reference no: 201101P
Publication date: 23 08 2024

Clinical Commissioning Policy:

Teriparatide for Osteoporosis in Men (Adults)

Summary

Teriparatide is recommended to be available as a routine commissioning treatment option for osteoporosis in men[1] (adults) within the criteria set out in this document.

The policy is restricted to certain age groups as there is insufficient evidence to confirm safety and/or it is not recommended through the licence authorisation process to be used in those age groups not included in the policy.

Committee discussion

Clinical Panel agreed with the policy and recommended this proceed as a routine commissioning policy.

What we have decided

NHS England has carefully reviewed the evidence to treat osteoporosis in men (adults) with teriparatide. We have concluded that there is enough evidence to make the treatment available at this time.

The evidence review which informs this commissioning position is at Annex A

Links and updates to other policies

The Clinical Commissioning Policy: Teriparatide for the treatment of osteogenesis imperfecta (Adults) Reference: NHS England: 16002/P remains extant.

Plain language summary

About osteoporosis in men (adults)

Osteoporosis is a condition affecting the bones which causes them to lose their strength and increases the chances of them breaking.

[1] In this policy the term ‘men’ is used, based on the source evidence used in its development. This policy is also relevant to people with male anatomy who do not identify as men.

Women who have completed the menopause are at the highest risk of developing osteoporosis but it also affects a significant number of men. Lack of awareness of the disease in men can lead to a delay in diagnosis and treatment.

Osteoporosis is a common systemic skeletal disease characterised by compromised bone density and quality, predisposing to an increased risk of fracture [NIH Consensus Statement (2000)]. Definitive clinical diagnosis requires measurement of bone mineral density (BMD). The current reference diagnostic standard is dual- energy x-ray absorptiometry (DXA) of the hip [Kanis et al 2000]. Osteoporosis is conventionally diagnosed when BMD values lie 2.5 standard deviations or more below the young adult reference age, i.e. a T-score less than -2.5. Studies suggest that about 20% of all western women over the age of 50 years have osteoporosis and that the prevalence increases exponentially with age [World Health Organisation 1994].

The clinical impact of osteoporosis is due to the increased fracture risk and the consequent increased morbidity and mortality. Within Europe, osteoporotic fractures account for almost 2% of the burden of non-communicable disease and are associated with more disability adjusted life-years (DALYs) than common cancers, with the exception of lung cancer. The DALY's lost in Europe due to osteoporosis (2.0 million) are greater than for rheumatoid arthritis (1.0 million). Osteoporosis increases the risk of bone fracture at all sites, but typical 'low-trauma' fractures occur at the distal forearm, humerus, vertebrae and hip. It has been estimated that nearly one woman in two will experience an osteoporosis related fracture following menopause [Chrischilles et al1991].

About current treatment

Alendronate and risedronate are first line treatments in men. Where these are contraindicated or not tolerated, zoledronic acid or denosumab are the most appropriate alternatives.

About teriparatide

Teriparatide is licensed for treatment of osteoporosis in postmenopausal women and men at increased risk of fracture and treatment of osteoporosis associated with sustained systemic glucocorticoid therapy in women and men at increased risk of fracture. Teriparatide is recombinant parathyroid hormone (PTH) 1-34 which is administered subcutaneously for up to two years. It is an anabolic agent whereas the majority of standard treatments act as antiresorptive agents.

Teriparatide is a drug that works by increasing the formation of bone and so reduces the risk of fractures. It is recommended for people who have had several fractures despite having tried other drug treatments. Currently the drug is recommended by NICE for the secondary prevention of osteoporotic fragility fractures in postmenopausal women (TA161), under specified criterial. This policy seeks to address equality issues by recommending use in men.

Epidemiology and needs assessment

In developed nations, around one in three women and one in five men aged 50 years or more will suffer a fragility fracture during their remaining lifetime. In the UK, around 536,000 people suffer fragility fractures each year, including 79,000 hip fractures, with a cost in 2010 estimated at £3·5 billion, expected to rise to £5·5 billion per year by 2025 [Hernlund et al 2013]. For the individual, a hip fracture can be devastating with loss of independence and less than one third of patients make a full recovery; mortality at one year post-fracture is approximately 20% [Sernbo et al1993].

Implementation

Inclusion criteria

Teriparatide is recommended as an alternative treatment option for the secondary prevention of osteoporotic fragility fractures in men.

Exclusion criteria

Patients are excluded if they meet any of the following criteria:

- Severe renal impairment.
- Paediatric patients (less than 18 years), or young adults with open epiphyses.
- Hypersensitivity to the active substance or to any of the excipients
- Pre-existing hypercalcaemia
- Metabolic bone diseases (including hyperparathyroidism and Paget's disease of the bone) other than primary osteoporosis or glucocorticoid-induced osteoporosis
- Unexplained elevations of alkaline phosphatase
- Prior external beam or implant radiation therapy to the skeleton
- Patients with skeletal malignancies or bone metastases should be excluded from treatment with teriparatide

In addition, caution should be exercised in moderate renal impairment.

