenia (10% vs 11%), pneumonia (8% vs 8%), thrombocytopenia (12% vs 14%).<sup>1</sup>

Phase 3 / Head-to-Head Trial / 2,049 Patients Breast Cancer Treated for Bone Metastases<sup>4</sup>

- Denosumab delayed time to first skeletal-related event by 18% compared to zoledronic acid. Overall survival (p=0.49) and disease progression (p=0.93) were similar between study groups.<sup>4</sup>
- Rates of severe adverse events (grade ≥3) and serious AEs (life threatening or requiring hospitalizations) were also similar between groups.<sup>4</sup>

Phase 3 Trials / FDA Approval & Labels Osteoporosis<sup>3,7</sup>

- Phase 3, randomized trial with 7,736 patients, show an absolute risk reduction of 7.6%, translating to 13 patients are needed to be treated with zoledronic acid to prevent 1 vertebral fracture (NNT=13)<sup>7</sup>
- Phase 3, randomized trial with 7,808 patients, show an absolute risk reduction of 7.6%, 21 patients are needed to be treated with denosumab to prevent 1 vertebral fracture (NNT=21)<sup>3</sup>



1. Raje N, Terpos E, Willenbacher W, et al. Denosumab versus zoledronic acid in bone disease treatment of newly diagnosed multiple myeloma: an international, double-blind, double-dummy, randomised, controlled, phase 3 study. *Lancet Oncol*. 2018;19(3):370-381. doi:10.1016/S1470-2045(18)30072-X.

3. Prolia [package insert]. Thousand Oaks, CA: Amgen Inc; 2020.

4. Stopeck AT, Lipton A, Body JJ, et al. Denosumab compared with zoledronic acid for the treatment of bone metastases in patients with advanced breast cancer: a randomized, double-blind study. *J Clin Oncol*. 2010;28(35):5132-5139. doi:10.1200/JCO.2010.29.7101.

7. Reclast [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; 2020.

12. CMS Average Selling Price File. <https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Part-B-Drugs/McrPartBDrugAvgSalesPrice/index>