


Comments on the National Institute for Health and Clinical Excellence
Health Technology Appraisal
Alendronate, etidronate, risedronate, raloxifene and strontium ranelate for the primary
prevention of osteoporotic fragility fractures in postmenopausal women
And
Alendronate, etidronate, risedronate, raloxifene and strontium ranelate and teriparatide
for the secondary prevention of osteoporotic fragility fractures in postmenopausal
women.


For
The Royal College of Pathologists

The comments that follow are given in accordance with the general headings requested by the Appraisal Committee

- 1) It is surprising that the documents comment on the fact that the guidance should be read in the context of the clinical guideline which is not available. The exclusions are inappropriate especially since a large amount of literature is available on primary prevention in women who are osteopenic.
- 2) A number of studies now question the relevance of statements on adequate calcium/vitamin D intake and what constitutes being replete. It is essential that this document addresses what is deemed to be a level of optimal vitamin D and calcium intake with references to published work on the subject or that the statements made incorporate specific guidance rather than waiting for the clinical guideline.
- 3) Work from Glasgow (McLellan AR et al Osteop Int 2003) questions the advisability of treating the elderly population without BMD measurements. Several other papers argue against this approach. I would recommend the committee read the work on the lack of age effects and fracture outcomes especially the NORA study which argued against an ageist approach (Siris E et al JBMR 2004).
- 4) It is difficult to agree that the alternative therapy recommended by the committee as alternative treatments to alendronate require patients to be suffering a greater degree of severity of illness. Surely an alternative therapy should be prescribed under the same clinical conditions as the initial recommended treatment.
- 5) HRT has been shown to be effective in several publications from the WHI study and yet has been ignored in this analysis.
- 6) Alendronate has been made the drug of choice in primary prevention. This commentator would like to see the evidence quoted from the literature that all generic forms of alendronate (“with the lowest acquisition price”) have the same efficacy as Fosamax and evaluate the outcome data to support their use before such a recommendation is made. There is some data that suggests this may not be the case (see Epstein S et al Curr Med Res Opin 2003, Hough S. SAfr Med J 2006)

- 7) The data on the effects of proton pump inhibitors on the efficacy of alendronate should be taken into greater account when making current recommendations.
- 8) It is very surprising that other efficacious agents have been excluded from use by these documents or given lower ratings based purely on cost. It appears that cost considerations are dominating this appraisal document and pronouncement. Surely the value of second line agents with effectiveness against fracture in post-menopausal women who are unable to tolerate the first line therapy should be recognised by the appraisal group.
- 9) In making the cost comparisons the etidronate assessment includes the costs of calcium but the alendronate costing does not appear to include this.
- 10) It would serve patients better if the NICE panel recognised that all, bisphosphonates are best taken on an empty stomach where possible to aid absorption rather than between meals as stated in the document (see etidronate recommendations). Also it is recommended that patients should not take any other treatment along with the bisphosphonate.
- 11) The recent identification of the serious side effect resulting from the use of strontium ranelate, DRESS, should be mentioned in the document (4.1.29).
- 12) The type of screening programme that could be implemented should be re-considered. Costs effective analyses based on peripheral scanning and other approaches should now be assessed in the light of the published literature (Siris E et al Osteop Int 2006, Miller P et al J Clin Densitometry 1998, Miller PD et al Arch Int Med 2004)
- 13) Having identified the very serious nature of this condition within the document the current provisional recommendations are not a sound and suitable basis for the preparation of guidance to the NHS.

Additional Comments Related to the Documentation

The Committee have disregarded the evidence presented that shows ways of improving persistence and compliance with bisphosphonate therapy for either primary or secondary prevention. For a small amount of investment a significant return can be obtained by using biochemical markers of bone metabolism or nurse/physician led feed back to patients on compliance (Delmas P et al JCEM 2007, Eastell et al JBMR 2003, Clowes et al JCEM 2004). The committee should review the literature that exists in this area of the technology appraisal. The implications of this data should be included in the economic analyses with increased persistence factored into the calculations and assumptions made. Although hip fracture is a “crucial goal” in the management of osteoporosis there is significant evidence pointing to the relatively “high cost” of vertebral fracture in terms of morbidity and the importance of reducing vertebral fracture incidence in patients with osteoporosis and this should not be underestimated by the committee (eg Borgstrom et al Osteop Int 2006).

Once again the committee have ignored the science base on the effect of strontium on calcium measurement. Despite previous responses on this matter the documentation still incorrectly has a statement that strontium, in the doses currently prescribed, can affect the measurement of calcium in the blood or urine (6.3). At the concentrations of strontium prescribed there is no statistically significant effect on calcium measurement in the blood.

There can be an effect at very high doses or immediately after a dose on urinary calcium excretion estimates but even this is minimal. I would like to see a reference quoted that backs up the current incorrect statement on this in the document.