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SENT BY EMAIL ONLY

9th July 2007

Dear Dr. Longson,

Joint appeal by the National Osteoporosis Society, the Society for Endocrinology, the British Society for Rheumatology and the Bone Research Society regarding the NICE Final Appraisal Determinations:

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

The National Osteoporosis Society (NOS), the Society for Endocrinology, the British Society for Rheumatology and the Bone Research Society ("the Societies") wish formally to notify the Institute of their intention to appeal the guidance contained in the above Final Appraisal Determinations (FADs). This appeal is on the grounds of fairness, of perversity, and of exceeding powers, as described in your letter of 18th June 2007 accompanying the FADs.

We believe that many of the problems relating to these appraisals have been due to the impasse between the Institutes' two advisory bodies; the Technology Appraisal Committee and the Guideline Development Group (GDG), both of whom have been considering the appropriate management of osteoporosis. These two advisory groups have repeatedly drawn different conclusions from the same data. The approach taken by the GDG has been consistent but for the reasons outlined in this letter we do not believe that they will be able to make clinically appropriate and cost effective recommendations in the Guideline if they have to encompass recommendations contained in these FADs.

1 Ground 1: NICE has failed to act fairly and in accordance with the appraisal procedure set out in the 'Guide to the Technology Appraisals Process'

We appeal under ground one in nine instances as set out below

1.1 *The Institute changed the scope for these appraisals part way through the process and without consultation*

The Institute originally published the scope for the appraisal "*prevention and treatment of postmenopausal osteoporosis*" in August 2002 at the start of the appraisal process. The objective of the appraisal was stated to be:

“to establish the clinical and cost effectiveness of selective oestrogen receptor modulators (SERMs), bisphosphonates and parathyroid hormone (subject to licensing) for the prevention and treatment of osteoporosis and the prevention of osteoporotic fractures in post-menopausal women and to provide guidance to the NHS in England and Wales.”

The population of patients to be considered in the appraisal was defined as:

“Post-menopausal women at risk of developing osteoporosis or having a related fracture. Risk factors include: low bone mineral density, smoking, low body mass index, early menopause, family history of osteoporosis, untreated hypogonadism, corticosteroid therapy, other diseases which affect bone metabolism”.

Further to the consultation on the first Appraisal Consultation Document (ACD), during December 2003, the appraisal was divided into two parts; primary and secondary prevention. There was no revision to the scope at this stage, and the original scope continued to apply to both appraisals. The appraisal of secondary prevention was completed and issued as guidance in January 2005 (TA87). The appraisal of primary prevention has not yet resulted in any guidance.

The appraisal of technologies used in primary prevention, therefore began in December 2003 (initially as part of an appraisal of both primary and secondary prevention) and has proceeded on the basis of the original scope since that date. The review of TA87 (secondary prevention) was notified to stakeholders on 3 June 2005. In view of the fact that strontium ranelate was incorporated into both the primary prevention appraisal and the review of TA87 (secondary prevention) some additional scoping work was carried out in relation to this technology. There was however no modification to the scope applicable to the appraisal of bisphosphonates, raloxifene and teriparatide.

The first ACD was issued in December 2003 as part of the combined appraisal. The preliminary guidance related to the initiation of treatment and second or subsequent line therapy. It was stated to be directed to all patients within the population identified in the scope, with the exception of women with corticosteroid induced osteoporosis. However, the fourth ACD, issued in the primary prevention appraisal in February 2007, departed substantially from the agreed scope and the direction of the appraisal up until that point. In particular, the 2007 ACD (and the FAD) excluded the following groups of women covered by the scope:

- Second line treatment in women who do not respond to or are unable to tolerate alendronate
- Women for whom alendronate is contra-indicated

No explanation for this departure from the terms of the agreed scope which had formed the basis for the appraisal to date was provided and the change was not subject to separate consultation. The FAD merely provided a statement referring to the clinical guideline on osteoporosis and stating that this

“will cover the treatment of women who are contra-indicated to or have withdrawn from initial treatment, who have osteopenia and who are on long-term corticosteroid therapy. This technology appraisal guidance should be read in the context of the clinical guideline when it is available.”

