Cost-effectiveness of denosumab (XGEVA®) for the prevention of skeletal related events in adults with bone metastases from solid tumours in Ireland.

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Summary

1. An economic evaluation on the cost-effectiveness of denosumab (Xgeva®) for the treatment of skeletal-related events in adults with bone metastases from solid tumours was submitted to the NCPE by Amgen Ltd in August 2011.

2. Denosumab is a fully human monoclonal antibody that binds to RANKL, a soluble transmembrane protein that binds to the RANK (receptor activator for nuclear factor) receptor. The binding of RANKL to RANK receptors enhances the formation, activation and survival of osteoclasts responsible for bone resorption. Denosumab binds to RANKL and antagonises its activity thereby reducing osteoclast activity and bone resorption.

3. A cost-utility analysis was provided which compared the use of denosumab (Xgeva®) versus zoledronic acid (ZA) in the prevention of skeletal-related events (SREs), i.e. pathological fracture, radiation to bone, spinal cord compression, surgery to bone in patients with bone metastases from solid tumours (specifically breast, prostate and other solid tumours excluding multiple myeloma). The perspective adopted was that of the Health Service Executive (HSE).

4. A Markov cohort model was used to demonstrate the cost-effectiveness of denosumab versus ZA for the prevention of SREs in each of three tumour types: breast cancer, prostate cancer and other solid tumours. Clinical outcome data were derived from studies from Stopeck *et al.,* 2010 (breast cancer), Fizazi *et al.*, 2010 (prostate cancer) and Henry *et al.,* 2010 (all other tumours). Costs and consequences were discounted at 4%. A ten year time horizon was adopted.

5. In the base-case analysis presented by Amgen, denosumab dominated ZA in all three cancer models. An alternative scenario was modelled by the review group (which included lower administration and acquisition costs for ZA). The incremental cost-effectiveness ratio (ICER) under these assumptions were €29,371/QALY (Prostate Cancer); €14,626/QALY (Breast cancer) and for all

other tumours denosumab dominated ZA. The ICER derived from the population weighted analysis was € 21,643/QALY.

6. In the alternative scenario modelled by the review group a deterministic sensitivity analysis demonstrated that the parameters with greatest effect on the ICER (for all three tumour types) included drug costs (denosumab and ZA), administration costs for denosumab under the HTD scheme, administration costs for ZA, and the relative SRE rate of denosumab vs ZA. In the alternative scenario the probability of denosumab being cost-effective at a willingness-to-pay (WTP) threshold of €20,000 per QALY gained was 38.9% in the prostate cancer model, 46.9% in the breast cancer model and 52.1% for all other tumours.

7. The submission included a budget impact assessment for denosumab therapy vs ZA. If the budget impact is estimated for the alternative scenario, which includes a lower administration cost and lower acquisition cost for ZA, the incremental budget impact would be €59,666 in 2012 increasing to €842,475 in 2016.

8. We believe that denosumab (Xgeva®) may be considered a cost-effective therapy for the prevention of skeletal-related events in adults with bone metastases from solid tumours in the Irish healthcare setting.