PTAC and Osteoporosis Subcommittee minutes for teriparatide (parathyroid hormone)

Osteoporosis Subcommittee October 2001

The subcommittee referred to a recently published study (N Engl J Med Vol. 344; No. 19; May 10, 2001 sponsored by Eli Lilly) regarding the treatment of postmenopausal women with parathyroid hormone. The subcommittee considered that the data suggested that it produced significant increases in bone mineral density and substantially decreased the risk of fractures. The subcommittee considered that although parathyroid hormone could be very effective in treating severe osteoporosis it was unlikely that it would be widely used as it had to be given by daily injections. The subcommittee considered that parathyroid hormone would likely be used together with an anti-resorptive therapy in patients with severe osteoporosis who have had multiple fractures and low BMD scores despite the anti-resorptive therapy. The subcommittee requested that once the product was approved for sale in New Zealand PHARMAC would consider it for funding.

Osteoporosis Subcommittee April 2009

The Subcommittee considered that there was a significant unmet need for anabolic therapy for osteoporosis. The Subcommittee considered that parathyroid hormone (PTH) could fill this unmet clinical need. PHARMAC staff noted that PTH was not registered for use in New Zealand. The Subcommittee **recommended** that PHARMAC staff follow-up with the supplier (Eli Lilly) around registration and pricing and look into the cost-effectiveness of PTH when used as a daily subcutaneous injection in patients unresponsive to other treatments with a T-Score ≤ -4 or a history of 3 significant osteoporotic fractures. Members considered that perhaps 100-200 patients would be eligible for treatment with PTH annually.

PTAC May 2010

The Committee noted that PHARMAC staff were seeking advice from PTAC in relation to several currently unfunded treatments for osteoporosis: risedronate, zoledronic acid and raloxifene as first-line or second-line treatments and teriparatide and strontium ranelate as second-line treatments only. The Committee noted that its advice would concentrate on the use of these treatments in postmenopausal osteoporosis (i.e., not glucocorticosteroid-induced osteoporosis or Paget's disease).

The Committee considered that of the funded treatments, alendronate was currently the first-line treatment of choice for osteoporosis. The Committee noted that usage of etidronate had declined over the past few years and considered that the available evidence suggested that it has only limited efficacy in osteoporosis.

The Committee considered that there was currently an unmet clinical need for a treatment for osteoporosis in patients who could not tolerate alendronate. The Committee considered that it would be useful to have a funded treatment with a different mechanism of action to bisphosphonates for patients who could not take bisphosphonates.

The Committee noted that all patients eligible for treatment with any of the five agents would require supplementation with calcium and vitamin D, and that funding a second-line treatment could increase prescribing of vitamin D, as patients would no longer be receiving vitamin D supplementation in the combination alendronate with cholecalciferol product.

The Committee noted that there did not appear to be any clinical trials comparing the treatments under discussion with each other, and indirect comparisons were difficult because of the different patient populations and treatment regimens used in the published trials of these treatments. In general, however, of the five unfunded treatments the Committee placed the greatest priority on funding zoledronic acid as a second-line treatment for osteoporosis in patients intolerant to alendronate, taking into account its efficacy, cost and tolerability profile. The recommendations for all other treatments were largely based on their cost relative to their benefits compared with currently funded treatments and alternative proposals for unfunded treatments. Members expressed a preference for strontium ranelate over raloxifene as a second-line treatment in patients intolerant to bisphosphonates, and considered that the superior efficacy of teriparatide for the same indication did not justify its cost (which is currently more than 15 times the cost of alendronate).

Application

The Committee noted that PHARMAC staff had sourced information on teriparatide (Forteo) for the Committee's review following a recommendation from the Osteoporosis Subcommittee to investigate this agent, and that Eli Lilly had provided an amended version of its Australian PBAC funding application to assist the Committee's review.

Recommendation

The Committee **recommended** that teriparatide be funded as a last-line treatment for osteoporosis subject to Special Authority criteria restricting its use to patients with evidence of ongoing fractures and/or T-scores < -3 after trying all funded osteoporosis treatments with a low priority and only if a significant price reduction could be achieved.

The Decision Criteria particularly relevant to this recommendation are: *(i) The health needs of all eligible people within New Zealand; (iii) The availability and suitability of existing medicines, therapeutic medical devices and related products and related things; (iv) The clinical benefits and risks of pharmaceuticals; (vi) The budgetary impact (in terms of the pharmaceutical budget and the Government's overall health budget) of any changes to the Pharmaceutical Schedule.*

Discussion

The Committee noted that teriparatide is a recombinant fragment of human parathyroid hormone and is an anabolic agent that stimulates new bone formation. It is indicated in New Zealand for use in the treatment of postmenopausal osteoporosis and in glucocorticosteroid-induced osteoporosis. It is administered as a 20 μg once-daily subcutaneous injection.

The Committee reviewed the key randomised controlled trial (Neer et al, N Engl J Med 2001;344:1434-41) in which 1,326 postmenopausal women with osteoporosis were assigned to receive teriparatide 20 μg daily, teriparatide 40 μg daily or placebo. Patients were intended to receive treatment for two years but the study was stopped early by the supplier because of findings that teriparatide increased the incidence of osteosarcoma in rats; as a result, the median duration of observation in the trial was 21 months. New vertebral fractures occurred in 14% of patients in the placebo group and in 5% and 4% of patients taking 20 μg and 40 μg teriparatide respectively; new non-vertebral fractures were seen in 6% of the placebo group and in 3% of patients in both teriparatide groups. Compared with placebo, teriparatide 20 μg increased overall BMD at most sites and both doses increased overall total-body BMD. Teriparatide was also found to reduce back pain and was associated with less height loss than placebo. Adverse events included nausea, dizziness and leg cramps.

The Committee noted that there was a lack of long-term safety data for teriparatide, which was reflected in the recommendation that patients receive a maximum of 18 months' treatment, although members noted that the supplier intended to apply for an extension of the maximum treatment time.

The Committee noted that the effectiveness of teriparatide is not reduced following bisphosphonate treatment. The Committee noted that the supplier had told PHARMAC staff that the benefits of teriparatide are only maintained if patients went on to bisphosphonate treatment after completion of teriparatide treatment.

The Committee considered that patients most likely to benefit from teriparatide would be patients with osteoporosis who do not respond adequately to bisphosphonate treatment. The Committee considered that it would be difficult to identify, and target treatment to these patients, but that an approximate measure would be evidence of ongoing fractures and those with T-scores < -3 despite ongoing treatment with bisphosphonates.

The Committee noted that teriparatide was significantly more expensive than all the other treatments under consideration and would, therefore, likely be dominated by the other options in any cost-utility analysis of teriparatide as a second-line treatment for osteoporosis.

The Committee considered that even if teriparatide was restricted to last-line use following failure of all other funded treatments there would be an unacceptably high financial risk at the current proposed price, because of the risk of extensive use in rest homes where patients would likely have tried all other options.