Similarly, the original appraisal for secondary prevention proceeded on the basis of the original scope issued in August 2002 and guidance was issued in January 2005 (TA87), consistent with that scope. The review of TA87, which commenced in June 2005, also approached the appraisal on the same basis and this was reflected in the first and second ACDs issued in September 2005 and 2006 respectively. It was only when a third ACD was issued in February 2007 that it became clear that NICE had sought to introduce a substantial change to the scope for the appraisal, consistent with that proposed for primary prevention. In our responses to the February 2007 ACD we noted the need for a mandating link to the Guideline should second line therapies not be included in the appraisals, but this has not been incorporated.

The scope for an appraisal defines the way in which that appraisal will be directed and focused. The Societies and other stakeholders agreed to participate in the appraisal on the basis of the agreed scope for these appraisals. The unilateral decision by the Institute to change the scope for the appraisal towards the conclusion of the process is wholly inconsistent with the Institute's procedures and fundamentally unfair. Stakeholders have a legitimate expectation that NICE will adhere to its published procedures and the Societies have directed their submissions in both appraisals on that basis.

For completeness, we would say that we do not believe that the reference in the FADs to the clinical guidelines, to be published at a future date, is any answer to our concerns. It is only technologies recommended by NICE in technology appraisal guidance, that are subject to mandatory funding in accordance with NHS Directions and we would have objected strongly had there been any suggestion that NICE's guidance should select only a part of the population of patients with established osteoporosis or at risk of developing osteoporotic fractures, to receive the benefit of this mandatory funding requirement. Therefore, in order for NICE to fulfil its obligations under the remit issued by the Department of Health and the agreed scope for this appraisal by reference to the Clinical Guidelines, it would be necessary for the Guidance to include an express statement incorporating the recommendations in the Clinical Guidelines relating to treatment in (a) women for whom alendronate is contra indicated and (b) second and subsequent line therapy, so that NHS Directions will require that funding for such treatment is made available, in the same way as treatment addressed directly in the Guidance.

The issues set out in this point of appeal also, we believe, raise issues under ground 3 of NICE's procedures, excess of powers. The remit provided to the Institute for an appraisal is determined by the Department of Health and the scope is formulated consistent with the terms of that remit. In these circumstances, we believe NICE had no proper power unilaterally to modify the scope of the appraisal without proper direction from the Department of Health and consultation with stakeholders.

1.2 *The Institute has inappropriately based treatment decisions on age, which goes against the principles for the development of NICE guidance laid out in their Social Values Judgments*

The Social Values Judgments document states that the Institute's general principle is that "*patients should not be denied NHS treatment simply because of their age*". Principle 6 is:

"NICE clinical guidance should only recommend the use of a therapeutic or preventive measure for a particular age group when there is clear evidence of differences in the

clinical effectiveness of the measure in different age groups that cannot be identified by any other means”

The primary prevention FAD makes recommendations for treatment that are dependent on a woman's age, yet we do not believe there is any evidence to support this methodology. Indeed in paragraph 4.1.2 the FADs state:

“For this appraisal, reductions in RR associated with treatment were pooled regardless of the baseline BMD and fracture status of the participants in the studies. It was also assumed that these reductions in RR remain constant at all ages....”

The failure to base guidance on overall risk of fracture, rather than simply by reference to age, is inconsistent with the principles laid out in Social Values Judgment and is therefore unfair.

1.3 *The Institute has acted unfairly by failing to provide consultees with a live version of the economic model*

There have been many different versions of the economic analyses published during the five year development of these FADs, with numerous sensitivity analyses modelled. Results have been consistently cut off at cost per quality adjusted life years (CPQ) values of either £20K or £30K meaning that consultees have been unable to examine the true effects of sensitivity analyses and to see when analyses have approached cost effectiveness.

