Comparison of hospitalization rates in patients with community-acquired pneumonia treated with telithromycin for 5 or 7 days or clarithromycin for 10 days

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 use of oral telithromycin, administered at a dose of 800 mg once daily (two 400-mg tablets) for either 5 or 7 days, was evaluated.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised adults (aged >/= 18 years) with CAP. The authors described numerous exclusion criteria. For example, severe CAP, CAP requiring immediate admission to an intensive care unit or parenteral antibacterial therapy, and those with infections attributable to sources other than community-acquired bacterial pathogens. Further exclusion criteria were patients who had risk factors for drug-resistant S. pneumonia, patients with a history of alcohol abuse, and immunocompromised patients.

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

Dates to which data relate
The effectiveness and resource use evidence were collected in 2000. The price year also appears to have been 2000, although this was not explicitly stated.

Source of effectiveness data
The effectiveness data were derived from a single study.

Link between effectiveness and cost data
The costing (which appears to have been performed retrospectively) was carried out on the same sample of patients as that used in the effectiveness study.

Study sample
The study sample was selected by including adult outpatients and inpatients considered suitable for oral therapy who had a suspected diagnosis of CAP. The authors stated that the study was powered to detect equivalence in clinical efficacy between treatments, although further information about the sample calculation was not reported. A total of 581
patients were enrolled into three groups. There were 193 patients (62.7% male) in the 5-day telithromycin group, 195 (52.8% male) in the 7-day telithromycin group and 187 (51.9% male) in the 10-day clarithromycin group. The mean ages of the patients were 45.8 years (5-day telithromycin), 45.7 years (7-day telithromycin) and 46.0 years (10-day clarithromycin), respectively. Six patients were not randomised because of a lack of chest X-ray findings consistent with bacterial CAP.

**Study design**
The analysis was based on a randomised, double-blind, parallel-group, Phase III clinical trial. The trial was multi-centred being based in 77 centres across 9 countries: Argentina (8), Brazil (5), Canada (14), Chile (2), Germany (6), South Africa (9), Spain (4), the UK (5) and the USA (24). The method and unit of randomisation were not reported, only that the patients were randomised according to a ratio of 1:1:1. The study investigators were blinded to the treatment assessed. The study patients were followed for 1 month with evaluations at pre-therapy/entry (day 1), on-therapy (days 3 - 5), end of therapy (days 11 - 13), post-therapy/test of cure (TOC) (days 17 - 24), and late post-therapy (days 31 - 36). There was no reported loss to follow-up.

**Analysis of effectiveness**
The analysis was reported to have been conducted on an intention to treat basis. A further analysis was performed in which only those patients who had clinical and radiologic confirmation of CAP were considered. The primary effectiveness outcomes were the clinical cure rates. The authors reported that they analysed other secondary efficacy variables, such as bacteriological outcomes at the post-therapy/TOC visit, clinical and bacteriological outcomes at the late post-therapy visit, and safety variables (e.g. electrocardiogram recordings and emergence of adverse events). In addition, the authors stated that there were no statistically significant differences across the treatment groups in terms of demographics, inpatient or outpatient status, or baseline clinical characteristics (as indicated by the Fine scale, which stratified patients according to demographic characteristics, co-morbidity, and abnormal physical or laboratory findings).

**Effectiveness results**
The clinical cure rates were 89.3% for 5-day telithromycin, 88.8% for 7-day telithromycin and 91.8% for 10-day clarithromycin. The differences between 5- or 7-day telithromycin versus clarithromycin were not statistically significant (-2.5%, 95% confidence interval, CI: -9.7 - 4.7 and -3.0%, 95% CI: -10.2 - 4.3, respectively).

These results were also supported when only patients with a clinical and radiologic confirmation of CAP were considered at analysis.

The authors reported that the bacteriological outcomes and tolerability profiles were similar for the three treatment regimens, although no evidence for this was presented.

**Clinical conclusions**
The clinical efficacy of the two technologies was statistically equivalent in terms of clinical cure rates.

**Measure of benefits used in the economic analysis**
The authors did not estimate a summary measure of benefits. Instead they reported that, since no significant clinical differences were observed between telithromycin and clarithromycin, a cost-minimisation analysis would be carried out.

