OSTEOPOROSIS: FRACTURE PROTECTION IN A REAL-WORLD SETTING Recent oral bisphosphonate data

Health professionals with an interest in women's health from around Australia joined a livestream webinar with German osteoporosis expert, Dr Friederike Thomasius, who described how key findings from a recent study of which she was the lead investigator can influence ongoing osteoporosis management to optimise patient outcomes in a real-world health setting. To access the presentation recording, please visit https://theramex.com.au/hcp-resources/#rwewebinar or scan

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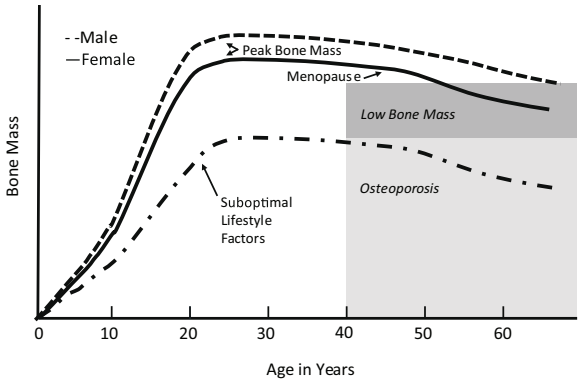
Osteoporosis across the life course

Osteoporosis is characterised by low bone mass and microarchitectural deterioration of bone tissue leading to enhanced bone fragility and a consequent increase in fracture risk.[1] Even though there is accumulating evidence that the risk of developing osteoporosis is accrued across the entire life course from childhood to old age, clinically osteoporosis is still often treated as an older person's condition.[2]

Changes in bone mass across the life course with optimal and suboptimal lifestyle choices[3]



Bone growth and development throughout life is influenced by both heredity and environmental factors. Many factors influence the accumulation of peak bone in early life which can have consequence on the risk of fractures later in life: bone strength, bone mass, nutrition, hormones, exercise, lifestyle and falls.

Determinants of osteoporosis across the life course[3,4]

Non-modifiable	Modifiable
Genetics	Poor nutrition
Age	Low calcium and vitamin D
Sex (female)	Smoking
Family history	Alcohol
Ethnicity	Physical inactivity
	Low body weight
	Medications

Osteoporosis trajectory in Australia, 2012 – 2022[6]

Prevalence of osteoporosis in Australia

Worldwide, osteoporosis is an under recognised health problem. In Australia 924 000 people self-report having osteoporosis (3.3% of the population) (about 29% women and 10% men aged over 75 years).[5] Over the 10-year period from 2012 to 2022 osteoporosis and osteopenia prevalence in men and women between 50 and 69 years is predicted to increase by 31%. Not only is the prevalence of osteoporosis increasing so too is the healthcare burden: the overall cost to Australians of osteoporosis in 2022 is estimated to be $3.84 billion.[6]

Importance of early diagnosis

Any osteoporotic fracture predisposes a person to at least a 2-fold risk in further fractures, significant morbidity and premature death.[7] It is important to identify patients with risk factors for osteoporosis and elevated fracture risk early in order to offer them appropriate treatment. There are 2 steps in the diagnosis of osteoporosis:

- Identifying patients at increased risk of fracture risk: using dual energy X-ray absorptiometry (DXA) measurements and further diagnostic procedures
- Identifying patients who may need specific treatment for osteoporosis in the future:
  - Garvan Fracture Risk Calculator www.garvan.org.au/bone-fracture-risk
  - Fracture Risk Assessment Tool (FRAX) www.shef.ac.uk/FRAX

Treatment strategies

The main goal of treatment for osteoporosis is fracture prevention.[7] Strategies should incorporate treatment to increase bone mineral density (BMD), to reduce future fracture risk and to prevent osteoporosis. These strategies usually involve a combination of drug therapy and risk factor modification (i.e. smoking, alcohol intake, medication that may induce accelerated bone loss, nutritional deficiencies and physical activity.

Australian guidelines recommend bisphosphonates and denosumab for first-line osteoporosis treatment.[7,8]

Oral bisphosphonates

Oral bisphosphonates are generally poorly absorbed.[9] The bioavailability of immediate release (IR) oral bisphosphonate is reduced if taken in close proximity to food or liquid intake, standard IR oral bisphosphonates should be taken on an empty stomach and at least 2 hours apart from calcium, iron, magnesium and antacids. This regimen can affect patient adherence to bisphosphonates.[9] Risedronate enteric-coated (EC) has the advantage of being absorbed even when taken with food. A recent study has tested whether its higher bioavailability translates into improved efficacy and a reduction in fracture rates compared to IR oral bisphosphonates.[10]

Real-world evidence and fraction prevention[10]

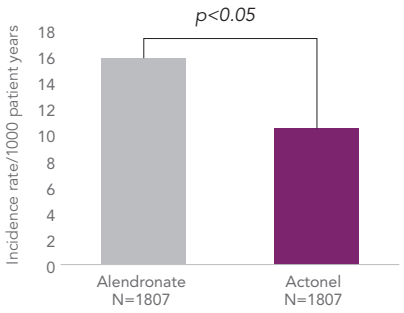
A retrospective, observational analysis of US healthcare claims database (2009-2019) compared the fracture rate and economic burden in over 5000 women with osteoporosis who were prescribed risedronate EC (n = 2726) with those treated with IR bisphosphonates (n = 2726). The majority of patients in the IR bisphosphonate cohort were on alendronate (66.3%). Patients were matched 1:1 based on characteristics, including baseline vertebral fractures and gastrointestinal conditions, and were observed for at least 2 years after treatment initiation for incidence of fractures and medication adherence.