The NOS requested a live version of the SchARR economic model in October 2006, but we were advised by the project manager at that time that NICE were unable to provide a copy of the model due to Academic in Confidence information that it contained. Instead the Society was provided with a password protected, read-only version of the model, comprising stripped excel spreadsheets. These spreadsheets did not allow us to look at the effects of the sensitivity analyses in detail and therefore limited our ability to comment on the modelling throughout the appraisal development process. We were unable to check the accuracy of the base case analysis included in the read-only version because the auditing function was disabled and there was no possibility to carry out any reviews of the other sensitivity analyses presented.

The lack of transparency is unfair; it has inevitably affected the substance and detail of the challenge stakeholders can make to the assertions both during the consultation period and in the appeal process.

The Societies believe that the economic model is a central piece of the evidence which forms the basis for NICE's conclusions on cost effectiveness and that it should be fully disclosed and open to review by consultees. This would reduce the possibility of error and permit greater dialogue regarding the appraisal of technologies under consideration.

1.4 The Appraisal Committee has been inconsistent in its use of inputs and assumptions in the economic model, making changes despite there being no new evidence. It is unclear which inputs/assumptions have been used during the development process and this has precluded our ability to comment on and to understand the basis of the Guidance

In order to enable effective engagement in the consultation and appeal process, it is vital that stakeholders are given clear and detailed explanations of why and how decisions are reached.

During the course of the development of these appraisals, alendronate became available as a generic. This resulted in a reduction in price from £22.80, used in the 2005 ACDs, to the current price of £4.87 for 4 weeks supply. We would have expected this very substantial price reduction to have recurred in a finding that alendronate is cost effective for all eligible patients. However, although there have been no other significant changes in the evidence base during the appraisal process, the assumptions used during the course of this appraisal, have varied considerably, without adequate or any explanation and this has resulted in higher Incremental Cost Effectiveness Ratios (ICER) values than we believe are appropriate.

Accordingly, during the course of these appraisals there have been many changes to the base case assumptions, with a large number of sensitivity analyses; many of these are unexplained and the source data have not been identified. We have attempted to summarise these in the attached table. We include below specific inputs/assumptions that we believe have been changed during the appraisal process without adequate explanation. The lack of clarity in relation to these data which are, in a number of instances, inconsistent with published peer reviewed evidence, has prejudiced our ability to comment on the conclusions reached by the Institute. Furthermore, the effects of changes to these reports and assumptions are significant; the parameters referred to below are largely independent of one another and each assumption is generally conservative. Any errors associated with each parameter would be compounded in the model, producing extremely conservative ICER values.

1. The disutility associated with vertebral fracture has been reduced from the value used in the original economic model to that of hip fracture despite the existence of peer reviewed vertebral fracture specific data supporting the original value

The impact on quality of life the first year after a hip fracture is based on empirical estimates and similar estimates were used for vertebral fracture in the 2005 ACDs and also in the assessment report in 2006. However, the adverse impact on quality of life for the first year of a vertebral fracture was reduced by 7.1 % from the value derived from empirical observations in later ACDs as well as in the most recent FADs. In other appraisals the committee has stipulated that the optimal strategy is to use evidence from trial data, however, on this occasion the committee has decided to make a "guess" at the disutility. The explanation provided in 4.3.10 of the primary prevention FAD (4.3.11 for secondary prevention) is that

"The Committee considered the utility multiplier for the first year after a vertebral fracture used in the base-case analysis and noted that it was considerably lower than that for a hip fracture. Although the Committee acknowledged that vertebral fracture can lead to greatly reduced quality of life, it considered that it was

implausible that this would so greatly outweigh the utility decrement associated with a hip fracture”

The Committee provides no explanation for its conclusion with respect to the disutility associated with vertebral fractures. Indeed the hip fracture utility multiplier used in the model is also very conservative. A systematic review of health state utility values for osteoporosis has shown that the value used is at the very top end of published estimates¹. This suggests that it is not the disutility associated with vertebral fracture that is too low but the disutility for hip fracture that is too high.

