

RGH Pharmacy E-Bulletin

Volume 33 (7): March 23, 2009

A joint initiative of the Patient Services Section and the Drug and Therapeutics Information Service of the Pharmacy Department, Repatriation General Hospital, Daw Park, South Australia. The RGH Pharmacy E-Bulletin is distributed in electronic format on a weekly basis, and aims to present concise, factual information on issues of current interest in therapeutics, drug safety and cost-effective use of medications.

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Denosumab

There are currently several effective agents available to treat osteoporosis and for the prevention of fractures. Calcium and vitamin D play an important role for fracture prevention and bisphosphonates are the most commonly used anti-resorptive agents. Partial oestrogen agonists such as raloxifene have a more limited role in the treatment of osteoporosis. Teriparatide, a recombinant human parathyroid hormone is approved for the treatment of osteoporosis in Australia but it does not attract a Pharmaceutical Benefit Scheme subsidy and its cost is widely regarded as prohibitive.

Denosumab is a novel therapy under investigation for the treatment of osteoporosis in post menopausal women. Receptor activity of nuclear factor kB ligand (RANKL) (a protein expressed by osteoblastic stromal cells) binds to receptor activator of nuclear factor k B (RANK) and is the primary mediator of osteoclast differentiation, activation and survival. RANKL is responsible for osteoclast mediated bone resorption. Osteoprotegerin, a soluble decoy receptor that binds RANKL is the key endogenous regulator of the RANKL-RANK pathway. Denosumab is a fully human monoclonal antibody that binds to RANKL with high affinity and specificity and blocks the interaction of RANKL with RANK mimicking the endogenous effects of osteoprotegerin, leading to decreased osteoclast action and subsequently less bone resorption.

Denosumab has been evaluated in a number of clinical trials and has been shown to improve bone density. In one recently published study it appears denosumab is more effective than alendronate in improving bone mineral density and also lowering markers of bone turnover. The researchers followed 1189 post menopausal women with low bone density who were assigned to receive either a 60 mg subcutaneous injection of denosumab every six months and a weekly oral placebo, or an injection of placebo every six months and a weekly oral dose of alendronate 70 mg. All subjects took calcium and vitamin D daily. The mean lumbar T spine score was -2.6. This study revealed that a greater number of patients in the denosumab treated group gained more than 3% of BMD (measured at the total hip and lumbar spine after 12 months) than those in the alendronate group. Gains in BMD at all 5 skeletal sites evaluated (total hip, lumbar spine, femoral neck, trochanter and radius) were also noted to be improved.

Common adverse events reported in some studies were arthralgias, upper respiratory symptoms and back pain. Rash was reported more frequently in denosumab treated subjects. Reported serious adverse events was higher in denosumab treated group including serious infections which required hospitalization, and cancer was reported in four denosumab treated patients versus one in the placebo group.

Denosumab may also have wider clinical benefits for the treatment of myeloma, metastatic breast cancer and rheumatoid arthritis. The manufacturer has submitted marketing applications for denosumab to the FDA in the USA, and also in Australia, European Union, Canada and Switzerland. A decision by the FDA is expected in late 2009.

Acknowledgment – This E-Bulletin is based on work by Margie Harlow, Drug Distribution Coordinator, RGH

FOR FURTHER INFORMATION – CONTACT THE PHARMACY DEPARTMENT ON 82751763 or email: chris.alderman@rgh.sa.gov.au
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