Starting criteria

Using the criteria in NICE TA161 as a guide, teriparatide is recommended as an alternative treatment option for the secondary prevention of osteoporotic fragility fractures in men:

- Who are unable to take alendronate and risedronate, or have a contraindication to or are intolerant of alendronate and risedronate (see below), or who have had an unsatisfactory response, which is defined as occurring when a man has another fragility fracture despite adhering fully to treatment for 1 year and there is evidence of a decline in BMD below his pre-treatment baseline, AND

- Who are 65 years or older and have a T-score of –4.0 SD or below, or a T- score of –3.5 SD or below plus more than two fractures, or who are aged 55– 64 years and have a T-score of –4 SD or below plus more than two fractures.

Because fracture incidence is related to absolute bone density regardless of gender it is important that this is taken into account when calculating fracture risk. Accordingly, T-scores used for fracture risk calculation in men should be based on the National Health and Nutrition Examination Survey (NHANES) female reference database. The online version of the FRAX Fracture Risk Assessment Tool does this automatically if absolute bone mineral density is entered and the manufacturer of the densitometer specified.

In line with the NICE guidance, intolerance of alendronate or risedronate is defined as persistent upper gastrointestinal disturbance that is sufficiently severe to warrant discontinuation of treatment, and that occurs even though the instructions for administration have been followed correctly.

Dose

The adult male dose is 20 micrograms daily for a maximum of 24 months.

Stopping criteria

Treatment may be stopped if the patient has adverse reactions. The maximum total duration of treatment with teriparatide should be 24 months. The 24-month course of teriparatide should not be repeated over a patient's lifetime.

Governance arrangements

The policy proposition should be used in conjunction with A03/S/a specialised endocrinology services (adult)

Mechanism for funding

Whilst Teriparatide is currently within tariff for osteoporosis in men and women it is important to acknowledge that prescribing of teriparatide should continue to follow the starting and stopping criteria contained within this policy. This ensures equity of access to treatment for both men and women based upon the guidelines contained within NICE TA161 for treatment in women.

Audit requirements

Clinical audit should be conducted periodically as part of the providers audit cycle.

Policy review date

This document will be reviewed when information is received which indicates that the policy requires revision. If a review is needed due to a new evidence base then a new Preliminary Policy Proposal needs to be submitted by contacting england.CET@nhs.net.

Our policies provide access on the basis that the prices of therapies will be at or below the prices and commercial terms submitted for consideration at the time evaluated. NHS

England reserves the right to review policies where the supplier of an intervention is no longer willing to supply the treatment to the NHS at or below this price and to review policies where the supplier is unable or unwilling to match price reductions in alternative therapies.

Equality statement

Promoting equality and addressing health inequalities are at the heart of NHS England's values. Throughout the development of the policies and processes cited in this document, we have:

- Given due regard to the need to eliminate discrimination, harassment and victimisation, to advance equality of opportunity, and to foster good relations between people who share a relevant protected characteristic (as cited under the Equality Act 2010) and those who do not share it; and

- Given regard to the need to reduce inequalities between patients in access to, and outcomes from healthcare services and to ensure services are provided in an integrated way where this might reduce health inequalities.

References

Chrischilles EA, Butler CD, Davis CS, Wallace RB. (1991) 'A Model of Lifetime Osteoporosis Impact' Arch Inter Med 151: pp 2026-2032.

Hernlund E, Svedbom A, Ivergård M, Compston J, Cooper C, Stenmark J, McCloskey EV, Jönsson B, Kanis JA. (2013) 'Osteoporosis in the European Union: Medical Management, Epidemiology and Economic Burden. A Report Prepared in Collaboration with the International Osteoporosis Foundation and the European Federation of Pharmaceutical Industry Associations (EFPIA)' Arch Osteoporos 8 (1-2): 136.

Kanis JA, Glüer CC. (2000) 'An Update on the Diagnosis and Assessment of Osteoporosis with Densitometry' Osteoporosis International 11 pp192-202.

NIH Consensus Statement (2000) Osteoporosis Prevention, Diagnosis, and Therapy. March 27-29;17: pp1–45.

Neer RM, Arnaud CD, Zanchetta JR, Prince R, Gaich GA, Reginster JY, Hodsman AB, Eriksen EF, Ish-Shalom S, Genant HK, Wang O, Mitlak BH. (2001) 'Effect of Parathyroid Hormone (1-34) on Fractures and Bone Mineral Density in Postmenopausal Women with Osteoporosis' New England Journal Med. May 10; 344(19), pp.1434-41Niimi R, Kono T, Nishihara A, Hasegawa M, Matsumine A, Kono T, Sudo A. (2015) 'Analysis of Daily Teriparatide Treatment for Osteoporosis in Men' Osteoporosis International 26:1303–1309.

Orwoll ES, Scheele WH, Paul S, Adami S, Syversen U, Diez-Perez A, Kaufman JM, Clancy AD, Gaich GA. (2003) 'The Effect of Teriparatide [Human Parathyroid Hormone (1-34)] Therapy on Bone Density in Men With Osteoporosis' Journal of Bone and Mineral Research Volume 18, Number 1.