Furthermore, although there is a considerable short term loss of utility after a hip fracture, post surgery this reduces. The Appraisal Committee does not appear to have considered the fact that, with a vertebral fracture, the disutility is frequently much longer lasting.

2. The Appraisal Committee have pooled the efficacy of alendronate and risedronate despite the fact that they have their own robust evidence bases

Since the publication of TA87 there has been a progressive reduction in the mean relative risk reduction calculated by the Appraisal Committee for hip fracture by alendronate from a RR of 0.49 (for secondary prevention from the FIT study) to 0.62 (from meta-analyses of both primary and secondary prevention) to 0.71 (alendronate pooled with risedronate) used in the FADs. This is despite the absence of new evidence and the fact that no explanation for the change in approach has been provided. Similar changes of efficacy for vertebral and wrist fractures have been used in the FADs.

The relative risk reductions associated with treatment with alendronate used in the FAD are based on the pooled effects of alendronate and risedronate. It is unclear as to why the combined efficacy has been used given that each treatment has its own robust evidence base that shows differences in their efficacy.

3. The use of Health Resource Group (HRG) data significantly underestimates the true cost to the NHS of fractures

Costs used in the 2005 ACDs were based on data published in 1998. In June 2006 SchARR reviewed the evidence available to produce updated costs for hip, vertebral, wrist and other non vertebral fractures. SchARR presented three different approaches to estimating costs, including a method based on length of stay and cost per bed day that was in press, Health Resource Group (HRG) data and a review of published literature. The Appraisal Committee have chosen to use the HRG data, despite the fact that there are a number of problems with using these data to estimate costs of osteoporotic fractures; they generated the lowest estimate of costs calculated by SchARR.

¹ Brazier *et al* (2001) A systematic review of health state utility values for osteoporosis-related conditions. *Osteoporosis International* 13: 768-776

Although there is evidence that the costs associated with fracture have increased, the HRG costs are lower than those used in the 2005 ACD. Furthermore, the HRG costs presented for hip fracture are unrealistic, being less than 50 % of those published in the literature.

In addition, HRG data are not available for vertebral fracture and are inappropriate for forearm fracture in the elderly.

4. New assumptions have been introduced about the impact of side-effects on cost-effectiveness. These were established on the basis of a systematic survey conducted by ScHARR on bisphosphonate-related side effects. The incidence of side effects defined by this survey has increased tenfold in the latest economic models and has been applied to all treatments, in the absence of any supportive evidence or justification.

Neither randomised studies of efficacy, nor studies of side effects, have shown significant differences between placebo and patients treated with bisphosphonates. Furthermore, in clinical practice, where side effects are reported, drug switching tends to be used rather than treating the side effects at extra cost.

In the 2005 ACD NICE did not incorporate any assumptions about side effects into the cost-effectiveness analysis. However, in the ACDs published for primary and secondary prevention more recently side effects have been included. The value used originally was calculated from a systematic review conducted by ScHARR; however, in the FADs the incidence of side effects as estimated from this review has been arbitrarily multiplied ten-fold. No explanation for this approach and, in particular, the figures used have been provided.

The overturning of the evidence-base by the adoption of extreme one-way assumptions (in this case, 10 times the side effects disutility), contrary to the available evidence requires proper explanation. This is not provided in the FAD.

We suggest that the way that the Appraisal Committee has utilised the model – repeatedly changing the inputs without explanation or evidence to support the changes – precludes effective consultation and has prevented proper consideration as a result.

The Societies are also concerned that the future work of the Guideline Development Group may be undermined if they are forced by the Institute to adopt estimates that are not based on the evidence, and do not reflect UK clinical practice.

