Complete Summary

GUIDELINE TITLE

Bisphosphonates (alendronate, etidronate, risedronate), selective oestrogen receptor modulators (raloxifene) and parathyroid hormone (teriparatide) for the secondary prevention of osteoporotic fragility fractures in postmenopausal women.

BIBLIOGRAPHIC SOURCE(S)

National Institute for Clinical Excellence (NICE). Bisphosphonates (alendronate, etidronate, risedronate), selective oestrogen receptor modulators (raloxifene) and parathyroid hormone (teriparatide) for the secondary prevention of osteoporotic fragility fractures in postmenopausal women. London (UK): National Institute for Clinical Excellence (NICE); 2005 Jan. 51 p. (Technology appraisal; no. 87).

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

SCOPE
METHODOLOGY - including Rating Scheme and Cost Analysis
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SCOPE

DISEASE/CONDITION(S)

- Osteoporosis
- Osteoporotic fragility fractures

GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness
Management

Prevention
Treatment

CLINICAL SPECIALTY

Endocrinology
Family Practice
Geriatrics
Internal Medicine
Preventive Medicine

INTENDED USERS

Advanced Practice Nurses
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

To review the clinical and cost-effectiveness of selective oestrogen receptor modulators (SERMs), bisphosphonates, and parathyroid hormone (PTH) (subject to licensing) for the prevention and treatment of osteoporosis and the prevention of osteoporotic fractures in post-menopausal women

TARGET POPULATION

Postmenopausal women with osteoporosis who have normal calcium levels and/or vitamin D levels and who have already sustained at least one fracture as a result of the disease

Note: This guidance does not include women with corticosteroid-induced osteoporosis.

INTERVENTIONS AND PRACTICES CONSIDERED

1. Bisphosphonates (alendronate, etidronate, risedronate)
2. Selective oestrogen receptor modulators (SERMs) (raloxifene)
3. Parathyroid hormone (teriparatide)

MAJOR OUTCOMES CONSIDERED

- Clinical effectiveness
    - Vertebral or nonvertebral fracture
    - Quality of life
    - Associated effects (both adverse and beneficial)
    - Continuance and compliance
- Cost effectiveness

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Clinical Excellence (NICE) commissioned an independent academic centre to perform a systematic literature review on the technology considered in this appraisal and prepare an assessment report. The assessment report for this technology appraisal was prepared by The University of Sheffield, School of Health and Related Research [ScHARR]. (See the "Availability of Companion Documents" field.)

Clinical Effectiveness

Search Strategy

Because of the range of interventions and comparators under review, the literature search aimed to identify all literature relating to the prevention and treatment of osteoporosis. The main searches were conducted in May and July 2002, and updated in September and October 2002. The utilities searches were performed in October and November 2002.

Sources Searched

Fourteen electronic bibliographic databases were searched, covering biomedical, science, social science, health economic, and grey literature. A list of the databases searched is provided in Appendix 2 of the Assessment Report (see "Availability of Companion Documents" field).

In addition, the reference lists of relevant articles and sponsor submissions were handsearched, and various health services research-related resources were consulted via the Internet. These resources included health economics and health technology assessment (HTA) organisations, guideline-producing agencies, registers of generic research and trials, and specialist sites. These additional sources are listed in Appendix 3 of the Assessment Report (see "Availability of Companion Documents" field).

Search Terms

A combination of free-text and thesaurus terms was used. General "population" search terms (e.g., osteoporosis, bone, density, diseases, fracture, etc) were used in order to identify all potentially relevant studies. "Intervention" terms were not used in the main searches since it was felt that these might restrict the results and cause possibly relevant articles to be missed. Utilities searches were performed for breast cancer and for osteoporosis fractures as part of the

economic evaluation section of the report. Copies of the Medline search strategies are included in Appendix 4 of the Assessment Report (see "Availability of Companion Documents" field). Search strategies for the other databases are available on request.

