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Dr Carole Longson
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23 April 2008

Dear Dr Longson

Re: Health Technology Appraisals: Primary and Secondary Prevention of Osteoporotic Fragility Fractures in Postmenopausal Women

The Society welcomes the opportunity to comment on these ACDs and hopes that the Institute will find our comments useful in developing your final guidance. We offer our general comments first followed by specific observations on each of the ACDs.

General comments

1. The Society remains concerned that the Institute seems to adopt the most conservative stance available whenever a choice of parameters in the cost effectiveness model has to be made. The result of this is the multiplication of errors all of which tend to be in one direction so that the final effect of the model is far too conservative and at variance with what is seen by any of us in clinical practice. By adopting this stance the Institute appears to be judging osteoporosis against a different set of criteria from those which would be used for the assessment of other disease states.

2. We were concerned to see the summary dismissal of the FRAX fracture risk estimator. This has been something that has been developed over a long period of time by the WHO and is likely to represent the international gold standard for the assessment of osteoporosis risk. Whilst we accept that the way that the risk generated by the FRAX calculator has not yet clearly been translated into a treatment decision we do believe that by such summary dismissal of something that is likely to assume major significance within the field in the very near future the Institute are likely to be producing guidance which may not be relevant to the clinical climate into which it is being released.

3. All our clinical members with whom we have consulted have expressed grave concerns about the way in which a patient who fails to tolerate generic alendronate needs to satisfy substantially more stringent criteria to become eligible for alternative therapies in either ACD. Whilst we understand the argument relating to cost effectiveness regarding this we do not believe that in reaching this decision the committee have taken sufficient cognizance of the adverse effect this is likely to have on the doctor patient relationship and the deleterious effect on an individual's quality of life when she knows that she is suffering from a condition which would justify treatment but has been told that as she cannot tolerate one treatment the NHS cannot "afford" the alternative unless her condition were to worsen.

4. We can see no reason in science or clinical practice why the committee have arrived at their list of risk factors. It is incomplete and if taken as an exclusive list is likely to mean that many patients who could benefit cost effectively from therapy will be denied that treatment.

5. We are concerned that etidronate is afforded equal status to that of risedronate despite the lack of convincing evidence for clinical effectiveness of the former against limb fractures.

6. The review date (2010) is likely to mean that new agents in the categories under consideration (ibandronic acid, zoledronic acid and PTH1-84) are not going to be subject to scrutiny by the Institute for a considerable length of time and may therefore not be used in a cost-effective manner in the NHS.

Primary prevention

7. The guidance offered here is far too complicated to be of any utility in the day-to-day management of patients unless the Institute is also able to offer some form of computer program or other decision support aid which would assist clinicians through the morass of guidance.

8. The categorisation of risk factors into those that are associated with low bone density and those which are associated with increased fracture risk independent of bone density is not something which is recognised by the clinical community. Furthermore it is actually doubtful whether any of the risk factors so identified by the appraisal committee actually neatly fall into the boxes assigned to them. Those factors which are said to be risk factors for fracture independent of bone density are reasonably good at predicting low bone mass and the fracture risk associated with risk factors said to only predict fracture by virtue of bone density is not completely abolished by correction for bone density. It can therefore be seen that the committee have taken a simplistic and not scientifically justified view in their arbitrary categorisation of risk factors. Of course were the committee to abolish this unjustified distinction and merely base the guidance on the number of risk factors this would, at a stroke, substantially simplify the guidance and therefore make it much more likely to be adopted in clinical practice.

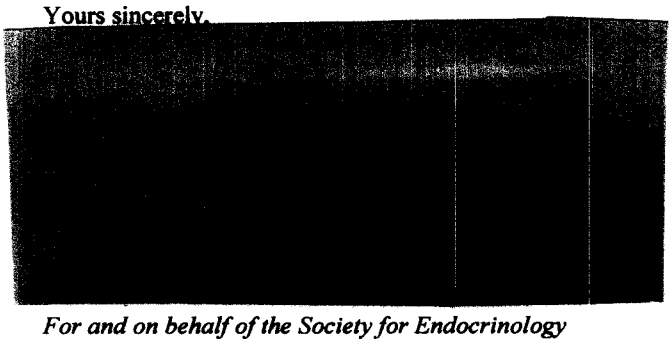
9. One of our members has examined the prevalence of the various risk factors identified by the committee in the Glasgow Fracture Liaison service. His observations would suggest that the actual prevalence of these risk factors in a large unselected fracture population is very low. Although we do not have as much similar data for an unselected population this does raise the possibility that the predictive value of these risk factors may not be particularly strong by virtue of their low prevalence within the British population. If that is indeed the case then one must wonder whether to seek out these risk factors will be cost effective any way.

Secondary prevention

10. We are not aware of any change in the clinical evidence available to the appraisal committee from the time when they developed TA87. However there are many clinical scenarios where TA87 would have permitted the use of risedronate in which that agent is now explicitly precluded. Clearly it is appropriate that, given the huge fall in the cost of alendronic acid, the cheaper agent should be used in preference to risedronate. The committee however find no explanation of why something that was cost effective three years ago is no longer considered cost effective despite there being no change in the evidence available to them and a small fall in the price of risedronate. In the interests of transparency we would expect the committee to make explicit the reasons for this change of heart.

We hope that the Institute finds these comments helpful and look forward to seeing your revised guidance. If you require any further information do not hesitate to contact us.

Yours sincerely,



For and on behalf of the Society for Endocrinology