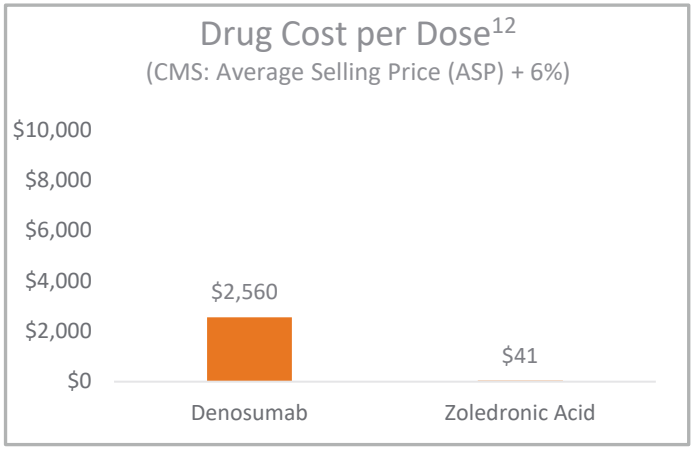
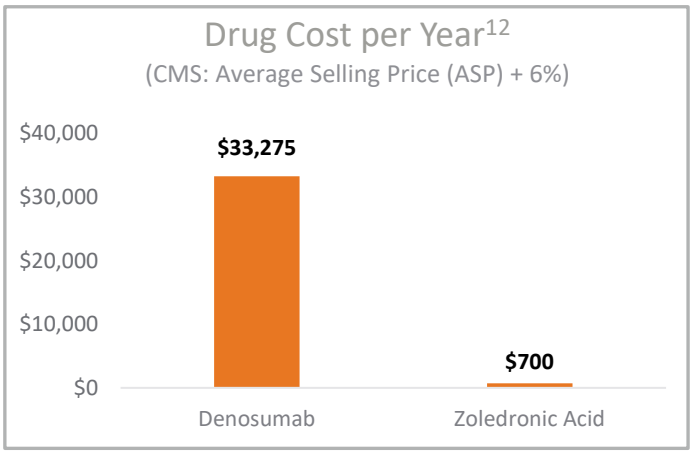
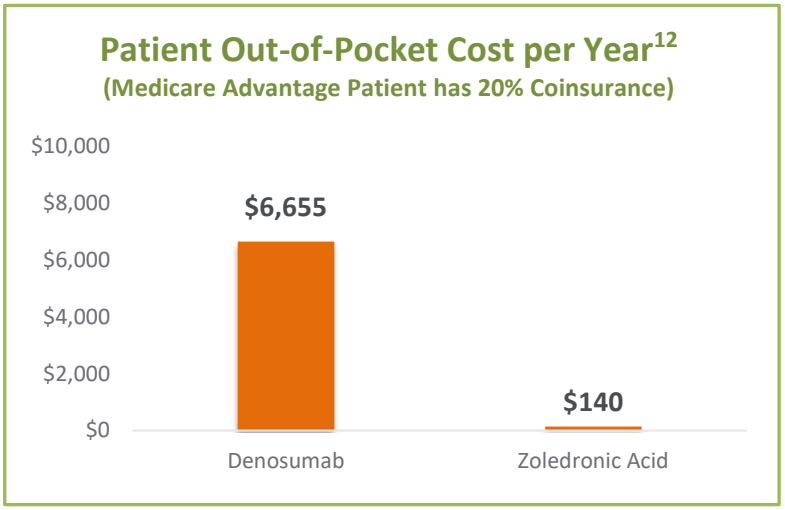
	Zoledronic Acid (ZA) / HCPCS J3489	Denosumab / HCPCS J0897
Efficacy | Clinical Trials and Outcomes		
Prevent Skeletal Related Events (SRE)	Multiple Myeloma (n=1,970)[2] • *Overall Survival* At 5.9 years, extended 6 months, HR 0.86; 95%CI (0.77-0.97) • *Progression-free survival* At 5.9 years, extended 1 month, HR 0.89; 95%CI (0.80-0.98)	Multiple Myeloma (n=1,178)[1] • *Time to first skeletal-related event* At 42 months, non-inferior vs ZA, HR 0.98; 95%CI (0.85-1.14) • *Overall Survival* At 42 months, non-inferior to ZA; HR 0.90; 95%CI (0.70-1.16)
Treat Bone Metastases/SRE	Bone Metastases in Solid Tumors (n=1,822)[4] • *Skeletal-related events (SRE)* At 2 years, 12-week dosing non-inferior to 4-week dosing in proportion of patient having 1 SRE. Risk difference 0.3%; 95% CI (-4% to ∞). Approximately 30% of patients experienced a SRE during 2 years study period.	Bone Metastases in Breast Cancer (n=1,026)[3] • *First skeletal related event* At 34 months, non-inferior to ZA delaying first SRE, HR 0.82; 95% (0.71-0.95)
Osteoporosis Vertebral Fractures	• *Vertebral Fractures (n=7,736)*[7] The reductions in vertebral fractures over three years were consistent (including new/worsening and multiple vertebral fractures), with a 3YR absolution risk reduction of 7.6% NNT (1/ARR) = 1/0.076 = 13	• *Vertebral Fractures (n=7,808)*[3] Incidence of new vertebral fractures at year 3 was 2.3% for the denosumab arm compared 7.2% in the placebo-treated arm compared The absolute risk reduction (ARR) of vertebral fractures was 4.8% at year 3. NNT (1/ARR) = 1/0.048 = 21
FDA Approved Indications & Other Uses	• treatment in patients with *multiple myeloma and metastatic bone lesions* • treatment of *bone metastases from solid tumors* • *hypercalcemia of malignancy* • Paget's disease of bone • osteoporosis • (off-label) adjuvant treatment in early breast cancer in postmenopausal females	• prevention of skeletal-related events in patients with *multiple myeloma or bone metastases from solid tumors* • *hypercalcemia of malignancy* • giant cell tumor of bone • osteoporosis • to increase one bone mass in men and women receiving hormone therapies for cancer
Safety | Adverse Drug Events (ADEs) >10%[5-8] | *see package insert for complete ADEs*		
Anemia	33%	22%
Arthralgia	21%	14%