Sernbo I, Johnell O. (1993) 'Consequences of a Hip Fracture: A Prospective Study Over 1 Year' Osteoporosis International 3(3): pp 148-53.

World Health Organisation (1994). Assessment of Fracture Risk and its Application to Screening for Postmenopausal Osteoporosis. WHO Technical Report Series, Geneva.

Evidence Summary

1. NHS England has considered the evidence submitted as part of the preliminary policy proposal to establish the interim clinical commissioning policy statement, including the clinical criteria for initiating and discontinuing the intervention. This includes up to three of the most clinically impactful publications, identified using a literature search strategy defined by the clinical lead. These publications are summarised below.

Publication 1

2. Neer RM, Arnaud CD, Zanchetta JR, Prince R, Gaich GA, Reginster JY, Hodsman AB, Eriksen EF, Ish-Shalom S, Genant HK, Wang O, Mitlak BH. (2001) 'Effect of Parathyroid Hormone (1-34) on Fractures and Bone Mineral Density in Postmenopausal Women with Osteoporosis' New England Journal Med. May 10; 344(19), pp.1434-41

3. A randomised controlled trial assigned 1637 postmenopausal women with prior vertebral fractures to either 20 or 40 µg of teriparatide or placebo. The study was sufficiently powered to demonstrate significant differences in bone density between placebo and teriparatide treated patients. Median duration of observation was 21 months. In the 20 µg treatment group there was a 65% reduction in the risk of one or more new vertebral fractures, 53% less likely to have one or more new non-vertebral fractures. Bone density increased by 9% at the lumbar spine and by 3% at the femoral neck in the 20 µg per day treatment group.

4. 11% of women in the 40µg group, 6% of women in the 20 µg group and 6% of women in the placebo group withdrew from the study due to an adverse event. The most commonly reported adverse events were nausea, headache and dizziness. No cases of osteosarcomas were reported. The authors concluded that treatment of postmenopausal osteoporosis with parathyroid hormone 1 – 34, teriparatide, decreases the risk of vertebral and non-vertebral fractures; increases vertebral, femoral and total body bone mineral density; and is well tolerated.

5. The strength of the study was the scale and power statistically to identify clinically meaningful change in terms of fracture risk reduction. The limitation of the study design was that it did not include men.

Publication 2

6. Orwoll ES, Scheele WH, Paul S, Adami S, Syversen U, Diez-Perez A, Kaufman JM,

7. Clancy AD, Gaich GA. (2003) 'The Effect of Teriparatide [Human Parathyroid Hormone (1-34)] Therapy on Bone Density in Men With Osteoporosis' Journal of Bone and Mineral Research Volume 18, Number 1.

8. This study aimed to extend the observations in women to determine whether equivalence was demonstrated in terms of bone density in men. In total, 437 men with low bone density (2 SD below young adult male mean) at the hip or spine were randomised to either placebo, teriparatide 20 µg or 40µg. The study ran for 11 months in total. Surrogate markers for fractures were analysed including bone mineral density. At the end of the study, bone mineral density had increased by 5.9% at the spine ($p<0.001$) and 1.5 % at the femoral neck for the 20µg group

(p=0.029).

9. Adverse events were similar in the 20µg and the placebo group. The most common reported adverse effects were nausea and headache. There were no cases of osteosarcoma. The authors concluded that the positive bone mineral density responses to teriparatide in men highlighted its potential utility as a therapy for men with osteoporosis.

10. The strength of this study is that it was a large scale study in men looking at surrogate markers for fracture, (positive) changes in bone mineral density. The limitation of the study is that it was of relatively short duration and was not powered to demonstrate incident fractures. The population studied was predominantly Caucasian which may limit the wider applicability to other ethnic groups.

Publication 3

11. Niimi R, Kono T, Nishihara A, Hasegawa M, Matsumine A, Kono T, Sudo A. (2015) 'Analysis of Daily Teriparatide Treatment for Osteoporosis in Men' Osteoporosis International 26:1303–1309

12. This was a retrospective study comparing the effects of daily teriparatide treatment in postmenopausal women with osteoporosis and men with osteoporosis. Markers of drug effect including changes in bone mineral density and changes in bone turnover markers were analysed. The study population was 488 women and 75 men.

13. All patients received the standard teriparatide dosage of 20 µg per day and study observations were made for the first 12 months. In men, the percentage change in lumbar spine bone density rose significantly by 11.3% and the femoral neck bone density increased by 0.4% at 12 months. In postmenopausal women, the percentage change in lumbar spine bone density increased by 9.6% at the spine and by 2.4% at the femoral neck at 12 months.

14. The percent and absolute bone density increases in lumbar spine and femoral neck between men and women were similar. Using P1NP as a bone turnover marker, the authors show that the absolute increases in this marker at four, eight and 12 months were similar in men and women. The authors concluded that daily teriparatide treatment was as effective in men as in postmenopausal women regardless of sex differences when analysed according to bone turnover markers and bone mineral density change.

15. The strength of this study is that there is a direct comparison between the effects of teriparatide in men and women, demonstrating no significant change according to sex. The limitation of the study is that only bone turnover markers and bone density was feasible to measure and there are no clear fracture outcome data.