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SUBMITTED BY EMAIL ONLY

Dear Dr Longson,

Primary and secondary prevention of osteoporotic fragility fractures in postmenopausal women

Further to your letter dated 28th January 2008, the National Osteoporosis Society has a number of comments and observations relating to the appeal panel decision. If the Appraisal Committee proposes to make final decisions on the information that it has already considered, we would be extremely concerned that the appraisals will not meet the needs of either health professionals or patients. We therefore hope that our submission is given full and proper consideration.

Before I refer to the further development of these appraisals there are a number of points that we would like to make regarding the appeal decision documents that we received in December 2007.

- Point 12 (primary and secondary) – "while it was open to the committee to consider the question with consultees, it was also open to the committee simply to explain to consultees what happened. The Committee chose the former course" – we believe that this should read "the latter course".
- Point 99 (primary) – states that there was a typographical error at paragraph 4.2.21 of the FAD – however, there is no paragraph of this number in the primary prevention FAD. We remain unclear as to which sensitivity analyses were favoured by the Committee for strontium ranelate and raloxifene and would like to see complete transparency around this in future documents.
- Page 22 (primary) – we note that after point 113 the NOS appeal points 3.1, 3.2 and 3.3 were considered. Although the Servier appeal points 3.1 and 3.2 are documented, similar points made by the National Osteoporosis Society, which were discussed are not. Similarly the NOS Ground 3 points made during the appeal on secondary prevention are also not included at page 19.

Although we are pleased that the Appraisal Committee will now be including recommendations for alternative first line and second line treatments, the Society has serious concerns regarding how these will be incorporated into the appraisals. Further to the appeal, we would like further clarification on which groups will now be covered by the Appraisal recommendations. The appeal panel stated that "*an appraisal that does not as a minimum examine all significant patient groups with in the scope, and make recommendations where the evidence permits this, is very likely to be rejected on any appeal*". The original scope (2002) for the primary prevention appraisal included postmenopausal women at risk of developing osteoporosis or having a related fracture, and corticosteroids were included as a risk factor. With this in mind we believe that the appraisals will now cover postmenopausal women with osteopenia who are at a high risk of fracture and women who have used glucorticoids, confirmation of this would be useful.

During recent years the Society has been working, through its helpline, conference and publications, to educate stakeholders about absolute fracture risk. Until recent years, the focus had been on T-score and it has been particularly difficult to explain to our members why their having a BMD of T≤ -2.5 does not automatically mean that they need a treatment. The publication of the World Health Organisation (WHO) fracture risk assessment tool (FRAX™), today (www.shef.ac.uk/FRAX), marks an important step forward in the assessment of fracture risk, setting BMD into a broader framework of risk factors. This tool will be disseminated widely and we believe that FRAX™ will be widely used by clinicians across the UK. Indeed we know that GPs in particular will value having a simple tool which they can implement in a similar way to the cardiovascular risk calculators that they already use routinely. Although we want to see the FRAX tool continue to evolve in line with new clinical evidence, we do see it as being a key component in helping health professionals improve their management of osteoporosis and fractures.

We acknowledge that the Appraisal Committee have considered the fracture risk data which forms the basis of FRAX™ and indeed that these data have partially been incorporated into the economic modelling. However, with the publication of this tool we believe that there now needs to be fuller consideration given as to how the appraisals are interpreted alongside absolute fracture risk data. Without this we cannot envisage how the Clinical Guideline, which must surely now incorporate FRAX™, could be interpreted alongside the Appraisal recommendations.

Since the Committee last requested additional economic modelling the tariff price for alendronate has reduced signficantly. It is now set at £4.12 (NHS Drug Tariff, 21st February 2008) for 4 tablets, giving a drug cost for one year of £53.56. This is some 44 % lower than the price of £95.03 per annum used in the FADs. As the Committee will require further economic modelling based on the new price, we would urge the committee to consider producing output based on absolute fracture risk.

Since the Department of Health referral for these appraisals, there have been several new treatments licenced, including ibandronic acid (monthly tablet or three monthly i/v), zoledronic acid and rh1-84 parathyroid hormone (Preotact). These new treatments have provided patients with welcome additional treatment choices. At this stage we are concerned about how recommendations for zoledronic acid in particular, which we believe will now be included in the Clinical Guideline, will work alongside the appraisals. Given that the drug has good efficacy data, will have high compliance and does not have the gastro-intestinal side effects that are associated with the oral bisphosphonates (this is particularly important given the recent data demonstrating that there is an increased fracture risk associated with proton pump

inhibitors), this treatment might be more cost-effective than some of the other second line treatments, which would mean that the appraisals no longer recommend the most cost effective treatment strategies.

In view of these points, we remain very concerned about how the Technology Appraisals and the Clinical Guideline are going to work together and would strongly encourage the NICE Executive to ensure that these two processes now work closely together to ensure that the result is a robust suite of clinically workable guidance for health professionals and patients. Our concern has been heightened by the fact that the two clinical experts originally nominated by the Society appear to have been excluded from the March Appraisal Committee meeting. We are suprised that the Institute has not seen fit to seek the opinion of the clinical experts originally recommended by the National Osteoporosis Society given the appeal findings. Without this clinical input we do not see how the Institute can develop guidance which is clinically relevant and applicable in the NHS.

I know that you are aware of the recent publication in Bone[1], which reports the cost effectiveness of alendronate for the treatment of osteoporosis and hope that this has been made available to the Appraisal Committee. The economic analyses, which incorporate sensitivity analyses previously explored by NICE, demonstrates significantly better cost effectiveness of alendronate and also provides scenarios where alternative treatments are cost effective. With the results of these analyses in mind, we urge the Committee to consider, where individual treatments are shown to be cost effective, using wording similar to the statins appraisal, which recommends "that therapy should usually be initiated with a drug with a low acquisition cost".

At this time we are aware that a number of our Scientific Advisory Group are now developing a clinical guideline based on this alternative economic analysis and the recently published FRAX™. We believe that their work will provide recommendations on all of the licensed treatments based on absolute fracture risks. When these guidelines are published they are likely to be viewed as an update to the RCP guidelines that are currently seen as best practice.

Although at this stage we have not been involved in this alternative guideline we are now minded to watch its progress closely. The Society began working with NICE as we believed that it would provide clinically workable osteoporosis guidance that, when implemented, would result in significant improvements in the identification and treatment of those patients who are at risk of suffering from painful and debilitating osteoporotic fractures. At this time we believe that there is a significant risk that NICE will not deliver this, and this alternative guideline could potentially be more relevant and valuable. We urge NICE to give this work serious consideration, with a view to incorporating key elements into the NICE Clinical Guideline and Technology Appraisals.

Carole, we remain committed to working with you and your colleagues to produce the Guidance that we need and look forward to reviewing further analyses from you later in the spring. We would however, like to be more fully engaged with your work on osteoporosis and to this end we have sought a meeting with Sir Michael Rawlins to discuss how these three pieces of osteoporosis guidance could best meet the needs of patients and clinicians.

[1] Kanis JA, Adams J, Borgström F, Cooper C, Jönsson B, Preedy D, Selby P and Compston J.(2008) The cost-effectiveness of alendronate in the management of osteoporosis. Bone; 42(1):4-15.

On a final note, I would be grateful if, further to the publication of the WHO analyses, you could facilitate release of the ScHARR economic model to the National Osteoporosis Society to allow us to more fully consider any additional analyses that may be presented.

If I can be any further help, please do not hesitate to contact me again.

Yours sincerely,

[redacted]

For and on behalf of the National Osteoporosis Society