

Cost-effectiveness of oral oxycodone/naloxone prolonged release tablet (Targin[®]) for severe pain, which can be adequately managed only with opioid analgesics



July 2010

Summary

1. In May 2010, Mundipharma submitted an economic dossier on the cost-effectiveness of oral oxycodone/naloxone prolonged release (PR) tablet (Targin[®]) to the National Centre for Pharmacoeconomics. Oxycodone/naloxone prolonged release (PR) is licensed for severe pain, which can be adequately managed only with opioid analgesics.
2. Oxycodone/naloxone PR tablet was compared with oxycodone PR tablet. A cost-utility decision tree model was developed in MS Excel. The time-horizon for the base case analysis was 301 days, in accordance with the average duration of oxycodone therapy for non-malignant pain in the UK. Analgesic efficacy of oxycodone/naloxone PR was found to be equivalent to oxycodone PR in a phase III randomised controlled trial (RCT). The proportion of patients with opiate induced constipation (OIC) in both arms of the economic model was estimated from the Phase III RCT OXN3001 and data from an open label unpublished study.
3. A phase III RCT (OXN3001) examining the effects of oxycodone/naloxone PR versus oxycodone PR on bowel function in patients with moderate to severe non-cancer pain over a 12 week period reported a statistically significant improvement in bowel function, as measured using the Bowel Function Index (BFI), in favour of oxycodone/naloxone PR.
4. The Review Group had a number of concerns with the trial data. The base case analysis of the economic evaluation assumes patients who develop OIC would be treated with two laxatives for 75% of the duration of opioid treatment. This is not reflective of the trial protocol and could potentially result in the benefit of oxycodone/naloxone PR being overestimated. Although it is stated that the BFI is an independently validated measure, the validation study was undertaken using data from the clinical development programme for oxycodone/naloxone PR. The estimates of the proportion of patients in each arm of the economic model that experienced OIC, were derived from an unpublished observational study.
5. Utility values were calculated directly from SF-36 data which was included as an exploratory measure in the Phase III RCT OXN3001 (unpublished). The Review Group have concerns about the generalisability of the trial data to clinical practice (see above). There was a numerical, but not statistically significant, difference in

utility values between the two arms by week 12. The difference in utility scores between the two treatment groups is the major driver of the cost-effectiveness results in the submission.

6. Utility values were estimated from the SF-36 data using three different methods: mapping to the EQ-5D using equations from Rowen *et al.* (base case) and Ara *et al.*, as well as the SF-6D. The average QALY gained with oxycodone/naloxone PR was approximately 0.030 using the mapping method by Rowen *et al.*, 0.027 using the method by Ara *et al.* and 0.0176 using the SF-6D method. Given the uncertainty and concerns with the SF-36 data (see above), the Review Group consider it appropriate to use the more conservative SF-6D utility estimates for the base case analysis.
7. The incremental cost-effectiveness ratio (ICER) ranged from €8,691/QALY and €10,813/QALY for the GMS and DP schemes respectively using the EQ-5D mapping equation (Rowen *et al.*) to €14,808/QALY and €18,607/QALY for the GMS and DP schemes respectively using the SF-6D model.
8. The ICER was sensitive to the utility values, the price of oxycodone/naloxone PR and the price of the comparator oxycodone PR. If post-patent price cuts of 20% and 35%, which may occur with the anticipated patent expiry of oxycodone PR, are included in the analysis the ICER would increase to €19,063 and €21,998/QALY respectively for the GMS scheme using the SF-6D model.
9. At a cost-effectiveness threshold of €20,000/QALY, the probability that oxycodone/naloxone PR is cost-effective is approximately 78% and 59% under the GMS and DP schemes respectively using the SF-6D model.
10. The total (gross) budget impact was estimated to increase from €0.4 million to €2.95 million by year 5. The incremental (net) annual cost to the HSE was estimated at €1.2 million in year 5. The incremental cost to the HSE, if the patent for oxycodone PR expires in 2012, was estimated to be €1.67 million in year 5.
11. Given the limitations and uncertainty associated with the utility data and the price differential (approximately double) between oxycodone/naloxone PR and its comparator oxycodone PR, the NCPE does not recommend this drug for reimbursement on the Community Drug Schemes at the proposed price.