Theramex meeting series

DISPELLING MYTHS ABOUT OSTEOPOROSIS TREATMENT

Australian Meeting Tuesday 16 June 2020

About 100 Australian osteoporosis health professionals came together in a live interactive masterclass to hear endocrinologist Associate Professor Terry Diamond share his clinical experience in treating people at high risk of fractures.

Associate Professor Terry Diamond
Department of Endocrinology
University of New South Wales
St George Hospital, Kogarah NSW

WHO NEEDS MEDICATION FOR OSTEOPOROSIS?

Osteoporosis is a serious condition, especially in elderly men and women, leading to an increase fracture risk, loss of quality of life and a 2-4-fold increased refracture risk and an increased mortality.[1]

Treatment options

Two of the most commonly used Pharmaceutical Benefits Scheme (PBS) reimbursed indications for osteoporosis are:

- **Established osteoporosis:** a minimal trauma fracture
- **Osteoporosis:** a bone mineral density (BMD) T-score (≤ -2.5) and 70 years or older.

MYTH Osteoporosis treatments have a high risk of ONJ and AFF

While osteonecrosis of the jaw (ONJ) occurs more frequently in cancer patients using high-dose intravenous bisphosphonates (zoledronic acid), the incidence of ONJ in osteoporosis patients is rare, estimated at 0.001% to 0.01%, marginally higher than the incidence in the general population (< 0.001%).[2]

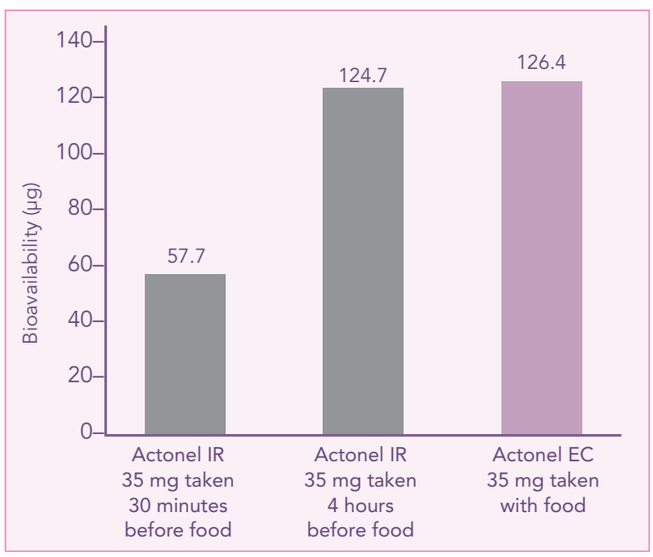
Long-term bisphosphonate use (over 5 years) may be associated with higher risk of atypical femoral fractures (AFF) in specific groups of people with osteoporosis.[1] However, the risk of AFF is generally 100 times lower compared to the risk of a major osteoporosis fracture in high-risk women.[3] Therefore, the benefits of osteoporosis therapy in reducing risk of future fractures strongly outweigh the risks of ONJ or AFF for most patients who have sustained a fragility fracture or are over the age of 70 and have low BMD.[4]

MYTH Patients need to fast before and after taking oral bisphosphonates

Food inhibits the uptake of oral bisphosphonates. Therefore, immediate release (IR) oral bisphosphonates need to be taken after overnight fasting followed by another 30 minutes of fasting after the bisphosphonate intake.[5,6] However, the oral bisphosphonate Actonel EC (enteric coated) is the only oral bisphosphonate that contains EDTA - a cation chelator - that binds to minerals such as calcium in food and allows the patient to take the tablet with their breakfast, without the loss of bioavailability or efficacy.[7]

Because of the enteric coating, Actonel EC dissolves in the small intestine and not the stomach, avoiding possible gastrointestinal issues.

The efficacy of bisphosphonates depends on two factors: bioavailability and bone affinity. Oral bisphosphonates are poorly absorbed and must be taken on an empty stomach, with a period of 30 minutes before taking any food or drink other than plain water.[8] However, an enteric-coated delayed-release formulation of risedronate (Actonel EC) removes the need for fasting without affecting its bioavailability or its efficacy. Because of the enteric coating, the tablet dissolves in the small intestine and not the stomach, avoiding possible gastrointestinal issues. Enteric-coated Actonel can be taken with or without food which has the added potential of improving adherence rates.[8]



The food effect in relation to the bioavailability of 35 mg Actonel enteric coated (EC) and immediate release (IR) tablets.[5]

