AWTTC
All Wales Therapeutics & Toxicology Centre
Canolfan Therapiwteg a Thocsicoleg Cymru Gyfan

Denosumab (Prolia®) for the treatment of osteoporosis in men at increased risk of fractures

March 2017

ONE WALES INTERIM COMMISSIONING DECISION

Denosumab (Prolia®) for the treatment of osteoporosis in men at increased risk of fractures

Date of advice: March 2017

The following Interim Pathways Commissioning Group (IPCG) recommendation has been endorsed by health board Chief Executives.

Denosumab (Prolia®) can be made available within NHS Wales for the treatment of osteoporosis in men at increased risk of fractures. Denosumab (Prolia®) should only be made available for men who fulfil the agreed criteria for treatment.

This advice will be reviewed after 12 months or earlier if new evidence becomes available.

Advice is interim to subsequent Health Technology Appraisal advice from AWMSG or NICE becoming available.

One Wales advice promotes consistency of access across NHS Wales.

Criteria for treatment with denosumab (Prolia®) for the treatment of osteoporosis in men at increased risk of fractures

These criteria have been adapted from NICE Technology Appraisal guideline TA204 Denosumab for the prevention of osteoporotic fractures in postmenopausal women[1].

Denosumab (Prolia®) can be made available for the primary prevention of osteoporotic fractures in men at increased risk of fractures:

- Who are unable to comply with the special instructions for administering alendronate and risedronate, or have an intolerance of, or a contraindication to, those treatments,
- Who are unsuitable for treatment with intravenous (IV) zoledronic acid and
- Who have a combination of bone mineral density T-score, age and number of independent risk factors as shown in the table below:

T-scores at or below which denosumab is recommended when oral bisphosphonates are not suitable

	Number of independent clinical risk factors*		
Age (years)	**0**	**1**	**2**
65–69	Not recommended	-4.5	-4.0
70–74	-4.5	-4.0	-3.5
≥ 75	-4.0	-4.0	-3.0
*Independent clinical risk factors are: parental history of hip fracture; alcohol intake of 4 or more units per day; and rheumatoid arthritis.			

Denosumab (Prolia®) can be made available for the secondary prevention of osteoporotic fragility fractures in men at increased risk of fractures who are unable to comply with the special instructions for administering alendronate and risedronate, or have an intolerance of, or a contraindication to, those treatments and who are unsuitable for treatment with IV zoledronic acid.

1. National Institute for Health and Care Excellence. Technology Appraisal 204. Denosumab for the prevention of osteoporotic fractures in postmenopausal women. Oct 2010.

KEY FINDINGS: This is an abbreviated summary of the evidence provided to IPCG

Report background
Denosumab was first licensed in May 2010 for the treatment of osteoporosis in postmenopausal women and for the treatment of bone loss associated with hormone ablation in men with prostate cancer. In June 2014 the European Medicines Agency granted an extension to the licence of denosumab to include the treatment of osteoporosis in men at increased risk of fractures. The National Institute for Health and Care Excellence (NICE) are currently in the process of appraising denosumab for this indication as part of a multiple technology appraisal, but the date that advice will be available has yet to be published. Clinicians in Wales consider there is an unmet need for this medicine in men and have identified a cohort of patients who could benefit from this treatment.

Efficacy/Effectiveness
In men with osteoporosis, a pivotal phase III randomised controlled trial demonstrated a statistically significant increase in lumbar spine bone mineral density (BMD) in the denosumab group compared with placebo. A randomised controlled study (RCT) in men receiving androgen-deprivation therapy for prostate cancer further supported the safety and efficacy of denosumab for the treatment of osteoporosis in men at increased risk of fractures. However, since the studies in men did not investigate the anti-fracture efficacy of denosumab and a similar association between BMD and fracture risk has been reported in men and in postmenopausal women, a phase III RCT in postmenopausal women was included in the licence application for men. This study demonstrated a significant decrease in the incidence of fractures following denosumab treatment versus placebo.

Safety
No new safety signals have been observed for denosumab for the treatment of osteoporosis in men at increased risk of fractures.

Patient factors
Denosumab is administered every six months by subcutaneous injection. It may be self-administered by the patient but is most likely to be administered by a primary care health professional.

Cost effectiveness
One study was identified assessing the cost-effectiveness of denosumab versus bisphosphonates, strontium ranelate and teriparatide in males aged 75 years and over with osteoporosis from a Swedish payer perspective. Cost effectiveness estimates have been calculated by the All Wales Therapeutics and Toxicology Centre (AWTTC) but are subject to large uncertainty due to the assumptions made in calculating these estimates. With this caveat, the estimated incremental cost-effectiveness ratio per quality-adjusted life-year gained was shown to be dominant for denosumab compared to strontium ranelate, teriparatide and zoledronic acid (i.e. shown to be more effective and less costly).

Budget impact
Denosumab is likely to be used third line after failure of two oral bisphosphonates in patients unsuitable for intravenous (IV) zoledronic acid, or fourth line after failure of IV zoledronic acid. Clinical experts estimate there to be 80–100 male patients in the third line setting and 20–30 male patients in the fourth line setting eligible for denosumab treatment. The estimated budget impact of denosumab third line is £44,200 in year one, increasing to £114,920 in year three as a proportion of patients will remain on therapy for two or more years. The budget impact assumes that 100 new male patients are treated each year and a 10% discontinuation rate and 4% mortality rate per annum. Budget estimates are based on the list price of denosumab as the company have not offered a Wales Patient Access Scheme (PAS), together with monitoring costs. There is no medicine displacement in the budget impact due to the absence of a suitable alternative treatment. In the absence of such treatment, a proportion of patients are receiving denosumab in current practice via local agreements within health boards.

Patient Access Scheme
AWTTC requested that the company submit a PAS as part of the submission to the One Wales Interim Commissioning Process. The company declined to submit a PAS the rationale being that denosumab represents a similarly cost-effective treatment option in the male population as in women. Denosumab has been approved by NICE for the prevention of osteoporotic fractures in postmenopausal women at the UK list price and deemed a cost effective use of resources.

Impact on health and social care services
Minimal increased use of existing services. Denosumab is currently available via shared care arrangements in some Health Boards for the treatment of postmenopausal osteoporosis.

Innovation and/or advantages
Denosumab offers an additional treatment option for this patient group and is relatively simple to administer.

Outcome data
Outcome data will be collected by the Welsh Osteoporosis Advisory Group.