

A Review of the economic evaluation of oral tapentadol
(Palexia[®]) for the management of adult patients with
severe chronic / acute pain



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Summary

1. In February 2011, Grunenthal submitted an economic dossier on the cost-effectiveness of oral tapentadol (Palexia[®]) prolonged release (PR) tablet to the National Centre for Pharmacoeconomics. Tapentadol PR is indicated for the management of severe chronic pain in adults, which can be adequately managed only with opioid analgesics. It is a Schedule 2 controlled drug with a dual mechanism of action (mu-opioid receptor agonist and noradrenaline reuptake inhibitor).
2. A full pharmacoeconomic assessment of tapentadol immediate release (IR) was not conducted because it has a lower drug acquisition cost than the comparator oxycodone IR (Oxynorm[®]).
3. Tapentadol PR was compared with oxycodone controlled release (CR) as a first line treatment option. Oxycodone CR was chosen as the comparator on the grounds that it is the most commonly prescribed strong oral opioid for chronic pain in Ireland. A cost-utility decision tree model was developed in Treeage. The time-horizon for the analysis was one year, with cycle lengths of four weeks.
4. Efficacy and tolerability data from a pooled analysis of three phase III randomised double blind active and placebo controlled trials in patients with chronic osteoarthritis / lower back pain over a period of 15 weeks (Lange *et al.* 2010) was included in the economic model. The clinical trial data suggests that tapentadol PR provided analgesic efficacy that is similar to that of oxycodone CR for the management of moderate to severe chronic pain.
5. The pooled clinical trial data (Lange *et al.*) reported a statistically significant difference in EQ-5D health status index scores between tapentadol PR and oxycodone CR in favour of tapentadol ($p < 0.0001$). The incidences of constipation, nausea and vomiting were significantly lower in the tapentadol PR group (16.9%, 20.7% and 8.2% respectively) than in the oxycodone CR group (33.0%, 36.2% and 21.0%) $p < 0.0001$. The times to first occurrence of gastrointestinal adverse events were all significantly longer in the tapentadol PR group compared with the oxycodone CR group ($p < 0.001$).

6. The Review Group had a number of concerns regarding the generalisability of the clinical trial data to clinical practice in the Irish setting. The doses of oxycodone CR administered in the clinical trial are higher than initiating and maintenance doses of oxycodone CR in clinical practice in Ireland, as observed in the GMS prescription database. Furthermore, prescriptions for laxatives and anti-emetics were more frequent in the titration phase (3 weeks) in patients receiving oxycodone CR vs tapentadol PR but was similar in the maintenance phase (12 weeks) of the clinical trials. The efficacy of tapentadol PR versus oxycodone CR plus regular laxatives and anti-emetics is uncertain.
7. The economic model assumes a titration phase of 4 weeks. At the end of the titration phase, patients may (1) tolerate therapy; (2) experience a mild to moderate adverse event (AE) and require symptomatic medication (i.e. a laxative or anti-emetic); (3) switch to an alternative strong opioid due to a severe AE or (4) switch due to lack of efficacy. The proportion of patients entering each of the four health states was determined from the adverse events reported in the pooled clinical trial data set (Lange *et al.*).
8. The incremental cost-effectiveness ratio (ICER) for tapentadol PR versus oxycodone CR on the GMS scheme ranged from dominated (i.e. tapentadol PR less costly and more effective) to €7,066/QALY depending on the method used to calculate drug costs in the model. For the DP scheme, the ICER ranged from €1,662/QALY - €11,038/QALY for the base case analysis.
9. The ICER was most sensitive to the probability of withdrawal due to an adverse event for oxycodone CR, the utility value for treatment tolerability, and the price of the comparator oxycodone CR. If the post-patent price cuts of 20% and 35%, which may occur with the anticipated patent expiry of oxycodone CR, are included in the analysis the ICER would increase to €8,247/QALY - €14,536/QALY and €14,991/QALY - €20,139/QALY respectively for the GMS scheme. The ICER also increases for the same scenario on the DP scheme (€12,200/QALY - €19,845 for a 20% post-patent price cut of oxycodone CR) and (€20,103/QALY - €26,450/QALY for a 35% post-patent price cut of oxycodone CR).

10. At a cost-effectiveness threshold of €20,000/QALY, the probability that tapentadol PR is cost-effective is approximately 91% - 97% under the GMS scheme and 83% - 97% under the DP scheme.

11. The gross budget impact on the GMS and DP schemes was estimated to range from €805,000 to €912,000 by year 5. The net budget impact was estimated to range from €254,324 to €284,420. This is based on the assumptions that only strong oral opioids will be replaced by tapentadol PR (not transdermal opioids), a post patent price cut of 20% in 2012 and 35% in 2014 for oxycodone CR, and an uptake of tapentadol PR of 20% by year 5.

12. The Review Group remain concerned in relation to the generalisability of the trial results to the clinical setting. Therefore we recommend that tapentadol should be reserved for those patients who cannot tolerate existing strong oral opioids. In view of this uncertainty, utilisation of tapentadol on the Community Drug Schemes should be closely monitored with the potential to reassess the cost-effectiveness of tapentadol if the budget impact and place in therapy is not consistent with this evaluation.