The objectives of this real-world study were to compare women with osteoporosis treated with oral bisphosphonates, either risedronate EC or IR bisphosphonates for the following:

- fracture rates
- health-care resource use and costs
- medication adherence.

The findings demonstrated a 17% reduction in incidence of any site fractures for patients taking risedronate EC compared with those taking oral IR bisphosphonates ($p < 0.05$). Time to first fracture was delayed for those receiving risedronate EC, reaching statistical significance at 36 months. The risedronate EC treatment group had a lower incidence of fracture compared to patients in the alendronate cohort, with statistically significant differences observed for any site of fractures.[10]

Patients on risedronate enteric-coated (EC) compared to alendronate, patients had a 31% relative risk reduction of spine fracture ($p < 0.05$)[10]



Compared to patients who were prescribed IR oral bisphosphonates, those who were prescribed risedronate EC had fewer hospital inpatient stays during the observation period .

Take home messages

- The convenient dosing administration of risedronate EC (Actonel EC) appears to improve the absorption of the bisphosphonate and helps patients with osteoporosis get an improved treatment benefit
- Patients prescribed Actonel EC have:
  - a lower incidence of fractures compared to those prescribed other oral bisphosphonates
  - lower use of inpatient services translating into lower inpatient costs
  - an improved medication benefit irrespective of fasting.

Independent of food intake, risedronate EC has a higher bioavailability and is a more effective therapy to reduce the risk of fractures in women with osteoporosis when compared to immediate release bisphosphonates.

References 1.Kanis JA, et al. J Bone Miner Res 1994;9:1137-41. 2. Harvey N, et al. J Bone Miner Res 2014;29:1917-25. 3. Weaver CM, et al. Osteoporos Int 2016;27:1281-386. 4. Pouresmaeili F, et al. Ther Clin Risk Manag 2018;14:2029-49. 5. AIHW. Osteoporosis [internet]. Cat. no: PHE 233. Last updated 25 August 2020. 6. Watts JJ, et al. Glebe; Osteoporosis Australia: 2013. 7. RACGP. 2nd edition. 2017. 8. Ebeling PR, et al. Healthy bones Australia. February 2021. 9. Pazianas M, et al. Ther Clin Risk Manag 2013;9:395-402. 10. Thomasius F, et al. Osteoporos Int 2021 Sep 6.

Please review the Product Information before prescribing.

Full Product Information is available from Medical Information: 1800 THERAMEX (1800 843 726) or online at https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2019-PI-01321-1&d=201905161016933

ACTONEL® EC 35 mg weekly MINIMAL PRODUCT INFORMATION.
INDICATIONS: Treatment of: 1) osteoporosis, 2) glucocorticoid-induced osteoporosis, 3) preservation of bone mineral density in patients on long-term corticosteroid therapy. **CONTRAINDICATIONS**: Risedronate: Hypersensitivity to the drug or ingredients, hypocalcaemia, inability to stand or sit upright for at least 30 minutes. **PRECAUTIONS**: Risedronate: Hypocalcaemia; bone and mineral metabolism dysfunction; calcium and vitamin D if dietary intake is inadequate; severe renal impairment; oesophageal reaction, inflammatory bowel disease; osteonecrosis of the jaw; osteonecrosis of the external auditory canal; dental examination with preventive dentistry; avoid invasive dental procedures; atypical stress fractures; pregnancy (Category B3); certain medications (e.g. calcium supplements, antacids) should not be taken with Actonel EC; patients with a history of oesophagitis, gastritis, oesophageal ulcerations and gastroduodenal ulcerations. **INTERACTIONS**: Risedronate does not induce or inhibit CYP450 enzymes. **ADVERSE EVENTS:** Risedronate: Very Common: nasopharyngitis. Common: abdominal and musculoskeletal pain, influenza, urinary tract infection, bronchitis, diarrhoea, constipation, vomiting, nausea, arthralgia, back pain, hypertension, hypercholesterolaemia. **DOSAGE AND ADMINISTRATION:** Tablet needs to be swallowed as a whole with plain water in an upright position (patient needs to stay upright for 30 minutes). **STORAGE**: store below 30°C. Refer to full PI before prescribing. Based on the PI last updated 9 April 2021.

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