Search Restrictions

No language, date or study-type restrictions were applied to the searches. However, the Biosciences Information Service (BIOSIS) search was performed as title only, and the Citation Indexes searches were limited with brief clinical trials, systematic reviews, guidelines, and economics filters, and to title only, in order to keep the number of hits to a sensible level. An randomized controlled trial (RCT) filter, an economics and quality of life evaluations filter, and a systematic reviews filter were used in the main searches performed in Medline and Embase to assist the identification of articles of these types (see Appendix 5 of the Assessment Report [see "Availability of Companion Documents" field]). After the searches were completed, because of the large number of references retrieved, only the articles identified using these specific filters, the articles from the databases that were not searched with filters (such as BIOSIS), and the papers found through handsearching etc, were reviewed.

Inclusion and Exclusion Criteria

Inclusion Criteria

Participants: Women with primary osteoporosis who were at least 6 months postmenopausal

Interventions:

- Bisphosphonates
    - Alendronate
    - Etidronate
    - Risedronate
- Selective oestrogen receptor modulators (SERMs)
    - Raloxifene
- Teriparatide (recombinant human parathyroid hormone (1-34))

Comparators:

- Vitamin D
- Calcitriol (a vitamin 1alpha-hydroxylated derivative)
- Pharmacological doses of calcium
- Oestrogens (opposed and unopposed)
- Exercise
- Placebo
- No treatment

Outcome Measures: Vertebral or nonvertebral fracture, associated effects, quality of life related to the study intervention, continuance and compliance

Study Design: Randomised controlled trials (RCTs). Trials were accepted as RCTs if the allocation of subjects to treatment groups was described by the authors as either randomised or double-blind.

A discussion of outcome measures is presented in section 3.1.2.1. of the Assessment Report (see "Availability of Companion Documents" field.)

Exclusion Criteria

Studies were excluded if they included participants with secondary osteoporosis (e.g., related to therapy with corticosteroids), or drew their participants exclusively from patients with specific diseases known to affect fracture rates (e.g., Parkinson's disease).

Only published studies (including those only available in abstract form) were included. As unpublished studies are more likely than published studies to demonstrate small or absent treatment effects, it is recognised that this approach is likely to overestimate the true effects of treatment. However, it was not possible in the time available to seek out unpublished studies.

It had originally been intended to include all relevant studies, whatever the language of publication. However, for practical reasons, it was in fact possible only to include those published in English, French, German, Italian or Spanish. This led to the exclusion of one possibly relevant study published only in Japanese.

Sifting

In principle, the references identified by the literature searches were sifted in two stages, being screened for relevance first by title and then by abstract. However, as it was not possible to identify all relevant studies with fracture outcomes from titles alone, the title sifting stage was used essentially to reject studies which were clearly irrelevant. Following this, the abstracts of all studies which used the relevant interventions in the relevant populations were screened (for studies which did not provide abstracts, the full studies were screened). Twenty-eight studies which had been identified by the literature searches were not identified as relevant at the abstract sifting stage, but were identified from other reviews as reporting fracture outcomes. The reason for this was that, as fracture was only a secondary outcome measure in many studies, it was therefore not reported in the abstract.

Economic Analysis

Identifying the Studies

The review has drawn on papers identified from a series of systematic searches undertaken for a Health Technology Assessment (HTA) review of treatment for osteoporosis. These include searches of papers reporting economic evaluation of the prevention and treatment of osteoporosis, and those reporting on quality of life associated with the main fracture states, breast cancer and coronary heart disease. Studies were identified through searches of electronic databases, hand searching, citation searching, reference list checking and those known to

researchers involved in the HTA review (Appendix 8 of the Assessment Report [see "Availability of Companion Documents" field]).

NUMBER OF SOURCE DOCUMENTS

Clinical Effectiveness

Ninety randomized controlled trials (RCTs) met the inclusion criteria relating to the five interventions (alendronate, etidronate, risedronate, raloxifene and teriparatide), and to five comparators (calcium, calcium plus vitamin D, calcitriol, HRT and exercise) as well as placebo or no treatment.

The Assessment Report reviewed data from 39 published RCTs in postmenopausal women where fracture or health related quality of life was a primary endpoint and where one of the five drugs of interest was compared with a relevant comparator.

Cost Effectiveness

The Assessment Group provided a cost-utility model.

