

30 June 2010

Proposal to fund zoledronic acid (Aclasta) and amend the alendronate Special Authority criteria

PHARMAC is seeking feedback on a proposal to fund zoledronic acid (Aclasta) for Paget's disease and osteoporosis (including glucocorticosteroid-induced osteoporosis), subject to Special Authority criteria, from 1 September 2010 through a provisional agreement with Novartis New Zealand Ltd.

If this proposal is approved, it is further proposed that the Special Authority criteria for alendronate are altered to ensure that patients who had previously had an approval for zoledronic acid would be able to access alendronate.

Feedback sought

PHARMAC welcomes feedback on this proposal. To provide feedback, please submit it in writing by **5 pm** on **Wednesday 14 July 2010** to:

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All feedback received before the closing date will be considered by PHARMAC's Board (or Chief Executive acting under delegated authority) prior to making a decision on this proposal.

Details of the proposal

- From 1 September 2010, zoledronic acid (Aclasta) 5 mg in 100 ml solution for infusion would be listed in Section B and in Part II of Section H of the Pharmaceutical Schedule at a price and subsidy of \$600.00 (ex-manufacturer, excluding GST).
- Zoledronic acid would be subject to the following restrictions in Section B of the Pharmaceutical Schedule:

Initial application – (Paget's disease) from any relevant practitioner. Approvals valid for 1 year for applications meeting the following criteria:

All of the following:

- 1 Paget's disease; and
- 2 Any of the following:
 - 2.1 Bone or articular pain; or
 - 2.2 Bone deformity; or
 - 2.3 Bone, articular or neurological complications; or
 - 2.4 Asymptomatic disease, but risk of complications; or

- 2.5 Preparation for orthopaedic surgery; and
- 3 The patient will not be prescribed more than one infusion in the 12-month approval period.

Initial application – (Underlying cause - Osteoporosis) from any relevant practitioner. Approvals valid without further renewal unless notified for applications meeting the following criteria:

Both:

- 1 Any of the following:
 - 1.1 History of one significant osteoporotic fracture demonstrated radiologically and documented bone mineral density (BMD) ≥ 2.5 standard deviations below the mean normal value in young adults (i.e. T-Score ≤ -2.5) (see Note); or
 - 1.2 History of one significant osteoporotic fracture demonstrated radiologically, and either the patient is elderly, or densitometry scanning cannot be performed because of major logistical, technical or pathophysiological reasons. It is unlikely that this provision would apply to many patients under 75 years of age; or
 - 1.3 History of two significant osteoporotic fractures demonstrated radiologically; or
 - 1.4 Documented T-Score ≤ -3.0 (see Note); or
 - 1.5 A 10-year risk of hip fracture $\geq 3\%$, calculated using a published risk assessment algorithm (e.g. FRAX or Dubbo) which incorporates BMD measurements (see Note); or
 - 1.6 Patient has had a Special Authority approval for alendronate (Underlying cause – Osteoporosis); and
- 2 The patient will not be prescribed more than one infusion in a 12-month period.

Initial application – (Underlying cause - glucocorticosteroid therapy) from any relevant practitioner. Approvals valid for 1 year for applications meeting the following criteria:

All of the following:

- 1 The patient is receiving systemic glucocorticosteroid therapy (≥ 5 mg per day prednisone equivalents) and has already received or is expected to receive therapy for at least three months; and
- 2 Any of the following:
 - 2.1 The patient has documented BMD ≥ 1.5 standard deviations below the mean normal value in young adults (i.e. T-Score ≤ -1.5) (see Note); or
 - 2.2 The patient has a history of one significant osteoporotic fracture demonstrated radiologically; or
 - 2.3 The patient has had a Special Authority approval for alendronate (Underlying cause – glucocorticosteroid therapy); and
- 3 The patient will not be prescribed more than one infusion in the 12-month approval period.

Renewal – (Paget's disease) from any relevant practitioner. Approvals valid for 1 year for applications meeting the following criteria:

Both:

- 1 Any of the following:
 - 1.1 The patient has relapsed (based on increases in serum alkaline phosphatase); or
 - 1.2 The patient's serum alkaline phosphatase has not normalised following previous treatment with zoledronic acid; or
 - 1.3 Symptomatic disease (prescriber determined); and
- 2 The patient will not be prescribed more than one infusion in the 12-month approval period.

The patient may not have had a prior approval for Paget's disease within the last 12 months.

Renewal – (Underlying cause was, and remains, glucocorticosteroid therapy) from any relevant practitioner. Approvals valid for 1 year for applications meeting the following criteria:

Both:

- 1 The patient is continuing systemic glucocorticosteroid therapy (≥ 5 mg per day prednisone equivalents); and
- 2 The patient will not be prescribed more than one infusion in the 12-month approval period.

