Asthma outcome changes associated with use of the leukotriene-receptor antagonist zafirlukast

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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 use of zafirlukast (20-mg tablets), a leukotriene-receptor antagonist, among patients with asthma.

Type of intervention

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients with asthma, aged between 12 and 64 years, who were covered by a large health insurer in the northeast of the USA.

Setting
The setting was a hospital. The study was carried out in the USA.

Dates to which data relate
The effectiveness and resource use data were collected between May 1996 and November 1998. The unit costs were obtained from studies published between 1996 and 1998. The price year was 1998.

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

Link between effectiveness and cost data
The costing was performed retrospectively on the same sample population as that used for the effectiveness analysis. Both the effectiveness and cost data were obtained from the integrated claims database of a large health insurer.

Study sample
No power calculations, to assure a certain power, appear to have been performed in the planning phase of the study. Patients who met the following criteria were considered for the effectiveness analysis:

at least one claim with a primary or secondary diagnosis of asthma;

continuous medical and prescription drug coverage;
not enrolled in any Medicare supplemental plans;

at least two zafirlukast prescriptions during the 90 days after the start of zafirlukast treatment; and

outcome information for the 6 months before and after the introduction of zafirlukast.

Among 104,416 patients with at least one diagnosis of asthma in the claims database used to extract the data, 599 patients met the study criteria. The mean age of the patients was 46.7 (+/- 12.6) years and 63% were females. Thirteen per cent had mild intermittent asthma, 27% mild persistent asthma, 50% moderate persistent asthma, and 10% severe persistent asthma. Asthma severity was measured on the basis of the asthma drug regimen used for each patient during the 90 days before the start of zafirlukast treatment. The authors did not report any evidence that the study sample was representative of the study population.

Study design
This was a retrospective, within-group comparison study, which appears to have been multi-centre. The period of follow-up was 12 months in total, 6 months before and 6 months after the introduction of zafirlukast. The outcome assessment was not reported to have been blinded.

Analysis of effectiveness
Only patients who had complete data for the 6 months before and the 6 months after the introduction of zafirlukast were considered for the main effectiveness analysis. The primary outcomes assessed were the percentages of patients experiencing at least one outpatient visit, one emergency department visit, one inpatient stay, and having at least one beta-adrenergic agonist prescription (this was used as an indicator of inadequate asthma control) before and after the introduction of zafirlukast. Also reported were:

the average number of outpatient visits, emergency department visits, inpatient stays, beta-adrenergic agonist prescriptions, and zafirlukast prescriptions; and

the percentage of patients that experienced either an increase or a decrease in these outcome events during the study period.

The authors did not report any information about changes in health status, or other relevant characteristics of the patients, that could have changed during the study period (i.e. before and after the introduction of zafirlukast).

Effectiveness results
After the introduction of zafirlukast, compared with the previous period:

the percentage of patients experiencing at least one outpatient visit was reduced by 9% (from 33.0 to 30.0%; mean frequencies: 3.97 versus 3.35),

the percentage of those experiencing one emergency department visit was reduced by 33% (from 7.2 to 4.8%; mean frequencies: 0.11 versus 0.08),

the percentage of those experiencing one inpatient stay was reduced by 34% (from 11.9 to 7.8%; mean frequencies: 0.17 versus 0.10), and

the percentage of those having at least one beta-adrenergic agonist prescription were reduced by 11% (from 81.1 to 71.8%; mean frequencies: 3.48 versus 2.68), (p<0.05 for all changes).

During the study period, the percentage of patients that experienced either an increase or a decrease in the frequency of events were:

4.0% versus 7.5% for outpatient visits,
3.3% versus 5.5% for emergency department visits,
5.2% versus 9.3% for inpatient stays, and
14.5% versus 38.2% for beta-adrenergic agonist prescriptions.

Clinical conclusions
The start of treatment with zafirlukast was associated with subsequent reductions in outpatient visits, emergency department visits, inpatient stays, and prescriptions for short-acting beta-adrenergic agonists in the 6 months following its introduction.

Methods used to derive estimates of effectiveness
The authors formulated an assumption to derive the effectiveness estimates.

Estimates of effectiveness and key assumptions
The authors assumed that all outpatient visits, emergency department visits, and inpatient stays during the study period were asthma-related.

Measure of benefits used in the economic analysis
No summary measure of benefit was used in the economic analysis. The study was therefore categorised as a cost-consequences analysis.