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Meta-Analysis of Randomized Controlled Trials
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Clinical Excellence (NICE) commissioned an independent academic centre to perform a systematic literature review on the technology considered in this appraisal and prepare an assessment report. The assessment report for this technology appraisal was prepared by The University of Sheffield, School of Health and Related Research [ScHARR]. (See the "Availability of Companion Documents" field.)

Clinical Effectiveness

Data Extraction Strategy

Data were extracted by one reviewer, using customised data extraction forms. Where available, the following data will be reviewed:

- Incident vertebral fractures
- Incident nonvertebral fractures
- Incident hip fractures
- Incident wrist fractures
- Quality of life
- Associated effects (both adverse and beneficial)
- Continuance and compliance

Quality Assessment Strategy

The methodological quality of all trials which met the inclusion criteria was assessed using the tool developed by Gillespie et al.* This tool was selected because it was intended specifically for the assessment of randomised or quasi-randomised trials of interventions designed to prevent fractures associated with osteoporosis.

The quality assessment tool included the following items:

- Adequacy of randomisation, and masking of randomisation
- Blinded assessment of outcomes—whether outcome assessors were blind to subjects' treatment allocation
- Withdrawals—whether the outcomes of people who withdrew were described and included in the analysis
- Comparability of groups at baseline
- Confirmation of diagnosis of hip or other appendicular skeleton fracture
- Method of diagnosis of vertebral fracture

Definitions of the various levels of randomisation and concealment of randomization derived from Prendiville et al. 1988** were incorporated in the tool (see Appendix 6 of the Assessment Report [see "Availability of Companion Documents" field]).

It is recognised that the quality assessment tool assesses reporting quality, and not necessarily the true methodological quality of each study. However, where trials were reported in more than one publication, the quality score was calculated on the basis of the combined data from all relevant publications.

Blinding of the quality assessors to author, institution or journal was not considered necessary.

The quality assessment of studies included in the review of clinical effectiveness was carried out by one researcher.

*Gillespie W, Avenell A, Henry D, O'Connell D, Robertson J. Vitamin D and vitamin D analogues for preventing fractures associated with involutional and post-menopausal osteoporosis. The Cochrane Library (Oxford) **2001 Issue 4 (27p) (27 ref 21 bib) Update Software, online of CD-ROM, updated quarterly, 2001; 2001-2ROM.

*Prendville W, Elbourne D, and Chalmers I. The effects of routine oxytocic administration in the management of the third stage of labour: an overview of the evidence from controlled trials. British Journal of Obstetrics & Gynaecology 1988; 95 3-16

Meta-Analysis Strategy

Studies which met the review's entry criteria were eligible for inclusion in the meta-analyses provided that they reported fracture incidence in terms of the number of subjects suffering fractures, as this enabled calculation of the relative risk of subjects in the intervention group developing a new fracture or fractures, compared with subjects in the control group. Studies which reported only numbers of fractures, or fracture rates (i.e., numbers of fractures per hundred or thousand patient years), could not be included in the meta-analyses unless it was possible to obtain from the authors unpublished information on the number of subjects who suffered fractures. The meta-analysis of data relating to numbers of fractures or fracture rates would have violated the basic statistical assumption that the occurrence of one event does not increase the likelihood of a subsequent event, since once a subject has suffered an osteoporotic fracture, the risk of a subsequent fracture increases.

Ideally, only those studies which had fracture as a primary endpoint would have been included in the meta-analyses. However, pragmatically this was not possible as very few studies met this criterion (see Appendix 7 of the Assessment Report [see "Availability of Companion Documents" field]). Meta-analysis was carried out using Review Manager using the random-effects model, as this both allows generalization beyond the sample of patients represented by the studies included in the meta-analysis and provides wider, more conservative confidence intervals than the fixed-effects model.

Since the endpoint of interest was fracture, it seemed appropriate (*pace* Meunier) to include open-label studies.

To ensure comparability, the meta-analyses of vertebral fractures only pooled data from studies which used the same definition of vertebral fracture. Where possible, data were pooled from studies using a definition which required a 20% or greater reduction in anterior, middle, or posterior vertebral height: as noted above, this definition was felt to identify fractures more reliably than a definition which required a 15% or greater reduction.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Considerations

Technology appraisal recommendations are based on a review of clinical and economic evidence.

