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## Cost-effectiveness analysis of pregabalin versus gabapentin in the management of neuropathic pain due to diabetic polyneuropathy or post-herpetic neuralgia

Rodriguez M J, Diaz S, Vera-Llonch M, Dukes E, Rejas E A

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### Record Status

This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

### CRD summary

The objective was to assess the cost-effectiveness of branded pregabalin (PGB) in comparison with generic gabapentin (GBP) in patients with neuropathic pain due to painful diabetic polyneuropathy or post-herpetic neuralgia. The authors concluded that PGB was a cost-effective alternative to GBP from the perspective of the Spanish health care system. The analysis was well conducted and reported. The authors' conclusions appear to be valid.

### Type of economic evaluation

Cost-effectiveness analysis, cost-utility analysis

### Study objective

The objective was to assess the cost-effectiveness of branded pregabalin (PGB) in comparison with generic gabapentin (GBP) in patients with neuropathic pain (NeP) due to painful diabetic polyneuropathy (DPN) or post-herpetic neuralgia (PHN).

### Interventions

The two treatments were PGB compared with GBP, at flexible doses. PGB was given at 150mg to 600mg daily (mean 457mg), while GBP was given at 900mg to 3600mg daily (mean 2400mg).

### Location/setting

Spain/secondary care.

### Methods

#### Analytical approach:

This economic evaluation used a Markov model based on individual patient simulations to examine the clinical and economic impact of the two treatments. The time horizon of the analysis was 12 weeks. The authors reported that the perspective of the Spanish National Health Care System was adopted.

#### Effectiveness data:

The clinical data were derived from a selection of known, relevant studies. Specifically, treatment effect for the two drugs was derived from three randomised controlled trials (RCTs), which were double-blind and placebo-controlled. The data on PGB were derived from a single trial, while data on GBP were obtained from two studies. Thus, no head-to-head trials were used as a source of clinical effectiveness. The patient characteristics were taken from the PGB trial. The key clinical outcome was reduction in pain with the two drugs.

#### Monetary benefit and utility valuations:

The utility valuations were derived from a combined analysis of two cross-sectional studies carried out on Spanish patients using the Spanish version of the Leeds Assessment of Neuropathic Symptoms and Signs and the Douleur Neuropathique Four scales. These were converted into utility weights using the Spanish version of the Health Utility Index Mark Three and a visual analogue scale.

#### Measure of benefit:

The summary benefit measures were quality-adjusted life-years (QALYs), days with no or mild pain, and number of patients with no or mild pain.

#### Cost data:

The direct medical costs were drugs, outpatient visits to specialists and the pain clinic, diagnostic tests, and non-pharmacological treatments. The side effects of the drugs had a negligible impact and were not included. The resource quantities were reported for different levels of pain intensity and unit costs were reported. The resource use for most items was determined from a panel of 13 experts in Spain. The direct health care costs were derived from a national health cost database. Drug costs were valued using public sales prices obtained from the Catalogue of Medicinal Products of the Spanish General Council of Official Pharmaceutical Colleges. All costs were in Euros (EUR) and the price year was 2006.

#### Analysis of uncertainty:

The decision model was replicated for 1,000 samples of 1,000 patients each to allow the calculation of 95% confidence interval (CI) for cost-utility and cost-effectiveness ratios. A probabilistic sensitivity analysis focused on variations in weekly mean pain changes. A deterministic sensitivity analysis investigated alternative assumptions and scenarios, especially around cost assumptions and utility values.

### Results

The expected QALYs were 0.1186 with PGB and 0.1138 with GBP.

The expected proportion of patients with no or mild pain at 12 weeks was 72% for PGB and 49.1% for GBP. The days with no or mild pain were 38 for PGB and 30 for GBP.

The total costs per patient were EUR 1,049.42 (standard error, SE: EUR 35.20) with PGB and EUR 950.82 (SE: EUR 37.71) with GBP.

The mean incremental cost, per day with no or mild pain, gained with PGB over GBP was EUR 12 (95% CI: EUR 1, EUR 24). The mean incremental cost, per patient with no or mild pain, gained was EUR 431 (95% CI: dominant, EUR 876). The incremental cost per QALY gained was EUR 20,535 (95% CI: EUR 1,607, EUR 40,345).

The sensitivity analysis indicated that the highest value of the incremental cost per QALY was EUR 33,498. These findings were sensitive to assumptions on the generic GBP dose.

### Authors' conclusions

The authors concluded that PGB was a cost-effective alternative to GBP for the treatment of NeP due to DPN, PHN or both, from the perspective of the Spanish health care system.

### CRD commentary

#### Interventions:

The two comparators were appropriately selected as available treatments for NeP. They were also compared with placebo in the RCTs.

#### Effectiveness/benefits:

The use of RCTs as sources of clinical evidence was appropriate given the robust design of this type of study. The randomised and double-blind approach should ensure the validity of the clinical findings. Furthermore, the authors stated that the three RCTs had similar populations and similar baseline pain values. Some information on follow-up and pain scores was provided. A potential limitation of this approach was that no direct head-to-head comparisons were available, thus the comparative efficacy of the drugs was obtained indirectly from their efficacy relative to placebo. The methodology used to pool the data from the two GBP studies was not described. The utility weights were taken from Spanish patients using appropriate instruments. QALYs are an appropriate benefit measure given the negative impact of the disease on quality of life. Furthermore, QALYs are validated measures which allow for cross-disease comparisons.

#### Costs:

The categories of costs were consistent with the perspective. Extensive information on resource use and costs was provided, especially with respect to the calculation of drug costs taking into account the dosages of drug administered. The sources of costs reflected the Spanish setting, but were varied in the sensitivity analysis. This was also the case for

data on resource consumption, which were based on the experience of a panel of experts. Other assumptions made in the economic analysis, and the price year were reported. In general, the economic analysis was carried out transparently. The authors pointed out that adopting a societal perspective (including indirect costs) favoured the PGB strategy.

**Analysis and results:**

: The costs and benefits were appropriately synthesised by means of average and incremental ratios. The issue of uncertainty was satisfactorily investigated in the sensitivity analysis by using probabilistic and deterministic approaches. The results of both the base-case and the sensitivity analysis were clearly presented and discussed. The statistical approach used in the analysis enhances the validity of the findings. The authors noted that the main limitations of the analysis were related to the available data sources, the assumptions required in the decision model, and the short time horizon. The authors also stated that these results should be considered to be specific to the Spanish context and that they were not likely to be transferable to other countries.

**Concluding remarks:**

The analysis was well conducted and reported. The authors' conclusions appear to be valid.

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**Bibliographic details**

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**Other publications of related interest**

Tarride JE, Gordon A, Vera-Llonch M, et al. Cost-effectiveness of pregabalin for the management of neuropathic pain associated with diabetic peripheral neuropathy and postherpetic neuralgia: a Canadian perspective. *Clin Ther* 2006;28:1922-34.

Rowbotham M, Harden N, Stacey B, et al. Gabapentin in the treatment of post-herpetic neuralgia: a randomised controlled trial. *JAMA* 1998;280:1837-42.

Freyhagen R, Strojek K, Griesing T, et al. Efficacy of pregabalin in neuropathic pain evaluated in a 12-week, randomised, double-blind, multicentre, placebo-controlled trial of flexible- and fixed-dose regimens. *Pain* 2005;115:254-63.

**Indexing Status**

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