**Direct costs**
The costing was carried out from the perspective of the US managed care payer, although it was unclear whether the payer might represent different organisations in the varying settings (e.g. third-party payer, government). Resource use was measured over the trial period from patients, using a Healthcare Resource Utilization Case Report Form for
protocol-driven costs (e.g. X-rays, electrocardiograms, visits, examinations, tests). In later visits, investigators collected information about non protocol driven costs (including emergency visits, additional general practitioner contact, home contacts, and additional ambulatory and inpatient tests or procedures). CAP-related hospitalisations were identified so as to estimate only those hospitalisation costs directly associated with CAP. The quantities were reported separately from the unit costs. The unit costs were obtained from hospitalisation data. Discounting was not required because of the very short time horizon. The price year was 2000. The costs estimated were the total hospitalisation costs per 100 patients.

**Statistical analysis of costs**
An analysis of variance applying the Dunnett adjustment was used to compare continuous variables and generate 95% CIs for the costs. Statistical significance was defined at a level of 5%.

**Indirect Costs**
The indirect costs, such as the implications of treatment for the wider society, were not estimated. The authors reported that this was beyond the scope of their study.

**Currency**
US dollars ($).

**Sensitivity analysis**
There was no report of sensitivity analyses being carried out.

**Estimated benefits used in the economic analysis**
See the 'Effectiveness Results' section.

**Cost results**
The hospitalisation cost per 100 patients was $46,099 for 10-day clarithromycin, $19,653 for 5-day telithromycin (difference versus clarithromycin -$26,446, 95% CI: -66,654 - 13,762) and $8,252 for 7-day telithromycin (difference versus clarithromycin -$37,847, 95% CI: -77,953 - 2,259).

These differences did not achieve statistical significance.

**Synthesis of costs and benefits**
Not relevant.

**Authors’ conclusions**
There were no statistically significant differences in the clinical efficacy between 5- and 7-day telithromycin and 10-day clarithromycin. As 5- and 7-day telithromycin were associated with a trend towards fewer hospitalisations, the projected hospitalisation costs related to community-acquired pneumonia (CAP) were "numerically reduced”.

**CRD COMMENTARY - Selection of comparators**
Clarithromycin was chosen as the comparator because it was reported to be a commonly recommended first-line treatment in the authors' setting for the treatment of outpatient adult patients with CAP. You should decide whether this is a widely used health technology for the treatment of CAP patients in your own setting.
Validity of estimate of measure of effectiveness
This was a double-blind, parallel-group Phase III clinical trial, which was appropriate for the study question. A relatively large sample was enrolled and this is likely to have been representative of the study population (since patients from many centres allocated in different countries were included). The sample appears to have been appropriate for the clinical question. The patients groups were comparable at baseline, and there was no evidence of confounding factors. The results were presented as point estimates as well as CIs. Statistical comparisons between 5- and 7-day telithromycin groups were not performed. As a limitation of the study, the authors mentioned that the trial was powered to detect clinical equivalence but not difference.

Validity of estimate of measure of benefit
No summary measure of benefit was used in the economic analysis, as the clinical study showed therapeutic equivalence of the treatment alternatives and therefore included only costs. Thus, the reader is referred to the comments in the 'Validity of estimate of measure of effectiveness' field (above).

Validity of estimate of costs
The costing was carried out from the perspective of the US managed care payer. The authors clearly stated that the indirect costs were beyond the scope of their study. As the cost-differences between the study groups did not achieve statistical significance, omissions in cost may alter the principle conclusions drawn. Examining the cost implications for individual countries might have revealed statistical significance in some countries, but not others, owing to the differing structures in the countries. This might have been a useful result for readers who were interested in their own specific country, or who were interested in generalising the results. Most of the unit costs and the quantities were reported separately, thus improving the readers' ability to understand the key cost drivers. In addition, this could facilitate limited reflation exercises in other settings. The potential miscategorisation of CAP-related hospitalisations might have introduced some bias into the cost estimation.

Other issues
The authors drew comparisons with findings of other authors highlighting, in particular, three studies with consistent findings in terms of healthcare resource utilisation. The authors presented valuable arguments to help explain the results that were observed, focusing on how clinically equivalent therapies can have potentially differing cost implications. Further, the authors reported that although this was a multinational study, the analysis was performed from a US managed care perspective and, therefore, the costing element may not be applicable to other countries. The authors acknowledged that, given the limitations of the study, the analyses should be regarded as "observational".

Implications of the study
The authors did not make any recommendations for policy or practice following on from their study. However, studies to support these preliminary analyses are recommended as a topic for future work.

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