Technology Appraisal Process

The National Institute for Health and Clinical Excellence (NICE) invites 'consultee' and 'commentator' organisations to take part in the appraisal process. Consultee organisations include national groups representing patients and carers, the bodies representing health professionals, and the manufacturers of the technology under

review. Consultees are invited to submit evidence during the appraisal and to comment on the appraisal documents.

Commentator organisations include manufacturers of the products with which the technology is being compared, the National Health Service (NHS) Quality Improvement Scotland and research groups working in the area. They can comment on the evidence and other documents but are not asked to submit evidence themselves.

NICE then commissions an independent academic centre to review published evidence on the technology and prepare an 'assessment report'. Consultees and commentators are invited to comment on the report. The assessment report and the comments on it are then drawn together in a document called the evaluation report.

An independent Appraisal Committee then considers the evaluation report. It holds a meeting where it hears direct, spoken evidence from nominated clinical experts, patients and carers. The Committee uses all the evidence to make its first recommendations, in a document called the 'appraisal consultation document' (ACD). NICE sends all the consultees and commentators a copy of this document and posts it on the NICE website. Further comments are invited from everyone taking part.

When the Committee meets again it considers any comments submitted on the ACD; then it prepares its final recommendations in a document called the 'final appraisal determination' (FAD). This is submitted to NICE for approval.

Consultees have a chance to appeal against the final recommendations in the FAD. If there are no appeals, the final recommendations become the basis of the guidance that NICE issues.

Who is on the Appraisal Committee?

NICE technology appraisal recommendations are prepared by an independent committee. This includes health professionals working in the NHS and people who are familiar with the issues affecting patients and carers. Although the Appraisal Committee seeks the views of organisations representing health professionals, patients, carers, manufacturers and government, its advice is independent of any vested interests.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

The Assessment Group provided a cost-utility model based on a modified, individualised Markov approach. The cost effectiveness was estimated separately for women at different ages (50, 60, 70, and 80 years), who have a T-score of –2.5 standard deviations (SD) and who have had a fragility fracture; this was the baseline risk in the modelling. As fracture risk can be increased by a further

decrease in bone mineral density (BMD) or by other clinical risk factors as described in section 2.6 of the original guideline document the Assessment Group also nominally increased the baseline risk by factors of 2 and 4 (respectively called 'doubled risk' and 'quadrupled risk' below).

The prevalence of fractures for women with a Z-difference of 0 was calculated and adjusted for different T-scores. For every age-cohort, the Z-difference was calculated as the difference between the T-score of the hypothetical patient (T-score of –2.5 SD) and the average T-score of the age-cohort. The Assessment Group model was based on BMD data from the United Kingdom (UK), and calculated fracture risk based on femoral neck T-scores. The model simulated patients either until they died or for up to 10 years (5 years of treatment plus 5 years linear fall time [that is, decline of effect to zero], except for teriparatide, where the fall time was 1 year). Although the time horizon was 10 years, the additional utility gained, through mortality prevented, was taken into consideration using a life-table approach. The comparator for the analyses was no treatment, but an adequate intake of calcium and vitamin D was assumed for all patients.

The cost-utility model included three additional variables to determine an appropriate cost per quality adjusted life year (QALY) for all technologies under appraisal: an age dependent gradient of hip fracture risk by Z-difference, the introduction of mortality related to vertebral and proximal humerus fractures, and an increase in the disutility associated with proximal humerus fractures.

See section 4.2. of the original guideline document for a detailed discussion of the cost-effectiveness analysis.

METHOD OF GUIDELINE VALIDATION

External Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Consultee organizations from the following groups were invited to comment on the draft scope, Assessment Report and the Appraisal Consultation Document (ACD) and were provided with the opportunity to appeal against the Final Appraisal Determination.

- Manufacturer/sponsors
- Professional/specialist and patient/carer groups
- Commentator organisations (without the right of appeal)

In addition, individuals selected from clinical expert and patient advocate nominations from the professional/specialist and patient/carer groups were also invited to comment on the ACD.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

This guidance covers the secondary prevention of osteoporotic fragility fractures in postmenopausal women who have sustained a clinically apparent osteoporotic fracture.

