

Thank you for inviting me to comment on the Appraisal Consultation Document for the Single Technology Appraisal of denosumab in the prevention of osteoporotic fractures in postmenopausal women. As regards the specific questions you raise, I should like to make the following comments:

Has all of the relevant evidence been taken into account?

Yes

Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence?

Yes, but I agree with the Expert Review Group that it is unlikely that the administration of denosumab will be provided in primary care as part of General Medical Services. This may therefore require additional funding as a Locally Enhanced Service, but the costs are likely to be modest.

Are the provisional recommendations sound and a suitable basis for guidance to the NHS?

I welcome the Appraisal Committee's recommendations on the use of denosumab for the secondary prevention of fragility fractures, which will allow postmenopausal women at increased risk of fractures to gain access to effective treatment for osteoporosis, if they are unable to take or tolerate oral bisphosphonates. Although the Committee's preliminary recommendations on the use of denosumab for the primary prevention of fragility fractures follow the approach adopted for second line agents in Technology Appraisal (TA) 160, I feel that the use of age, T-Scores and number of clinical risk factors for fracture, rather than absolute risk of fracture calculated by FRAX[®], may be difficult to use in clinical practice. Furthermore, as with TA 160 and TA 161, some women who meet the criteria for treatment with generic alendronate, but are unable to take or tolerate this medication, will need to lose bone before qualifying for treatment with denosumab or an alternative agent. This is a difficult situation for a clinician to explain and justify to a patient.

Are there any aspects of the recommendations that need particular consideration to ensure we avoid unlawful discrimination against any group of people on the grounds of gender, race, disability, age, sexual orientation, religion or belief?

The one area of potential discrimination is the situation of primary prevention in a postmenopausal woman with swallowing problems as a result of disabling stroke disease, who is otherwise eligible for treatment with oral alendronate, but does not fulfill the criteria for denosumab or other treatments.

Other Comments

3.25: The Expert Review Group concluded that data on morphometric vertebral fractures were not relevant, so did not use them in their modelling, but the Study of Osteoporotic Fractures from the US showed that although morphometric fractures may not come to clinical attention, they are associated with increased back pain and functional limitation (Nevitt et al, Ann Intern Med 1998; 128: 793–800).

4.5: This paragraph implies that oral bisphosphonates should only be taken whilst standing. The general recommendation is that these agents should be taken standing **or** sitting, as lying down immediately after ingestion may lead to the drug refluxing into the oesophagus.

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