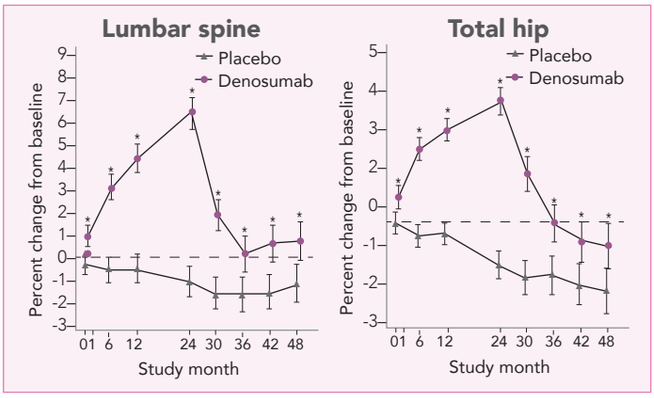
MYTH

Patients can safely stop osteoporosis treatment without the risk of rebound fractures

Bisphosphonates have a high affinity for bone and can remain in the skeleton for several years, even after treatment discontinuation.[9] Ceasing bisphosphonates therefore does not result in rebound-associated vertebral fractures and fracture protection may continue for up to several years after treatment cessation.[3,10,11.]

Denosumab, like bisphosphonates, is a very effective treatment for osteoporosis. Denosumab however does not integrate into the bone. When treatment is ceased or delayed, BMD levels have been shown to rapidly decline and rebound-associated multiple vertebral fractures have been reported shortly after cessation of treatment.[12,13] Clinical studies are needed to determine the best treatment strategy following denosumab discontinuation. However, researchers and societies across the world are advocating for prompt initiation of oral bisphosphonates or immediate recommencement of denosumab (re-inforcing the need for strict adherence to therapy).[3,4,14,15] Cessation of osteoporosis treatment is not advised in people with severe osteoporosis and at high fracture risk.

If … denosumab treatment cannot be continued, transition to an oral bisphosphonate for at least 12 months may be preferable, commencing within 4 weeks of the missed dose.[4]



Percentage change from month 0 in lumbar spine and total hip BMD over 48 months; treatment discontinued at 24 months; P = 0.0071[12]

MYTH

Most patients receive an oral bisphosphonate after stopping denosumab

A recent study in Australian general practice found over 80% of Australian osteoporosis patients stopping denosumab had no record of substituting other anti-osteoporotic therapies such as oral bisphosphonates. With the widespread use of denosumab in Australia many patients may be at risk of rebound-associated vertebral fractures if they are not being prescribed an oral bisphosphonate treatment quickly after denosumab treatment is discontinued.[16]

References 1. Royal Australian College of General Practitioners. Melbourne: RACGP; 2017. 2. Khan AA, et al. J Bone Miner Res 2015;30:3-23. 3. Meier C, et al. Swiss Med Wkly 2017;147:w14484. 4. Ebeling PR, et al. Osteoporosis Australia. July 2019. 5. Product Information. Actonel EC. 19 March 2019. 6.Product Information. Alendro (alendronic acid) tablets. 28 April 2017. 7. McClung MR, et al. Osteoporosis Int 2012;23:267–76. 8. Pazianas M, et al. Ther Clin Risk Manag 2013;9:395-402. 9. Fu K, Diamond T. Medicine Today 2018:12-24. 10. Watts NB, et al. Osteoporos Int 2008;19:365-72. 11. Eastell R, et al. J Clin Endocrinol Metab 2011;96:3367-73. 12. Bone HG, et al. J Clin Endocrinol Metab 2011;96:972-80. 13. Product Information. Prolia® (denosumab). Revised: 10/2019. 14. Leder BZ, et al. Bone 2017;98:54-8. 15. Kanis JA, et al. Osteoporos Int 2019;30:3-44. 16. Naik-Panvelkar P, et al. BMC Fam Pract 2020;21:32.

PBS Information: Actonel EC
Restricted benefit for osteoporosis, established osteoporosis and corticosteroid-induced osteoporosis.

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 whole with a full glass of plain water in an upright position and patient needs to stay upright for 30 more minutes. See full PI for further information. **STORAGE**: store below 25 °C. Sponsored in Australia by Theramex Australia Pty Ltd, ABN 37 623 186 845, Level 34, 60 Margaret Street, Sydney, NSW 2000. www.theramex.com Based on PI last updated 19 March 2019.

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