This guidance covers the treatment of postmenopausal women who have normal calcium levels and/or vitamin D levels. Unless clinicians are confident that women who receive osteoporosis treatment have an adequate calcium intake and are vitamin D replete, calcium and/or vitamin D supplementation should be provided.

This guidance does not cover the treatment of corticosteroid-induced osteoporosis.

1. Bisphosphonates (alendronate, etidronate, and risedronate) are recommended as treatment options for the secondary prevention of osteoporotic fragility fractures:
    - In women aged 75 years and older, without the need for prior dual energy X-ray absorptiometry (DEXA) scanning
    - In women aged between 65 and 74 years if the presence of osteoporosis is confirmed by DEXA scanning
    - in postmenopausal women younger than 65 years of age, if they have a very low bone mineral density (BMD, that is with a T-score of approximately –3 standard deviations (SD) or below*, established by a DEXA scan), **or** if they have confirmed osteoporosis plus one, or more, additional age-independent risk factor: low body mass index (<19 kg/m^2); family history of maternal hip fracture before the age of 75 years; untreated premature menopause; certain medical disorders independently associated with bone loss (such as chronic inflammatory bowel disease, rheumatoid arthritis, hyperthyroidism or coeliac disease); conditions associated with prolonged immobility.

2. In their choice of bisphosphonate, clinicians and patients need to balance the drug's overall proven effectiveness profile against tolerability and adverse effects in individual patients.
3. Raloxifene is recommended as an alternative treatment option, under the circumstances specified in Section 1 above, in women:
    - For whom bisphosphonates are contraindicated (see Summaries of Product Characteristics), **or**
    - Who are physically unable to comply with the special recommendations for use of bisphosphonates, **or**
    - Who have had an unsatisfactory response to bisphosphonates (as defined in Section 5 below), **or**
    - Who are intolerant of bisphosphonates (as defined in Section 6 below)

4. Teriparatide is recommended as a treatment option for the secondary prevention of osteoporotic fragility fractures in women aged 65 years and older who have had an unsatisfactory response to bisphosphonates or intolerance to bisphosphonates (as defined in Sections 5 and 6 below, respectively), **and**:
    - Who have an extremely low BMD (with a T-score of approximately –4 SD or below), **or**
    - Who have a very low BMD (with a T-score of approximately –3 SD or below) plus multiple fractures (that is, more than two) plus one, or

more, additional age-independent risk factor: low body mass index (<19 kg/m^2); family history of maternal hip fracture before the age of 75 years; untreated premature menopause; conditions associated with prolonged immobility

5. For the purpose of this guidance, an unsatisfactory response occurs when a woman has another fragility fracture despite adhering fully to treatment for 1 year and there is also evidence of a decline in BMD below her pre-treatment baseline.
6. For the purpose of this guidance, intolerance of bisphosphonates is defined as oesophageal ulceration, erosion, or stricture, or severe lower gastrointestinal symptoms, any of which warrants discontinuation of treatment with a bisphosphonate.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of evidence supporting the recommendations is not specifically stated.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Appropriate use of alendronate, etidronate, risedronate, raloxifene, or teriparatide in postmenopausal women to reduce the risk of osteoporotic fracture
- All five interventions have been shown to reduce the risk of vertebral fracture in women with severe osteoporosis with adequate calcium intakes. Alendronate and raloxifene have also been demonstrated to reduce the risk of vertebral fracture in women with adequate calcium or vitamin D intakes who have osteoporosis without fracture. However, only risedronate and teriparatide have also been demonstrated to reduce the risk of nonvertebral fracture in women with severe osteoporosis and adequate calcium intakes. Alendronate has been shown to do so in women with osteoporosis with or without fracture and with adequate calcium or vitamin D intakes. However, none of these drugs have been demonstrated, by direct comparison, to be significantly more effective than either each other or the other active interventions reviewed in this report.

