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## Sativex in multiple sclerosis spasticity: a cost-effectiveness model

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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

This study evaluated the cost-effectiveness of Sativex for patients with moderate-to-severe spasticity from multiple sclerosis (MS), who had not responded adequately to other anti-spasticity medications. The authors concluded that Sativex was a cost-effective treatment. Some effort was made to obtain relevant evidence and the methods were adequately reported in parts, but the uncertainty in the effectiveness methods and estimates, means that it is not clear that the authors' conclusions are appropriate.

### Type of economic evaluation

Cost-utility analysis

### Study objective

This study evaluated the cost-effectiveness of Sativex (nabiximols), when used in clinical practice, for patients with moderate-to-severe spasticity from multiple sclerosis (MS), who had not responded adequately to other anti-spasticity medications.

### Interventions

Sativex, as an addition to standard care, for four weeks, followed by continued treatment for those who demonstrated a clinically significant improvement, was compared with standard care. Patients used 6.9 sprays per day in the first four weeks, and 8.3 sprays per day in the 12-week continuation period. Standard care was the prescribing practice, which varied between Germany and Spain; the percentages of patients receiving each treatment were reported.

### Location/setting

Spain and Germany/out-patient care.

### Methods

#### Analytical approach:

The economic evaluation was based on one clinical trial. A Markov model was used for the ongoing risks of treatment discontinuation, disease progression, and death, over five years. The costs and benefits were aggregated over this period. The authors stated that a health care system perspective was adopted.

#### Effectiveness data:

The primary clinical data were the probability of reaching the minimum improvement at four weeks, on Sativex, and the probability of disease progression each month, over the five years. The probability of death and treatment discontinuation were incorporated. There were two stages to the clinical trial. At four weeks, 241 of the initial 572 patients had responded to Sativex and were randomised to Sativex or placebo. After the 12 weeks of the second part of the trial, patients were assumed to remain at the same spasticity severity up to the five years of the study, unless they discontinued treatment. Discontinuation rates were from the trial and from a long-term, open-label UK study.

#### Monetary benefit and utility valuations:

The utility values were obtained for mild, moderate and severe spasticity states. They were from the 241 trial participants, who completed the EQ-5D questionnaire at the end of the 12-week second part of the trial. Any quality-of-life effects associated with adverse events were assumed to be captured in the utility questionnaire.

#### Measure of benefit:

The measure of benefit was the quality-adjusted life-year (QALY). Benefits were discounted at an annual rate of 3.5%.

#### Cost data:

The resources included the medications; administration of botulinum toxin and intrathecal baclofen; tenotomy and rhizotomy surgery; health care visits for the management of MS; and tests that included the identification of responders at four weeks. The percentage of patients receiving each treatment in standard practice, was estimated by a Delphi survey of 16 neurologists (eight from Germany and eight from Spain). The resource consumption was estimated separately for patients with mild, moderate, and severe MS spasticity. The annualised resource use was valued using 2010 unit costs. Drug price lists, published sources and public information were used for the unit costs. Separate unit costs were derived for Germany and for Spain. The costs were reflatd to 2010 prices, where necessary, using published country-specific inflation rates. They were reported in Euros (EUR) and discounted at an annual rate of 3.5%.

#### Analysis of uncertainty:

One-way sensitivity analyses were conducted to investigate the impact on the results of varying the input parameters across a defined range of values. The results were presented in tornado diagrams. The range of parameter values was defined as  $\pm 20\%$  of the initial estimate. Alternative resource use data from a German retrospective study were tested.

### Results

The total discounted incremental cost of Sativex, per 100 patients, over the five years, was EUR 359,672 in Germany. In Spain, there were EUR 367,870 of savings, per 100 patients with Sativex. Cost savings were obtained from the reduced cost of managing more severe MS spasticity.

Sativex resulted in 32.07 incremental QALYs, per 100 patients, in Germany and 32.53 in Spain.

The incremental cost-effectiveness ratio for Sativex was EUR 11,214 per QALY gained in Germany. In Spain, Sativex dominated standard care as it was cost saving and more effective.

The results were most sensitive to changes in the cost of Sativex, over the  $\pm 20\%$  parameter ranges specified.

### Authors' conclusions

The authors concluded that Sativex was a cost-effective treatment, under the study assumptions.

### CRD commentary

#### Interventions:

The intervention and comparator were adequately described. This study evaluated the cost-effectiveness of Sativex as an addition to usual care, in Spain and Germany. It did not assess the most effective treatment combination or sequence. The authors noted that a few studies had suggested that intrathecal baclofen could be cost-effective for severe refractory cases.

#### Effectiveness/benefits:

This study evaluated Sativex as an addition to standard care, which differed in Germany and Spain. The selection criteria for the trial were not stated. It seems that all patients were given Sativex in the first four weeks, and only those who responded to treatment were randomised to Sativex or placebo, for the second part of the trial. It is not clear how well these data applied to the study context. As external data were used to model the disease progression for standard care, a risk ratio may have been used, but this was not reported nor discussed. It was acknowledged that the lack of evidence on the effectiveness of Sativex beyond the end of the trial was a limitation of the study. It was not clear if the measurement of utility at one time point accurately captured the incidence of adverse events.

#### Costs:

It was acknowledged that the Delphi survey method of estimating the resource use was not the ideal method. The resources relevant to the decision problem appear to have been included. The sources for the cost data and cost adjustment details were adequately reported. The unit costs were reported separately to the resources, which should make the study replicable in other settings.

#### Analysis and results:

The model structure and results were adequately reported. It was not clear that the range of parameter values, defined as  $\pm 20\%$  of the initial estimate, adequately covered the plausible range of values for each parameter. The authors

discussed some limitations to their analysis, which have been mentioned.

**Concluding remarks:**

Some effort was made to obtain relevant evidence and the methods were adequately reported in parts, but the uncertainty in the effectiveness methods and estimates, means that it is not clear that the authors' conclusions are appropriate.

**Funding**

Not stated.

**Bibliographic details**

Slof J, Gras A. Sativex in multiple sclerosis spasticity: a cost-effectiveness model. Expert Review of Pharmacoeconomics and Outcomes Research 2012; 12(4): 525-538

**PubMedID**

22681512

**DOI**

10.1586/erp.12.40

**Original Paper URL**

<http://www.expert-reviews.com/doi/abs/10.1586/erp.12.40>

**Indexing Status**

Subject indexing assigned by NLM

**MeSH**

Cost-Benefit Analysis; Drug Costs; Drug Resistance; Germany; Humans; Markov Chains; Multiple Sclerosis /drug therapy /economics /physiopathology; Muscle Spasticity /drug therapy /economics /etiology; Plant Extracts /economics /therapeutic use; Quality-Adjusted Life Years; Severity of Illness Index; Spain

**AccessionNumber**

22012038026

**Date bibliographic record published**

12/02/2013

**Date abstract record published**

29/05/2013