Back pain	15%	12-21%
Cough	22%	15%
Diarrhea	24%	34%
Dyspnea	27%	21%
Edema	21%	5-17%
Fatigue	39%	45%
Headache	19%	4-13%
Hypophosphatemia	13%	32%
Nausea	46%	32%
Administrative		
Dosing	• Oncology: 4 mg every 3-4 weeks • Osteoporosis & bone loss: 4 mg every 6 months or 5 mg yearly	• Oncology: 120 mg every 4 weeks • Osteoporosis & bone loss: 60 mg every 6 months
Products Available	Reclast: Bottle | 5 mg/100mL (various) Zometa: Bottle | 4 mg/100mL; SDV | 4 MG/5 ML (various)	Prolia: PFS | 60 MG/1 ML (Amgen) Xgeva: SDV | 120 MG/1.7 ML (Amgen)







References

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.
2. Morgan GJ, Davies FE, Gregory WM, et al. First-line treatment with zoledronic acid as compared with clodronic acid in multiple myeloma (MRC Myeloma IX): a randomised controlled trial. Lancet. 2010;376(9757):1989-1999. doi:10.1016/S0140-6736(10)62051-X.
3. Prolia [package insert]. Thousand Oaks, CA: Amgen Inc; 2020. https://www.pi.amgen.com/united_states/prolia/prolia_pi.pdf
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.
5. Himelstein AL, Foster JC, Khatcheressian JL, et al. Effect of Longer-Interval vs Standard Dosing of Zoledronic Acid on Skeletal Events in Patients With Bone Metastases: A Randomized Clinical Trial. JAMA. 2017;317(1):48-58. doi:10.1001/jama.2016.
6. Xgeva [package insert]. Thousand Oaks, CA: Amgen Inc; 2019.
7. Reclast [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; 2020. https://www.novartis.us/sites/www.novartis.us/files/reclast.pdf
8. Zometa [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; 2018.
9. Zometa. Lexi-Drugs. Lexicomp. Wolters Kluwer Health, Inc. Riverwoods, IL. Available at: http://online.lexi.com. Accessed June 6, 2020.
10. Fizazi K, Carducci M, Smith M, et al. Denosumab versus zoledronic acid for treatment of bone metastases in men with castration-resistant prostate cancer: a randomised, double-blind study. Lancet. 2011;377(9768):813-822. doi:10.1016/S0140-6736(10)62344-6.
11. Camacho PM, Petak SM, Binkley N, et al. American Association of Clinical Endocrinologist/American College of Endocrinology Clinical Practice Guidelines for the Diagnosis and Treatment of Postmenopausal Osteoporosis-2020 UPDATE. Endocr Pract. 2020;26(Suppl 1):1-46. doi:10.4158/GL-2020-0524SUPPL
12. CMS Average Selling Price File. https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Part-B-Drugs/McrPartBDrugAvgSalesPrice/index