Society for Endocrinology

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, strontium ranelate and teriparatide for the secondary prevention of osteoporotic fragility fractures in postmenopausal women.

Whilst the Society welcomes the fact that the long drawnout process of the Institute offering advice on the management of osteoporosis is coming to a resolution, we do have some concerns that the current analyses will result in advice that may not offer optimal therapy for people with osteoporosis. We therefore offer the following observations in the hope that the appraisal committee will be able to develop guidance that takes into account not only the clinical and cost effectiveness issues raised in the assessment report, but also the concerns that affect clinicians in their day-to-day dealing with patients.

General Issues

We are concerned that the basis on which the decision regarding cost effectiveness of treatment has been made has been changed from the previous advice on osteoporosis, moving from a cost per QALY of £30,000 to the much more stringent £20,000. Not only does this have significant implications for the outcome of the recommendations, but it also leads to the inescapable conclusion that osteoporosis is not as important as many other diseases upon which the Institute has recently given advice. Whilst we realise that it is within the discretion of the committee to advise the level of cost per QALY threshold it seems strange to change this from the threshold used for previous advice without offering any explanation.

We suspect that, largely as a result of the above change in the cost effectiveness threshold, the advice recommended in this assessment report is very different from that which had previously been issued regarding the use of bisphosphonates in the secondary prevention of osteoporotic fractures. Whilst we understand that medical practice must change with the advent of new knowledge, we are not aware of any information that would lead to such a downgrading of advice that assessment for the possibility of osteoporosis is not even recommended for a postmenopausal woman presenting with a fragility fracture under the age of 55. Even after 55 such women would not be eligible for further assessment in the absence of additional clinical risk factors until the age of 70. Under current advice all these patients would have been eligible for bone density assessment and possible treatment depending on the results of that assessment. Most international opinion has actually held that the Institute's current advice is leaning towards the conservative side of acceptable clinical behaviour and although it has been accepted by clinicians in this country, any attempt to rein in the use of investigation and treatment in this particular at-risk group of patients is likely to alienate large sections of the clinical community and patient population.

Whilst the splitting of patient groups into those who present with an obvious risk of osteoporosis

and those who do not is necessary in order to apportion the cost of ascertainment, it does not necessarily represent the reality of clinical practice. There are certain disease states where osteoporosis, and subsequent fracture, is a well recognised complication and it would be judged a breach of clinical duty for a clinician not to explore the possibility of osteoporosis in these circumstances. Indeed, in such situations the Courts have found against clinicians who have failed to undertake DXA scanning in patients who have subsequently gone on to fracture. In these cases, where assessment of osteoporosis risk is considered part and parcel of management of the underlying disease, we believe that at the very least they should be explicitly included as 'self identifying risk factors'. This is particularly important in an area of practice where many diseases affecting the endocrine system have profound effects on the skeleton. In the population of women over the age of 50 who are being considered in this appraisal such diseases would include: premature menopause; hyperthyroidism; hypoparathyroidism; Cushing's disease; and acromegaly. In various areas of clinical practice other diseases and treatments, including many gastrointestinal and renal conditions, would also fall into this category.

With the WHO recommendations on identification of people at risk of osteoporotic fracture due to be published in the very near future we fear that adoption of an overly prescriptive approach might leave the NHS appearing to be very much at odds with the rest of the world. In addition the inevitable publicity that will surround the WHO initiative is likely to lead to some confusion amongst clinicians. It is therefore disappointing that the assessment report did not give the cost effectiveness of treating at a given level of fracture risk (expressed as 10y probabilities as per the WHO) and then give advice as to how that level of risk might be attained for each age group according to clinical risk factors and BMD whilst we await the final WHO document.

Specific Issues

For many of the scenarios, the cost per QALY appears to be well under the stated threshold of £20,000. However, no information is given as to the effect of altering the identification criteria (for example a change of T score threshold from -2.5 to -2.0) on the cost per QALY of that intervention. Without such information it is very difficult to comment on the figures in front of us. Furthermore, it will be very difficult for the committee to decide on the appropriate intervention if the calculated cost per QALY was actually £20,001 and was therefore excluded from the report as being above the 'magic' threshold.

The cost of medication is now out of date. The latest drug tariff cost for 70 mg alendronic acid is £13.27 per four tablets (http://www.ppa.org.uk/edt/August_2006/mindex.htm) which equates to a total annual cost of £172.51. Because alendronic acid is now within category M, this cost is likely to decrease at intervals of three months until the cheapest price currently being offered to pharmacists is reached. Likewise the current drug tariff price for a month's supply of omeprazole at 20 mg per day is £7.54 (http://www.ppa.org.uk/edt/August_2006/mindex.htm). If these prices are not reflected in the advice then clearly the cost effectiveness of the interventions will have been grossly misinterpreted. We would therefore recommend that, rather than adopting the base case scenario, the committee base their recommendations on the sensitivity analysis in which the cost of alendronate has been halved, although we would prefer to see a new analysis undertaken using the correct price with appropriate sensitivity analysis to allow for future price reductions.

The utility multipliers associated with the various clinical states appear to bear little relationship to the reality of the clinical situation. In particular, the disutility associated with gastrointestinal side-effects has been set at the same as that associated with ongoing vertebral fracture. In our clinical experience this is a gross distortion of reality.

The strategy associated with the development of gastrointestinal side-effects in the assessment report does not reflect clinical reality. In most cases cessation of treatment with a bisphosphonate is always necessary to achieve a rapid resolution of symptoms. If this fails to improve symptoms then a proton pump inhibitor is prescribed. Most clinicians would not agree that there is a case for the use of H2 antagonists in the first line management of dyspeptic

symptoms today.

29 August 2006

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