POTENTIAL HARMS

Adverse Effects of Medication

- *Alendronate*: Adverse upper gastrointestinal (GI) events including nausea, dyspepsia, mild oesophagitis/gastritis and abdominal pain were reported in

about one-third of the participants in studies of alendronate. However, only one study found the increased frequency of these symptoms to be statistically significant relative to placebo. This is consistent with post-marketing studies indicating that around one-third of alendronate users experience upper-GI adverse events. In order to avoid oesophagitis, the Summary of Product Characteristics now recommends that alendronate should be taken upon rising for the day with a full glass of water. It is possible that these instructions were not followed in all of the studies, particularly the earlier ones.

- *Etidronate*: Higher rates of upper-GI adverse effects were found in the etidronate groups of four randomised controlled trials (RCTs), although the differences were not always statistically significant. However, non-RCT evidence and testimonies from clinical experts and patient experts suggested that etidronate may be associated with fewer upper-GI adverse effects than are other bisphosphonates.
- *Risedronate*: Overall and upper-GI adverse events were similar in the risedronate and placebo groups in all of the studies.
- *Raloxifene*: The most serious adverse effect associated with raloxifene is the approximately three-fold increased risk of venous thromboembolism. Statistically significantly higher incidences of hot flushes, arthralgia, dizziness, leg cramps, influenza-like symptoms, endometrial cavity fluid, peripheral oedema and worsening diabetes have also been found with raloxifene compared with placebo.
- *Teriparatide*: Nausea and headaches occurred more frequently with 40 micrograms/day teriparatide in the main placebo-controlled trial. In the smaller placebo-controlled trial, a proportion of women taking teriparatide were reported to suffer mild discomfort at the injection site. A systematic review of parathyroid hormone reported that treatment in a small proportion of women was associated with hypercalcaemia.

For full details of side effects and contraindications, see the Summary of Product Characteristics, available at http://emc.medicines.org.uk/.

CONTRAINDICATIONS

CONTRAINDICATIONS

Bisphosphonates (Alendronate, Etidronate, Risedronate)

- The use of bisphosphonates is contraindicated in people with hypocalcaemia. The use of risedronate and etidronate is contraindicated in people with severe renal impairment.
- Bisphosphonates should be used cautiously with women who have active upper gastrointestinal problems.

Raloxifene

Particular contraindications include a history of venous thromboembolism, hepatic impairment, cholestasis, severe renal impairment, undiagnosed uterine bleeding, and endometrial cancer. Raloxifene should not be co-administered with systemic oestrogens and, in patients with breast cancer, it should not be used for

osteoporosis treatment and prevention until treatment of the breast cancer, including adjuvant therapy, has been completed.

Parathyroid Hormone: Teriparatide

Particular contraindications include pre-existing hypercalcaemia, severe renal impairment, metabolic bone diseases other than primary osteoporosis (including hyperparathyroidism and Paget's disease of the bone), unexplained elevations of alkaline phosphatase, and previous radiation therapy to the skeleton.

For full details of side effects and contraindications, see the Summary of Product Characteristics, available at http://emc.medicines.org.uk/.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

This guidance represents the view of the Institute, which was arrived at after careful consideration of the available evidence. Health professionals are expected to take it fully into account when exercising their clinical judgement. This guidance does not, however, override the individual responsibility of health professionals to make appropriate decisions in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

Implementation and Audit

- All clinicians in National Health Service (NHS) Hospital and Primary Care Trusts who care for postmenopausal women who have had an osteoporotic fragility fracture should review their current practice and policies to take account of the guidance (see the "Major Recommendations" field).
- Local guidelines, protocols or care pathways that refer to the care of postmenopausal women who have had an osteoporotic fragility fracture should incorporate the guidance.
- To measure compliance locally with the guidance, the following criteria could be used. Further details on suggestions for audit are presented in Appendix C of the original guideline document.
    - For a woman aged 75 years or older who has had an osteoporotic fragility fracture, bisphosphonates are considered as treatment options for the secondary prevention of an osteoporotic fragility fracture, without the need for dual energy X-ray absorptiometry (DEXA) scanning.
    - For a woman aged between 65 and 74 years old who has had an osteoporotic fragility fracture, bisphosphonates are considered as treatment options for the secondary prevention of an osteoporotic fragility fracture, with DEXA-confirmed osteoporosis.

