[redacted]

Tuesday 23rd April 2008

Jeremy Powell
National Institute for Health and Clinical Excellence
Peter House
Oxford Street
Manchester
M1 5AN

BY E-MAIL

Dear Jeremy,

MULTIPLE TECHNOLOGY APPRAISAL –
Alendronate, etidronate, risedronate, raloxifene and strontium ranelate for the primary prevention of osteoporotic fragility fractures in postmenopausal women

Alendronate, etidronate, risedronate, raloxifene, strontium ranelate and teriparatide for the secondary prevention of osteoporotic fragility fractures in postmenopausal women

Thank you for sending us the Appraisal Consultation Documents (ACDs) for the above technology appraisals.

Our feedback is provided below as per the requested ACD response structure.

1 WHETHER YOU CONSIDER THAT ALL OF THE RELEVANT EVIDENCE HAS BEEN TAKEN INTO ACCOUNT

It is suggested in the ACD that there is a different willingness to pay for a QALY between primary and secondary prevention. The rational being that "in primary prevention where an asymptomatic group of adult patients with a high number needed to treat to avoid a fracture is under consideration" one would expect a lower willingness to pay than in secondary prevention where there is a smaller number under consideration.

Rather than suggesting a different value of a QALY between the two analyses, we consider that the uncertainty around whether an individual is going to be suitable for treatment should be accounted for in the costs and benefits assumed in the model.

2 WHETHER YOU CONSIDER THAT THE SUMMARIES OF CLINICAL AND COST EFFECTIVENESS ARE REASONABLE INTERPRETATIONS OF THE EVIDENCE AND THAT THE PRELIMINARY VIEWS ON THE RESOURCE IMPACT AND IMPLICATIONS FOR THE NHS ARE APPROPRIATE

There appears to be a discrepancy between the Evaluation Report and the ACD for primary prevention in the following subgroup:

- Age >75; 2 risk factors; T-Score -2.5 to -3.0; ICER: £13,380

The use of 2nd line bisphosphonates in the above subgroup appears cost effective with an ICER below the £20,000 threshold and yet this is not recommended in the ACD. This appears to be inconsistent with the remainder of the recommendations, which are inline with the Evaluation Report results.

Cost effectiveness estimates for etidronate were not provided in the Evaluation Report, however risedronate appears cost effective in subgroups of patients that are not recommended for treatment with "second-line bisphosphonates", risedronate and etidronate, in the ACD. This is due to the exclusion of guidance (in the ACD) on patients with more than 2 risk factors or osteopenia. One might interpret the recommendation tables (p. 5 of secondary prevention ACD and p. 4 primary prevention ACD) to mean that "second-line bisphosphonates" are not cost effective for the following subgroups, where according to the Evaluation Report they are:

Secondary Prevention

- Age 50-69; 3 risk factors; T-Score -2.5 to -3.0; ICER: £24,852 to £18,141
- Age 70-75; 2 risk factors; T-Score -1.5 to -2.5; ICER: £30,100 to £18,383
- Age 70-75; 3 risk factors; T-Score -1.0 to -2.5; ICER: £28,875 to £9,236
- Age >75; 2 risk factors; T-Score -1.0 to -2.5; ICER: £28,666 to £11,861
- Age >75; 3 risk factors; T-Score -1.0 to -2.5; ICER: £14,943 to £2,390

Primary Prevention

- Age 65-69; 3 risk factors; T-Score -3.0 to -3.5; ICER: £12,348
- Age 70-75; 3 risk factors; T-Score -2.5 to -3.0; ICER: £10,509
- Age >75; 3 risk factors; T-Score -1.5 to -2.5; ICER: £19,171 to £9,220

3 WHETHER YOU CONSIDER THAT THE PROVISIONAL RECOMMENDATIONS OF THE APPRAISAL COMMITTEE ARE SOUND AND CONSTITUTE A SUITABLE BASIS FOR THE PREPARATION OF GUIDANCE TO THE NHS

Aside from the points raised above the provisional recommendation appears a suitable basis for the preparation of guidance to the NHS.

We hope that our feedback is helpful to the Appraisal Committee in its subsequent deliberations.

Yours sincerely,