Direct costs
The direct costs included in the study were those of the third-party payer. These included the costs of outpatient visits, emergency department visits, inpatient stays, rescue medication (i.e. beta-adrenergic agonist), and zafirlukast. The authors reported that due to data limitations, some relevant costs (i.e. glucocorticoid and other asthma treatments beyond zafirlukast and short-acting beta-adrenergic agonists) were not included. The resource quantities were reported separately from the unit costs, and the price year was 1998. Resource use was obtained from the integrated claims database used for the effectiveness analysis, while the unit costs came from published studies. Therefore, the costs were estimated using actual data. Discounting was not performed, although it was not relevant since the period considered for the economic evaluation was shorter than 2 years. The study reported the cost-savings per patient after the introduction of zafirlukast.

Statistical analysis of costs
Since resource use was used as a proxy of the primary outcomes in the effectiveness analysis, and some statistical analyses were reported for the resources used, it can be considered that the costs were treated stochastically. However, no statistical analyses to compare the total costs before and after the introduction of zafirlukast were reported. According to the distribution of the data, the McNemar test, chi-squared test and Fisher's exact probability test were used to compare the resources used.

Indirect Costs
The indirect costs were not reported.

Currency
US dollars ($).
Sensitivity analysis
A sensitivity analysis was performed to test the robustness of the study results when a longer follow-up period was considered. For this, a smaller group of patients (203 of the total study sample) with claims information in the 12 months before and the 12 months after the introduction of zafirlukast treatment was analysed. This group of patients was shown to be similar to the study sample used in the effectiveness analysis in terms of age, gender, asthma severity, insurance type, and number of zafirlukast prescriptions per month.

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

Cost results
The cost-saving per patient was $101 for the 6 months following the introduction of zafirlukast, compared with the 6 months before.

Synthesis of costs and benefits
The estimated health benefits and costs were not combined given the cost-consequences approach undertaken. The results of the sensitivity analysis (i.e. patients with data for a 12-month follow-up period) showed that, although patients presented a decrease in the number of outpatient visits, emergency department visits and inpatients stays after the introduction of zafirlukast, the difference was not statistically significant. However, the decrease in the number of beta-adrenergic agonist prescriptions remained significantly lower after the introduction of zafirlukast. The cost-saving per patient decreased to $11 during the 12 months following the introduction of zafirlukast, compared with the 12 months before.

Authors' conclusions
Zafirlukast would appear to be a preferred strategy for patients with mild-to-moderate persistent asthma, improving outcomes at a lower total treatment cost.

CRD COMMENTARY - Selection of comparators
The comparator chosen was not specified clearly. Although it was the treatment strategy used for asthma patients in the authors' setting before the introduction of zafirlukast, no further details of it were given. This limits the comparisons performed, as there is not a clear treatment with which to compare the results of the introduction of zafirlukast.

Validity of estimate of measure of effectiveness
The authors reported that, because of the retrospective nature of the effectiveness analysis, some relevant factors (e.g. changes in health status, changes in health insurance coverage, non-compliance, and switching to other medications) could not be evaluated. These might have influenced the effectiveness results. Moreover, the effectiveness results were subject to the assumption that all the events were asthma-related. Since some relevant confounding factors (such as comorbidity) could not be assessed, it could not be inferred whether this assumption was actually met. Therefore, the effectiveness results might have been biased. The authors reported a further limitation in that the results of the study might have been subject to the potential bias of regression to the mean. All these facts introduced uncertainty into the reliability of the effectiveness results.

Validity of estimate of measure of benefit
No summary measure of health benefit was used in the economic analysis. The study was therefore categorised as a cost-consequences analysis.

Validity of estimate of costs

As the authors reported, not all the relevant costs related to the perspective adopted could be included, owing to the lack of data. The resource quantities were reported separately from the costs, and the price year was stated, which will enhance the feasibility of reflation exercises to other settings. Appropriate statistical analyses to compare resource use appear to have been performed, although none were carried out to detect significant differences in costs between the two treatment periods. A sensitivity analysis allowed the two treatment periods to be compared when a longer follow-up period was considered. Discounting was not performed, but it was not necessary since the period considered for the main analysis was less than 2 years.

**Other issues**
The authors reported that the results of this study were similar to those obtained by other clinical trials in terms of the reduction in resource use experienced by patients treated with zafirlukast. The issue of the generalisability of the results to other settings was not addressed.

**Implications of the study**
The findings suggested that clinical outcomes could be improved at lower cost by the use of zafirlukast, implying that this is a highly cost-effective option. However, the authors recommended further research to address the limitations inherent in this study. These limitations must be considered when interpreting the results obtained.

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