Costs and outcomes of extended-release vs. immediate-release clarithromycin for lower respiratory tract infections

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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.

Health technology
The study considered the first-line treatment of lower respiratory tract infections (RTIs) with extended-release (ER) clarithromycin (1,000 mg once daily for 7 days). If this treatment failed, second-line treatment with levofloxacin (500 mg once daily for 10 days) was used.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients with a lower RTI.

Setting
The setting was primary and secondary care. The economic study was carried out in the USA.

Dates to which data relate
The clinical effectiveness data were taken from studies published between 1990 and 2002. The resource use data related to data collated between 1998 and 2000. No clear price year was reported.

Source of effectiveness data
The effectiveness data were derived from a review or synthesis of published studies.

Modelling
A decision analysis model was used to identify the clinical and cost implications of treatment with ER versus IR clarithromycin.

Outcomes assessed in the review
The model parameters identified from published studies were the cure rates for ER and IR clarithromycin and levofloxacin, and the discontinuation of ER and IR clarithromycin because of adverse events.

Study designs and other criteria for inclusion in the review
All studies published between 1990 and 2003 that provided clinical effectiveness for the study treatments and an
assessment of the treatments in line with the US Food and Drug Administration classification of "cure" and "failure" for community-acquired pneumonia were used.

**Sources searched to identify primary studies**
Not reported.

**Criteria used to ensure the validity of primary studies**
Not reported.

**Methods used to judge relevance and validity, and for extracting data**
Not reported.

**Number of primary studies included**
The model parameters were identified from 20 primary studies.

**Methods of combining primary studies**
The results of the primary studies were combined using weighted average values based on sample size.

**Investigation of differences between primary studies**
Not reported.

**Results of the review**
The following model parameters were identified.

The cure rate was 86.0% for ER clarithromycin, 74.6% for IR clarithromycin and 86.3% for levofloxacin (second-line therapy).

Discontinuation because of adverse events was 2.4% with ER clarithromycin, and 3.7% (randomised blinded studies) and 4.9% (all studies) with IR clarithromycin.

**Measure of benefits used in the economic analysis**
The measure of health benefit used was the percentage of patients cured using the US Food and Drug Administration definition for community-acquired pneumonia.

**Direct costs**
The costs of the health care payer were identified in this study. The unit costs of drugs were based on wholesale costs from the Price Probe Database. The unit costs of physician visits and chest radiographs were taken from the 2002 Physician Fee and Coding Guide. Resource use for physician visits and chest radiographs were taken from the 1998 National Ambulatory Medical Care Survey and the National Hospital Ambulatory Medical Care Survey. Drug use was modelled using the model described earlier. Resource use information was dated between 1998 and 2000. The unit costs and resource use were identified separately in the paper. No clear price year was identified. The costs were not discounted.

**Statistical analysis of costs**
The cost data were treated deterministically.
Indirect Costs
No indirect costs were identified in this study.

Currency
US dollars ($)

Sensitivity analysis
Three sensitivity analyses were undertaken. One considered the impact of deriving model parameters only from studies that were blind, randomised controlled trials. A threshold sensitivity analysis was performed to determine the cure and discontinuation rates at which the two treatment options would be equal. Finally, a one-way sensitivity analysis that varied treatment adherence for the two treatments was also conducted.

Estimated benefits used in the economic analysis
The model estimated that 97.7% patients receiving ER clarithromycin as first-line treatment and 95.7% receiving IR clarithromycin were cured.

Cost results
The total cost of treatment with ER clarithromycin as first-line treatment was $172.05 per patient, compared with $204.15 for patients given IR clarithromycin as first-line treatment.

Synthesis of costs and benefits
Treatment with ER clarithromycin had a higher cure rate and lower costs than IR clarithromycin, therefore the benefits and costs were not combined.

The sensitivity analysis showed that taking parameter data only from blind, randomised controlled trials did not alter the model results. For the two treatments to be equal, the cure rate for IR clarithromycin would have to rise to 96.4% or the cure rate for ER clarithromycin would have to decrease to 66.7%. The discontinuation rate for ER clarithromycin would have to increase by 41.9% for the costs to be equal. Even if the discontinuation rate of IR clarithromycin decreased to 0%, ER clarithromycin would still be less expensive.

Authors' conclusions
Extended-release (ER) clarithromycin was cost-saving in comparison with immediate-release (IR) clarithromycin for the treatment of lower respiratory tract infections (RTIs).

CRD COMMENTARY - Selection of comparators
This study compared the treatment of lower RTIs with ER versus IR clarithromycin. The authors did not justify their choice of the comparator. You should consider how these treatment options compare to usual practice in your own setting.

Validity of estimate of measure of effectiveness
The measure of health benefit was modelled using a decision analysis model. The model parameters were taken from published studies. The authors did not state how they identified these primary studies. They indicated that studies published between 1990 and 2003 were found, but did not report the sources searched. The data from the primary studies were combined using weighted averages. The paper did not include any investigation of the differences between the primary studies used to identify model parameters. However, the authors considered the impact of only taking effectiveness data from blind, randomised controlled trials.
Validity of estimate of measure of benefit
The measure of health benefit used in the economic analysis was taken from the model discussed above.

Validity of estimate of costs
The paper did not explicitly state the economic perspective adopted in the study, but it appears to have been that of a health care payer. However, the costs of hospitalisation were not included in the study. The unit costs and resource use data were reported separately in the paper. This will enhance the scope for generalising this study to other settings. The generalisability of the study was further increased by the sensitivity analyses. These identified the impact of variation in the effectiveness data, but did not consider the impact of variation in resource use on the estimate of costs. No clear price year was reported, which will hinder future reflation exercises. The cost data were not discounted. However, as the time period of the cost data was not stated in the paper, it is unclear whether this was appropriate.

Other issues
The authors presented their data in a comprehensive manner and their conclusions reflected their results. They did not compare their findings with those from similar studies. This study was designed to reflect the situation in the USA, but the authors did not consider how their results could be generalised to other settings.

Implications of the study
The authors did not make any recommendations for changing practice or for further research.

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