1.5 *The approach followed in relation to the appraisals of osteoporosis treatments is not consistent with other appraisals and has significantly reduced cost-effectiveness estimates*

Stakeholders are entitled to expect that NICE will adopt a consistent approach when carrying out appraisals. This is a fundamental part of equality of treatment which is a requirement of a fair procedure. In addition to the procedural requirements for consistency, an inconsistent approach is arbitrary, raising an inference of perversity. However in several important respects, the approach followed in these appraisals is inconsistent with that followed in other appraisals.

- Within the appraisal of osteoporosis therapies for primary prevention, the Institute has included the costs of BMD assessment of the entire population of potential patients when evaluating the cost-effectiveness of treatment in those patients ultimately found to require it. The inclusion of screening costs reduces the cost

effectiveness of the treatments and may be viewed as determining the outcome of the appraisal.

In this regard it is significant that in the NICE appraisal of statins, the Institute did not take account of screening costs, despite issuing guidance for primary prevention of cardiovascular disease, requiring patient screening, a situation closely comparable to that in the appraisal of osteoporosis. We believe that a consistent approach requires that osteoporosis treatments are considered in the same way.

Furthermore, when modelling "opportunistic" and "self identifying" case finding strategies, it was stated that patients with rheumatoid arthritis and those that are concerned about their risk of osteoporosis are included in the "self-identifying" category as they do not have to be identified from the general population. However, these patients, who are included in the primary prevention Guidance do have opportunistic case finding costs applied.

- In addition, the economic analysis used to calculate the cost effectiveness of statins was modelled over a remaining lifetime horizon, which is the standard and recommended approach for chronic disease. However, the model used for osteoporosis was run over a ten year time horizon. The effect of this has been to significantly reduce the cost effectiveness of treatment as it captures all the costs of assessment and treatment, but loses a component of the benefit.

The NOS believe that the approach to this appraisal has been inconsistent and unfair and has resulted in the devaluing of osteoporosis as a disease.

1.6 No explanation has been provided for the categorisation of clinical risk factors used to identify patients at the highest risk of fractures.

The use of clinical risk factors to improve a clinician's ability to identify patients at the highest risk of fracture is well established. There is now published evidence providing data on the contribution of individual risk factors to overall fracture risk. The use of risk factors in the primary prevention FAD, however, is inconsistent with their use in the ACDs.

In TA87 risk factors were included to improve the specificity of case finding. These risk factors were chosen as they were indicative of low bone mineral density and some are also independently related to fracture risk. The age-independent risk factors included were low BMI (less than 19kg/m²), maternal hip fracture before the age of 75, untreated early menopause, medical conditions that increase the risk of osteoporosis and those associated with prolonged immobility.

Since the publication of TA87 the risk factors used in subsequent osteoporosis ACDs have varied as illustrated in the attached table. The risk factors included in the FAD for primary prevention at section 1 are divided into two; those associated with low BMD and those associated with increased fracture risk. Women aged younger than 70 may be considered for treatment only if they have one condition suggestive of low BMD and at least one clinical factor suggestive of increased fracture risk. These requirements may produce arbitrary results. A patient who has two clinical risk factors (e.g. parental history of hip fracture and severe and long-term rheumatoid arthritis) - but none of the features listed as suggestive of low BMD - will be denied therapy. Similarly a patient with a very low T-score (T≤-4), Crohn's disease and a premature menopause would also be denied treatment despite their high risk of fracture. Additionally, the division of risk factors has resulted in combinations that would rarely or never be seen in clinical

practice, for example a patient with ankylosing spondylitis and concurrent rheumatoid arthritis. No explanation for this approach, which appears illogical and arbitrary, has been provided in the FAD.

We believe the requirement for clarification is heightened by the apparent inconsistency of the recommendations at section 1 of the FAD for primary prevention with the conclusion of the Committee at section 4.3.16 which states

“Therefore the committee concluded that women under 70 years of age with severe and long-term rheumatoid arthritis, ankylosing spondylitis, Crohn’s disease and conditions that have resulted in prolonged immobility, provided that they have one or more additional clinical risk factors, should be considered for DXA scanning and treatment initiated with alendronate if osteoporosis is confirmed.”

