Health Technology Appraisal

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

Assessment Report
for The Royal College of Pathologists

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.

The evidence for a greater effect of Strontium than Raloxifene on reduction of non-vertebral fractures has been taken in to account in the current recommendation. Strontium is apparently more cost effective in the analyses and is a basis for the graded recommendation. However the data on Strontium would appear to depend on an age effect and this should be taken in to account when making the graded recommendation within the current guideline.

Great care is required when making recommendation for use of teriparatide in "….medical conditions independently associated with bone loss…." This needs to be in light of the contraindications for use as specified in the data sheet and conditions that might predispose to hypercalcaemia/hypercalciuria.

As can be seen in the ACD under "Consideration of the Evidence" the committee recognised that the new modelling identified women under the age of 65 who would benefit from teriparatide treatment if treatment with the bisphosphonates and strontium ranelate (which compose "the expanded treatment options") was contra-indicated. This surely forms the sound basis for a recommendation to use teriparatide in this sub group of women and the guideline should be altered to take account of the committee's own assessment. The previous recommendation is not satisfactory when this new evidence is available.

It is good to see an attempt to define an unsatisfactory response to bisphosphonates included but this should be expanded. If a patient suffered multiple fragility fractures on a bisphosphonate within 6-12 months would this not be evidence of failure to respond since most of the data that looks at the 6 months time frame of treatment shows a reduction in fractures?

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.

Consideration of the Evidence

The new modelling based on the WHO data is to be applauded and the update of Appraisal No 87 welcome.

It is surprising that the committee agreed that the modelling indicated that teriparatide would be cost effective in a small number of women under 65 with very low T-scores in whom bisphosphonates and strontium ranelate is contra-indicated but then stated “given the increased treatment options for such women, on balance, its prior guidance was satisfactory”. This is completely contradictory and needs to be changed and the recommendation for use allowed for under 65 year olds. How can it be stated that the increased treatment options are all contra-indicated but the committee then not recommend teriparatide be used in this age group?

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

These should take account of previous comments.