Cost effectiveness of bendamustine (Levact®) for the treatment of chronic lymphocytic leukaemia

November 2012

Summary

1. An economic evaluation was submitted in March 2012 by Mundipharma to assess the cost effectiveness of bendamustine (Levact®) as compared to chlorambucil in patients with stages B and C chronic lymphocytic leukaemia (CLL) unable to take the first-line combination of fludarabine and cyclophosphamide. Following amendments requested by the review group, an amended dossier was submitted in August 2012.

2. Bendamustine (Levact®) is an alkylating anti-tumour agent. It is licensed for the first-line treatment of chronic lymphocytic leukaemia (CLL), Binet stages B and C, in patients for whom a fludarabine/cyclophosphamide combination is unsuitable. It is a hospital only product.

3. The manufacturer provided a cost-utility analysis comparing bendamustine with chlorambucil for first-line therapy in patients with CLL unable to tolerate a combination of fludarabine and cyclophosphamide. A complex lifetime Markov model in which all patients begin treatment in a stable disease state and transition to a best overall response state based on efficacy data was presented. A cycle length of three months was used. The time horizon for the model was 10 years and the perspective was that of the HSE as the healthcare payer. A discount rate of 4% was applied to costs and outcomes as is appropriate.

4. The efficacy of bendamustine is derived from one phase III, open-label, parallel group, multi-centred trial (02CLLIII) (Knauf *et al* 2009), which compared bendamustine to chlorambucil (N=319). The overall response rate ((ORR), defined as patients with complete response, partial response or progression free survival), for bendamustine was 68% (110/162) compared to 31% (48/157) for chlorambucil ($p<0.001$). A complete response rate of 31% was obtained for bendamustine compared to 2% for chlorambucil ($p<0.001$).

5. The base case analysis resulted in an incremental cost per QALY gained of €12,961/QALY for bendamustine vs. chlorambucil.

6. Probabilistic sensitivity analysis indicated that the probability of cost effectiveness was 100% at a willingness to pay threshold of €45,000/QALY and 98% at a threshold of €20,000.

7. The NCPE calculated the Expected Value of Perfect Information (EVPI). The analysis determined that at a threshold of €20,000 per QALY, the 10 year Population EVPI (PEVPI) is estimated to be about €0.03 million. At a threshold of €45,000 per QALY, the 10 year PEVPI is zero. The impact of changing the threshold is considerable; the PEVPI ranges from about €13.08 million (at €0 per QALY) to zero at thresholds greater than €22,000 per QALY.

8. Based on the projected market share, the gross budget impact for bendamustine was estimated in the submission at €439,361 in Year 1 (n=75 patients) rising to €544,808 in Year 5 (n=93 patients). Based on these figures the 5 year cumulative gross budget impact was estimated by the review group at €2,548,295. The net budget impact provided was €426,353 in Year 1 rising to €528,678 in Year 5 (n=93 patients) equating to a net budget impact of €2,472,848.

9. The NCPE considers bendamustine to be a cost-effective strategy for first-line treatment of patients with CLL who are unable to tolerate a combination of fludarabine and cyclophosphamide. Patients who may benefit most treatment with bendamustine are those in the lower spectrum of the older age cohort and with milder Stage B disease.