Furthermore, no proper explanation has been provided for the exclusion of important risk factors, such as treatment of women with breast cancer with aromatase inhibitors from the list of clinical risk factors at sections 1.3 and 1.4 of the FAD. Exclusion of such factors and ignoring serious risk factors such as corticosteroid use will lead to excess fractures and is contrary to good clinical practice.

1.7 *The Societies believe that the factors taken into account by the Appraisal Committee in reaching its conclusions with respect to technologies for osteoporosis have lacked transparency.*

In the “Guide to the Methods of Technology Appraisal”, (the Methods Guide) sections 6.2.6.10 and 6.2.6.11, the criteria for judgements about the acceptability of a technology as an effective use of NHS resources are laid out. Those sections define the acceptability of ICERs below £20,000/QALY, between £20,000-30,000/QALY and above £30,000/QALY.

There is no indication that the Appraisal Committee has considered the application of these factors in the context of this appraisal or even put itself in a position where it is able to do so. The Appraisal Committee’s decision to present only ICERs below £20,000 for primary prevention have meant that it has been impossible for us to see the effects of sensitivity analyses or the final conclusions reached by the Appraisal Committee as to the cost effectiveness of these technologies and therefore to understand why decisions have been made. We believe that the Appraisal Committee is required to consider and to explain its reasons for rejecting technologies where the ICER exceeds £20,000 by reference to the factors identified at sections 6.2.6.10 and 6.2.6.11 of the Methods Guide. That reasoning is absent in this case.

1.8 *No explanation has been provided for the Appraisal Committee’s apparent decision to set different cost-effectiveness thresholds for primary and secondary prevention.*

There is a further inequality in the use of ICERs in these appraisals with the ICER for primary prevention being set at £20,000 and the one for secondary prevention at £30,000/QALY. There is no difference between the morbidity, loss of quality of life or health economic burden in respect of a woman suffering a hip fracture who has not had a prior fragility fracture compared with a woman who has. The Appraisal Committee has not been transparent in their reasoning behind this decision. Furthermore, the approach used is inconsistent with the approach used, for example,

in the appraisal of statins for primary prevention of coronary heart disease, where a cut off of £30,000/QALY was applied.

In section 5.2.2.1 of the Methods Guide it states that

“consistency between submissions is needed to allow comparisons between appraisals of different technologies over time”

In circumstances where different QALY thresholds are set for different populations within the same therapeutic area, we believe that transparency requires a considered and carefully reasoned explanation of the approach followed.

1.9 The recommendations contained in the FAD will limit innovation in the field of osteoporosis

Paragraph 1.2.9 of NICE's Guide to the Technology Appraisal Process provides:

“The Institute also takes into account the longer-term interests of the NHS in encouraging innovation in technologies that will benefit patients”

We suggest that by only mandating one of the range of treatments for osteoporosis the Institute will in fact discourage innovation in the field of osteoporosis. Furthermore, the lack of guidance mandating second and subsequent line treatment or treatment for patients who cannot take alendronate will increase the current NICE blight, where PCTs are refusing to fund osteoporosis treatments in the absence of NICE guidance and will lead to “postcode prescribing”.

Indeed the governments own response to the Health Committee's second report of session 2001-02 on NICE warns that

“To reduce the appraisal programme substantially in favour of guidelines could result in significant innovations being omitted and the resurgence of postcode prescribing which NICE was intended to tackle”

In adopting the highly restrictive approach proposed in the FAD, NICE has seemingly failed to take this important requirement of its own procedures into account.

2 Ground 2: The Institute has prepared guidance which is perverse in the light of the evidence submitted

We appeal under ground two on the following points.

2.1 The estimated incidence of side effects with bisphosphonates (multiplied by ten times) has been applied to all of the other treatments appraised which is perverse given that each of the other treatment classes have different modes of action, different side effect profiles and their own evidence base

In section 4.2.21 in the secondary prevention FAD it states that the rate of bisphosphonate associated side effects (24 % in the first month and 3.5% thereafter) was also applied to raloxifene, strontium ranelate and teriparatide. These data were calculated from a systematic review carried out by SchARR into side effects from and compliance with the bisphosphonates alendronate, risedronate and etidronate. The application of these data to other treatments is perverse given that raloxifene, strontium ranelate and teriparatide are totally different classes of treatments with independent side effect profiles.