The patient may not have had a prior approval for underlying cause glucocorticosteroid therapy within the last 12 months.

Renewal – (Underlying cause was glucocorticosteroid therapy but patient now meets the 'Underlying cause – osteoporosis' criteria) from any relevant practitioner. Approvals valid without further renewal unless notified for applications meeting the following criteria:

Both:

- 1 Any of the following:
 - 1.1 History of one significant osteoporotic fracture demonstrated radiologically and documented BMD ≥ 2.5 standard deviations below the mean normal value in young adults (i.e. T-Score ≤ -2.5) (see Note); or
 - 1.2 History of one significant osteoporotic fracture demonstrated radiologically, and either the patient is elderly, or densitometry scanning cannot be performed because of major logistical, technical or pathophysiological reasons. It is unlikely that this provision would apply to many patients under 75 years of age; or
 - 1.3 History of two significant osteoporotic fractures demonstrated radiologically; or
 - 1.4 Documented T-Score ≤ -3.0 (see Note); or
 - 1.5 A 10-year risk of hip fracture $\geq 3\%$, calculated using a published risk assessment algorithm (e.g. FRAX or Dubbo) which incorporates BMD measurements (see Note); or
 - 1.6 Patient has had a Special Authority approval for alendronate (Underlying cause was glucocorticosteroid therapy but patient now meets the 'Underlying cause – Osteoporosis' criteria); and
- 2 The patient will not be prescribed more than one infusion in a 12-month period.

Notes:

a) BMD (including BMD used to derive T-Score) must be measured using dual-energy x-ray absorptiometry (DXA). Quantitative ultrasound and quantitative computed tomography (QCT) are not acceptable.

b) Evidence used by National Institute for Health and Clinical Excellence (NICE) guidance indicates that patients aged 75 years and over who have a history of significant osteoporotic fracture demonstrated radiologically are very likely to have a T-Score ≤ -2.5 , and therefore do not require BMD measurement for treatment with bisphosphonates.

c) Osteoporotic fractures are the incident events for severe (established) osteoporosis, and can be defined using the WHO definitions of osteoporosis and fragility fracture. The WHO defines severe (established) osteoporosis as a T-score below -2.5 with one or more associated fragility fractures. Fragility fractures are fractures that occur as a result of mechanical forces that would not ordinarily cause fracture (minimal trauma). The WHO has quantified this as forces equivalent to a fall from a standing height or less.

d) A vertebral fracture is defined as a 20% or greater reduction in height of the anterior or mid portion of a vertebral body relative to the posterior height of that

body, or a 20% or greater reduction in any of these heights compared to the vertebral body above or below the affected vertebral body.

- Hospital sales and community claims of Aclasta would be subject to a rebate which would reduce the net price and subsidy paid by the Funder.
- Aclasta would have protection from subsidy reduction and delisting until 1 September 2013.
- The Special Authority for alendronate would be amended to add “patient has had a Special Authority approval for zoledronic acid” in the same places that the “patient has had a Special Authority approval for alendronate” criterion appears in the proposed Special Authority for zoledronic acid.

Background

Zoledronic acid (Aclasta) is a bisphosphonate treatment for Paget’s disease and osteoporosis (including glucocorticosteroid-induced osteoporosis). It is administered as an intravenous infusion.

The funding of zoledronic acid (Aclasta) has been considered by the Pharmacology and Therapeutics Advisory Committee (PTAC) in July 2008 and May 2010 and by the Osteoporosis Subcommittee of PTAC in March 2009. Full copies of the relevant minutes can be found on PHARMAC’s website: www.pharmac.govt.nz/PTACminutes and www.pharmac.govt.nz/PTACSCMinutes.

In summary, zoledronic acid has been recommended for funding in Paget’s disease with a high priority, as a second-line bisphosphonate treatment for osteoporosis in patients intolerant to alendronate with a medium-high priority and as a first-line bisphosphonate treatment (ie as an alternative to alendronate) for osteoporosis if it was cost-neutral versus alendronate.

We have reached a provisional agreement with Novartis for the funding of zoledronic acid as a first-line bisphosphonate treatment for osteoporosis that we consider addresses the issues.

We note that zoledronic acid is administered as an intravenous infusion, with a minimum 15 minute infusion time. PTAC and the Osteoporosis Subcommittee of PTAC have advised that zoledronic acid should be considered a community medicine given its relatively short infusion time, and that the majority of General Practice surgeries would be capable of delivering it.

If this proposal is approved by PHARMAC’s Board, it would address all outstanding funding applications for zoledronic acid that have been received by PHARMAC.