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## Cost-effectiveness of citicoline versus conventional treatment in acute ischemic stroke

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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 study examined the clinical and economic impact of neuroprotection with citicoline, compared with no intervention, in patients with acute ischaemic stroke. The authors concluded that treatment with citicoline was a highly cost-effective alternative to placebo in the setting of the Spanish health care system. The quality of the study methodology was good and the methods and results were presented clearly. The authors' conclusions appear valid.

### Type of economic evaluation

Cost-effectiveness analysis

### Study objective

The aim of the study was to examine the clinical and economic impact of neuroprotection with citicoline, compared with no intervention, in patients with acute ischaemic stroke.

### Interventions

The study examined the addition of citicoline (from a minimum of 500 to a maximum of 2,000 mg/day for 6 weeks) to the standard therapy for ischaemic stroke. The intervention was compared with placebo, that is, standard therapy alone.

### Location/setting

Spain/hospital.

### Methods

#### Analytical approach:

A simplified decision model was developed on the basis of published evidence in order to simulate the natural history of disease and patient management under the two scenarios (citicoline versus placebo). The time horizon of the analysis was 3 months. The authors stated that the study was carried out from the perspective of the Spanish National Health System.

#### Effectiveness data:

A systematic review of the literature was undertaken to identify meta-analyses of placebo-controlled, double-blind, randomised clinical trials (RCTs) of citicoline versus placebo. The databases searched and inclusion criteria were described. No restrictions on the study country or language were applied. Two meta-analyses were identified. The first pooled study included 4 RCTs that enrolled 1,672 patients (pooled analysis), while the second included 8 RCTs that enrolled 2,063 patients (Cochrane study). In the current study, only 1,372 patients were included in the pooled analysis and 1,048 in the Cochrane study, given some specific inclusion and exclusion criteria. The key clinical estimate was the probability of recovery after acute ischaemic stroke with citicoline or placebo.

#### Monetary benefit and utility valuations:

None.

#### Measure of benefit:

The model outputs used in the analysis were the probability of death or disability and the probability of recovery. Each of them was derived from the two studies identified in the review. No discounting was applied.

#### Cost data:

The health service costs included in the analysis were intensive care unit stay, hospital ward stay, consultations

(cardiology, nephrology and endocrinology), physiotherapy, rehabilitation services (physiotherapy and speech therapy) and medications (citicoline at different dosages). The resource use data were derived from a panel of experts from four acute-care teaching hospitals in Spain. The unit costs were derived from the participating hospitals, consultation with experts and bibliographic sources. An annual increment of 3% was applied to take into account the inflation rate for data taken from old studies. The costs were in euros (EUR). The price year was not reported.

#### **Analysis of uncertainty:**

A deterministic sensitivity analysis was undertaken to assess the robustness of the model results, using published confidence intervals (CIs) for clinical estimates and ranges of values for economic inputs. Different scenarios were also considered on the basis of data from the expert panel in relation to the use of health care services for the management of patients with (not recovered) and without (recovered) functional disability.

#### **Results**

The median rate of death or disability was 0.548 (95% CI: 0.518 to 0.578) with citicoline and 0.647 (95% CI: 0.613 to 0.681) with placebo.

The median rate of recovery was 0.252 (95% CI: 0.222 to 0.282) with citicoline and 0.202 (95% CI: 0.169 to 0.234) with placebo.

When including only inpatient care services, the expected costs per patient were EUR 3,026.1 with citicoline and EUR 3,127.3 with placebo using the Cochrane study. The corresponding values when using the pooled analysis were EUR 3,493.6 and EUR 3,480.3.

When including inpatient and outpatient care services after discharge, the expected costs per patient were EUR 3,633.5 with citicoline and EUR 3,759.9 with placebo using the Cochrane study. The corresponding values when using the pooled analysis were EUR 4,151.89 and EUR 4,151.28.

The incremental analysis showed that citicoline treatment was the dominant treatment when using the Cochrane study, as placebo was both less effective and more expensive. When data from the pooled analysis were used, the incremental cost per additional patient recovered was EUR 266.43 when including only inpatient care and EUR 12.08 when including both inpatient and outpatient care after discharge.

The sensitivity analysis corroborated the base-case findings.

#### **Authors' conclusions**

The authors concluded that treatment with citicoline in acute ischaemic stroke was a highly cost-effective alternative to placebo in the setting of the Spanish health care system.

#### **CRD commentary**

##### **Interventions:**

The authors did not provide an explicit justification for their choice of the comparators. Nevertheless, the selection of placebo as the alternative strategy appears to have been appropriate in the authors' setting.

##### **Effectiveness/benefits:**

The identification of the sources of clinical estimates was carried out satisfactorily. The authors reported extensive information on the methods and conduct of the systematic review. The quality of the two studies included was good and key issues of heterogeneity, adequate sample size and the quality of individuals RCTs were well addressed. The results from the two meta-analyses were reported clearly. The authors carried out two separate analyses using clinical data from each source, which provided different benefit measures. Both of them might be of relevance to decision-makers. The benefit measure would appear to be appropriate for stroke, although not fully comparable with other diseases.

##### **Costs:**

The analysis of the costs was consistent with the perspective adopted in the study. A breakdown of the cost items was provided. The sources of the costs were reported clearly for each item. The approach used to derive data on resource

use through the panel of experts was described. This method strengthens the validity of the data on consumption of health care services since it is representative of the authors' setting. The resource quantities were reported for several items, which enhances the transparency of the cost analysis. However, the price year was not reported, which could limit the possibility of conducting reflation exercises in other time periods.

**Analysis and results:**

The use of an incremental analysis was appropriate to synthesising the costs and benefits of the alternative strategies. The sensitivity analysis addressed some areas of uncertainty using published estimates for clinical data and expert opinion for economic inputs. The results of both the base-case and the sensitivity analyses were presented clearly, which enhances the external validity of the study. However, in some cases the terminology of the study was not fully appropriate for an economic evaluation (e.g. marginal cost-effectiveness rather than incremental cost-effectiveness).

**Concluding remarks:**

The quality of the study methodology was good and both the methods and results were presented clearly. The authors' conclusions appear valid.

**Funding**

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**Bibliographic details**

Casado A, Secades J J, Ibarz R, Herdman M, Brosa M. Cost-effectiveness of citicoline versus conventional treatment in acute ischemic stroke . Expert Review of Pharmacoeconomics and Outcomes Research 2008; 8(2): 151-157

**Other publications of related interest**

Davalos A, Castillo J, Alvarez-Sabin J, et al. Oral citicoline in acute ischemic stroke. An individual patient data pooling analysis of clinical trials. Stroke 2002;33:2850-7.

Adibhatla RM, Hatcher JF. Citicoline mechanisms and clinical efficacy in cerebral ischemia. J Neuroscience Res 2002;70:133-9.

Payne KA, Huybrechts KF, Caro JJ, et al. Long-term cost-of-illness in stroke: an international review. Eur J Neurol 2002;20:813-25.

**Indexing Status**

Subject indexing assigned by CRD

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