2.2 *The price for alendronate is already out of date and does not reflect the current price for this technology.*

The FAD, states that the price for alendronate is £7.31 for four 70mg tablets (four weeks treatment) giving an annual drug cost of £95.03. However, while this price was taken from the 1 November 2006 edition of the NHS Drug Tariff (paragraph 3.2 of the FAD) it is now out of date and the price has been reduced in July 2007 to £4.87 for four tablets. Such a reduction will inevitably exert a significant effect on the cost effectiveness of alendronate. We believe that guidance issued by NICE should be current and relevant at the date it is issued and that reliance on old pricing data to form the basis of recommendations, is perverse.

3 Ground 3: The Institute has exceeded its powers

We believe the Institute has exceeded its powers in the following three areas.

3.1 *The Institute has exceeded its powers in making changes to the scope referred by the Department of Health*

As indicated above (paragraph 1.1), the Societies believe that the changes made to the scope for this appraisal part-way through the appraisal process and contrary to the remit issued by the Department of Health, exceed the powers delegated to the Institute. We refer to the matters raised under paragraph 1.1 above.

3.2 *The Institute has exceeded its powers by making recommendations inappropriately based on age*

NICE's limitation of access to treatment, based restrictively by reference to age, rather than clinical need, represents a breach of article 8 and article 14 of the European Convention of Human Rights (ECHR).

Article 8 covers a range of personal interests raised by any characteristic of an individual affected by a particular decision.

In this case, access to treatment for primary prevention of osteoporotic fractures is determined primarily by reference to the age of the woman under consideration. Therefore, paragraph 1.1 of the FAD provides that women aged 70 years or older are required only to have one clinical factor suggestive of increased fracture risk or one medical condition suggestive of a low BMD together with a T-score of minus 2.5 SD or below. However, women younger than 70 years are required to have at least one medical condition suggestive of low BMD and at least one clinical factor suggestive of increased fracture risk together with a T-score of minus 2.5 SD or below. Whilst age is one of the risk factors associated with fracture risk, it is not the only determinant. The imposition of a 70 year threshold above which access to treatment is made easier, fails to recognise the risks that may be experienced by women below that threshold, who do not have the combinations of clinical risk factors identified in the FAD. Such women are treated adversely on the basis of a personal characteristic (age) contrary to the ECHR. We believe that this regime is not permitted as a result of article 14 of the ECHR because two women with equal risk of fracture would be treated differently, merely because one was over age 70 and one was below that age.

The Societies believe there can be no justification of such discrimination as a requirement for NICE to achieve its aims.

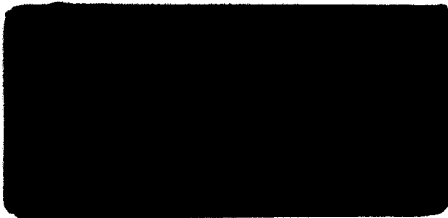
3.3 The inclusion of screening costs in the cost effectiveness analysis is outside NICE's remit

The inclusion of screening costs to identify women with a low BMD is inconsistent with the approach followed in other appraisals and outside NICE's remit for this appraisal. We refer to the matters set out at paragraph 1.5 above.

In conclusion, we believe that the FAD fails on grounds of fairness, perversity, and that the Institute may be exceeding its powers.

The Societies will be very happy to continue to work with NICE to ensure a satisfactory outcome to these appraisals.

Yours sincerely



Chief Executive, National Osteoporosis Society

For and on behalf of the National Osteoporosis Society, the Society for Endocrinology, the British Society for Rheumatology and the Bone Research Society

Enc. Table detailing changes in assumptions with time