    - For a postmenopausal woman younger than 65 years of age who has had an osteoporotic fragility fracture, bisphosphonates are considered as treatment options if the woman has a very low bone mineral density or confirmed osteoporosis plus one or more additional age-independent risk factors.
    - For a postmenopausal woman with osteoporosis who has had an osteoporotic fragility fracture, raloxifene is considered as an alternative treatment option, under the circumstances specified above if she meets any of the following.
        - She has a contraindication to bisphosphonates.
        - She is physically unable to comply with the special recommendations for use of bisphosphonates.
        - She has had an unsatisfactory response to bisphosphonates.
        - She is intolerant of bisphosphonates.
    - For a woman aged 65 years or older who has had an unsatisfactory response to bisphosphonates or intolerance to bisphosphonates, teriparatide is considered as a treatment option for the secondary prevention of an osteoporotic fragility fracture **only** if the woman either has an extremely low bone mineral density (BMD) or has a very low BMD plus multiple fragility fractures plus one or more age-independent risk factors.
- Local clinical audits on the care of women who have experienced an osteoporotic fragility fracture also could include criteria related to the prevention of falls based on the standards in the National Service Framework for Older People or criteria based on the clinical guidelines for prevention and treatment of osteoporosis published by the Royal College of Physicians. Issues that could be addressed in local clinical audits on osteoporosis include identifying high-risk patients, maintaining patient adherence with bisphosphonate drug therapy, educating patients about the condition and treatments, appropriate investigation and the involvement of the multiprofessional team in managing patients with osteoporosis.

IMPLEMENTATION TOOLS

Audit Criteria/Indicators
Foreign Language Translations
Patient Resources
Quick Reference Guides/Physician Guides

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness
Staying Healthy

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

National Institute for Clinical Excellence (NICE). Bisphosphonates (alendronate, etidronate, risedronate), selective oestrogen receptor modulators (raloxifene) and parathyroid hormone (teriparatide) for the secondary prevention of osteoporotic fragility fractures in postmenopausal women. London (UK): National Institute for Clinical Excellence (NICE); 2005 Jan. 51 p. (Technology appraisal; no. 87).

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2005 Jan

GUIDELINE DEVELOPER(S)

National Institute for Health and Clinical Excellence (NICE) - National Government Agency [Non-U.S.]

SOURCE(S) OF FUNDING

National Institute for Health and Clinical Excellence (NICE)

GUIDELINE COMMITTEE

Appraisal Committee

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) format from the National Institute for Health and Clinical Excellence (NICE) Web site.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Bisphosphonates (alendronate, etidronate, risedronate), selective oestrogen receptor modulators (raloxifene) and parathyroid hormone (teriparatide) for

the secondary prevention of osteoporotic fragility fractures in postmenopausal women. Quick reference guide. London (UK): National Institute for Health and Clinical Excellence (NICE); 2005 Jan. 4 p. (Technology appraisal 87). Available in Portable Document Format (PDF) from the National Institute for Health and Clinical Excellence (NICE) Web site.

- The clinical effectiveness and cost effectiveness of prevention and treatment of osteoporosis. Assessment report. The School of Health and Related Research (ScHARR), University of Sheffield. 2003 Dec. Electronic copies: Available from the NICE Web site.

Print copies: Available from the National Health Service (NHS) Response Line 0870 1555 455. ref: N0786. 11 Strand, London, WC2N 5HR.

Additionally, Audit Criteria can be found in Appendix C of the original guideline document.

PATIENT RESOURCES

The following is available:

- Bisphosphonates (alendronate, etidronate, risedronate), raloxifene and teriparatide for the secondary prevention of osteoporotic fragility fractures in postmenopausal women. Understanding NICE guidance – information for women with postmenopausal osteoporosis who have had a fracture as a result of the disease, their families and carers, and the public. London (UK): National Institute for Health and Clinical Excellence (NICE); 2005 Jan. 124 p. (Technology appraisal 87).

Electronic copies: Available in English and Welsh in Portable Document Format (PDF) from the National Institute for Health and Clinical Excellence (NICE) Web site.

Print copies: Available from the NHS Response Line 0870 1555 455. ref: N0787. 11 Strand, London, WC2N 5HR.

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