PUBLIC SUMMARY DOCUMENT

Product: Ibandronic Acid, tablet, 150 mg, Bonviva® Once Monthly

Sponsor: Roche Products Pty Ltd

Date of PBAC Consideration: March 2007

1. Purpose of Application

The resubmission requested an authority required PBS listing for the treatment of established postmenopausal osteoporosis in patients with fracture due to minimal trauma.

2. Background

This was the second submission to PBAC for Bonviva Once Monthly.

At its July 2006 meeting, the PBAC rejected the submission because of the inadequate evidence of demonstrating no difference between ibandronate and alendronate.

There is a Public Summary Document for the ibandronic acid application to the July 2006 PBAC meeting at:
www.health.gov.au/internet/wcms/publishing.nsf/Content/pbac-psd-ibandronic-july06.

3. Registration Status

Bonviva Once Monthly was registered by the TGA on 4 July 2006 for treatment of postmenopausal osteoporosis. Bonviva Once Monthly increases BMD and reduces the risk of fractures. Osteoporosis may be confirmed by the finding of low bone mass (at least 2.0 SD below the normal mean) or by the presence or history of osteoporotic fracture.

4. Listing Requested and PBAC's View

Authority Required
Initial treatment as the sole PBS-subsidised anti-resorptive agent for established postmenopausal osteoporosis in patients with fracture due to minimal trauma. The fracture must have been demonstrated radiologically and the year of plain x-ray or CT-scan or MRI scan must be included in the authority application.
A vertebral fracture is defined as a 20% or greater reduction in height of the anterior or mid portion of the 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;

Continuing treatment as the sole PBS-subsidised anti-resorptive agent for established postmenopausal osteoporosis in patients with fracture due to minimal trauma, where the patient has previously been issued with an authority prescription for this drug.

See Recommendation and Reasons for the PBAC's views.

5. Clinical Place for the Proposed Therapy

In the treatment of postmenopausal osteoporosis, ibandronic acid provides an alternative treatment to other bisphosphonates and raloxifene.

6. Comparator

The comparator, as previously agreed by the PBAC, was alendronate 70 mg/week once weekly.

7. Clinical Trials

The submission made no changes to the trial data presented in the previous submission to the July 2006 meeting, with the exception of the addition of one year data in the MOBILE Long Term Extension (LTE) Study, and the inclusion of results of the intermittent dosing regimens in the BONE study (20 mg ibandronic acid) and the MOBILE study (100 mg ibandronic acid).

The evidence provided in the re-submission, was a distant indirect comparison:
Stage 1:

- 150mg ibandronate taken once monthly is non-inferior to 2.5mg ibandronate taken daily (MOBILE trial, based on BMD outcomes)
- 70mg alendronate, taken once per week is non-inferior to 10mg alendronate daily (Schnitzer and Rizzoli trials, based on BMD outcomes)

Stage 2

- 2.5mg ibandronate taken daily vs. placebo (BONE trial, fracture data)
- 10mg alendronate daily vs. placebo (FIT and Liberman trials, fracture data)

8. Results of Trials

For new vertebral fractures, new or worsening fractures and new clinical vertebral fractures, both ibandronic acid 2.5 mg/day and alendronate 10 mg/day were statistically superior to placebo. The indirect comparison results suggested that there was no statistically significant difference between the drugs in reducing the risk of each type of fracture. However, for new clinical vertebral fracture, the results were consistent with a possible increased risk with ibandronic acid. For new vertebral fractures, the baseline risk between the populations of the BONE and FIT/Liberman trials were different, as shown by the placebo arms of those trials (8.1% vs. 18.5%) raising the possibility that there might be important differences between studies which increased the uncertainty of the results from the indirect comparison. A similar observation was made for the placebo arms in the analysis of new or worsening vertebral fractures (8.9% vs. 18.5%), but not for new clinical vertebral fractures.

The PBAC accepted the arguments presented in the sponsor's Pre-PBAC response that the BONE study population had a lower risk of fracture than those of other similar studies, including the FIT study.

The three year efficacy and safety data were presented for the MOBILE long term extension (LTE) study. Overall adverse events were similar between the ibandronic acid 150 mg/month and ibandronic acid 100 mg/month doses in the MOBILE LTE study**.** The

PBAC noted the approved Product Information for ibandronic acid now contains warnings regarding osteonecrosis of the jaw (ONJ) and adynamic bone disease (ABD). The warnings suggest that this is more a class effect rather than directly related to ibandronic acid.

9. Clinical Claim

The submission claimed that ibandronic acid 150 mg/month was no worse than alendronate 70 mg/week.

See Recommendation and Reasons for PBAC's views.

10. Economic Analysis

The submission provided an updated preliminary (trial-based) economic evaluation. A cost-minimisation approach was presented in this resubmission on the basis that ibandronic acid 150 mg/monthly and alendronate 70 mg/weekly were equi-effective doses.

11. Estimated PBS Usage and Financial Implications

The likely number of patients was estimated to be between 100,000 - 200,000 in Year 5 of listing accounting for market share.

The estimated financial cost per year to the PBS (excluding co-payments) was > $100 million per year in Year 5 for all bisphosphonates. The net cost of ibandronic acid to the PBS after subtracting patient co-payments is < $10 million per year in year 5 of listing.

The estimates of costs to the PBS were based on the assumption that there would be no additional increase in the usage of bisphosphonates, as ibandronic acid would be substituted for existing bisphosphonates (predominantly alendronate) and therefore there will be minimal net impact to PBS expenditure.

12. Recommendation and Reasons

The PBAC recommended listing on a cost-minimisation basis with alendronate for the treatment of established osteoporosis, with the equi-effective doses being ibandronic acid 150 mg/month and alendronate 70 mg/week. The pricing calculation is to be based on 12 doses of ibandronic acid, with each dose given on a calendar monthly basis, being equivalent to 52 doses of alendronate, with each dose given on a weekly basis.

The PBAC recommended the 20 day safety net rule should apply on the basis that the rule does apply to other PBS listed bisphosphonates.

Recommendation
Ibandronic acid, tablet, 150 mg,

Authority Required
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fracture must have been demonstrated radiologically and the year of plain x-ray or CT-scan or MRI scan must be included in the authority application.
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Maximum quantity: 1
Repeats: 5

13. Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised in Australia. It considers submissions in this context. A PBAC decision not to recommend listing or not to recommend changing a listing does not represent a final PBAC view about the merits of the medicine. A company can resubmit to the PBAC or seek independent review of the PBAC decision.

14. Sponsor's Comment

The sponsor has no further comment.