

Which factors should be considered when prescribing a bisphosphonate for frail or older adults living in long-term care?

Conclusion: Older adults living in long-term care and people with frailty are underrepresented in bisphosphonate clinical trials. In the long-term care setting, consideration should be given to their complex administration instructions, contraindications, and the delayed time-to-benefit.

The BC Provincial Academic Detailing (PAD) service's topic <u>Medications for osteoporosis: an update</u> looks at the evidence for bisphosphonates, denosumab, raloxifene, teriparatide and romosozumab. Click to <u>book a session</u> with an academic detailing pharmacist in your area. We received this question during PAD sessions: **How does the evidence apply to frail or older adults living in long-term care?**

- a) Clinical trial evidence:^{1,2} People with multimorbidity, polypharmacy and persons living in long-term care have been underrepresented in bisphosphonate clinical trials. Recently, the first bisphosphonate fracture trial in ambulatory females living in long-term care was completed (ZEST II). After 3 years, the rate of fractures was similar in the zoledronic acid and placebo groups (1.06 and 1.01 fractures per person-year, respectively).
- b) **Time-to-benefit:** ^{1,3} In clinical trials of healthy, postmenopausal females the onset of symptomatic or hip fracture risk reduction appears approximately 12 months after initiating bisphosphonate treatment. In addition to the results of the ZEST II trial, this might have relevance when prioritizing essential medications for people with limited life-expectancy.
- c) Administration:¹ Determine if a person with frailty and/or the long-term care facility has the capacity to follow the administration instructions of oral bisphosphonates intended to reduce the risk of esophagitis, esophageal ulcers, erosions, stricture, and perforation. Refer to Table 1.
- d) **Renal function:**^{1,4} Declining renal function may preclude oral and intravenous bisphosphonate use. Further, the risk of acute kidney injury with zoledronic acid requires adequate hydration, pre and post infusion. Refer to Table 1.

Table 1. Bisphosphonate contraindications & administration instructions ¹		
alendronate (Fosamax®, Fosavance®) risedronate (Actonel®, Actonel DR®)	contraindications	 abnormalities of the esophagus inability to sit or stand upright for at least 30 minutes following administration inability to swallow ≥ 120 – 200 mL of plain water hypocalcemia CrCl < 30-35 mL/min
	administration	 take on empty stomach upon arising for the day avoid taking any other medications (including vitamins and antacids) for at least 30 minutes
zoledronic acid (Aclasta®)	contraindications	 inability to appropriately hydrate pre and post infusion hypocalcemia CrCl < 35 mL/min (C-G formula using actual body weight)
	administration	 ≥ 500 mL of fluids before and after infusion infusion time: minimum 15 minutes

¹BC PAD Service Medications for Osteoporosis: An Update (December 2023 updated); ²Zoledronic Acid for Osteoporotic Fracture Prevention (ZEST II) ClinicalTrials.gov NCT02589600; ³DEARDORFF JAMA Int Med 2022;182:33-41 (PMID:34807231); ⁴Health Canada Drug Product Database Aclasta