Health Technology Appraisal

Appraisal Consultation Document
Alendronate, etidronate, risedronate, raloxifene and strontium ranelate for the primary prevention of osteoporotic fragility fractures in postmenopausal women

Assessment Report

Preliminary Recommendations

A recommendation on how a patient is assessed as calcium and vitamin D replete is required. Although a matter for debate biochemical evidence showing a PTH within the reference range, a urine calcium and plasma adjusted calcium within the reference range and a total 25 OH vitamin D >50nmol/L would be a consensus from the literature that may be acceptable to the committee currently.

It is surprising that all three bisphosphonates have been recommended without expressing a preference for use. As the appraisal identified "….the data for alendronate generally provide the best case in terms of cost effectiveness". The most recent comparative data available indicates greater effects of alendronate on BMD and bone marker changes than risedronate. These surrogates are now accepted by other regulating bodies as markers of efficacy yet NICE do not appear to wish to move with the times in accepting this evidence. The preliminary views are only acceptable if such evidence is ignored and that is not a sound basis for recommendations and guidance to the NHS. This is particularly relevant to statement 1.2.

There has been no comment on the dose of drug to be used as a preventative measure although the literature has cited different doses of alendronate in studies on prevention and treatment.

It is surprising that Raloxifene is not recommended for prevention especially in light of the reduction in breast cancer seen in women treated in the MORE study. The benefit in younger women in the analyses was surely a factor that would result in the recommendation for use in the long-term. The previous decision (NICE Technology Appraisal No.87) not to include the breast cancer benefit is regrettable and to the detriment of this population of women.

The lack of recognition of the analyses showing that many women below the age of 70 can be treated cost effectively is a serious omission. Several identification methods have been published in the literature that have not been explored in the technology and this posses a serious issue and therefore this is not a sound basis for recommendation of the current guideline to the NHS.

The data on corticosteroid use in younger women is clear in recommending the benefit of prophylactic treatment to prevent fractures. This needs to be highlighted and an appropriate age banding change recommended in the current guideline. The current ACD is liable to result in dangerous practice in relation to this area of therapeutics.

The Technologies

Within the technologies alendronate has been costed using previous prices. The availability of generic alendronate will change the cost estimates and this should be performed as an addendum to the recommendation as soon as possible.

Proposed Recommendations for Further Research

Since head to head studies are being recommended it would be interesting to know how these are going to be funded, under whose auspices these should be conducted and what end points should be assessed.

The glib statement regarding bone quality is interesting and it would be important to detail which aspects of bone quality are assessable and quantifiable at present.

In previous comments it has been pointed out that the effect on measurement of serum/plasma calcium is minimal but a more significant effect may be seen on urine calcium with certain biochemical

methods particularly in relation to the timing of the dose prior to sampling. This statement should be altered appropriately.

Proposals for Implementation and Audit

The proposal that Raloxifene should not be considered at all as a treatment option is not acceptable. This is influenced by the fact that previous appraisals including the breast cancer efficacy showed the cost-effective benefit of such treatment. If a patient is not suitable for oral bisphosphonate and is intolerant to strontium then the possibility of prescribing Raloxifene should be retained within the recommendation. To be so dogmatic as the current recommendation would be a disservice to a large cohort of women in the UK.