Zafirlukast: the first leukotriene-receptor antagonist approved for the treatment of asthma

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Authors' objectives
To review the pharmacology, pharmacokinetics, clinical efficacy, and adverse effects of zafirlukast for the treatment of asthma.

Searching
MEDLINE was searched, but no details of the search strategy were provided.

Study selection
Study designs of evaluations included in the review
Double-blind, placebo-controlled trials were included.

Specific interventions included in the review
Zafirlukast (both oral and aerosol).

Participants included in the review
Patients with asthma were included.

Outcomes assessed in the review
Asthma symptoms, concomitant beta-agonist use, pulmonary function, and the safety profile were assessed.

How were decisions on the relevance of primary studies made?
The author does not state how the papers were selected for the review, or how many of the reviewers performed the selection.

Assessment of study quality
The author does not state that they assessed validity.

Data extraction
The author does not state how the data were extracted for the review, or how many of the reviewers performed the data extraction.

Methods of synthesis
How were the studies combined?
The studies were combined in a narrative description.

How were differences between studies investigated?
Differences between the studies were described in the narrative.

Results of the review
There were 11 trials evaluating the efficacy of zafirlukast in patients with asthma, including 8 trials where asthma was experimentally induced.

According to the results from 8 trials, zafirlukast antagonised exercise-induced bronchoconstriction, and blockws both early- and late-phase responses following allergen provocation in patients with atopic asthma.
A 6-week, multicentre, double-blind, randomised, dose-ranging study evaluated the efficacy of oral zafirlukast (20, 10 or 5 mg twice daily) versus placebo. Of the three zafirlukast dosages, the 20-mg twice-daily dosage produced consistently significant \( p<0.05 \) improvements relative to placebo, by reducing night-time awakenings, first-morning asthma symptoms, daytime asthma symptom scores and albuterol use, and by increasing peak expiratory flow rates and forced expiratory volume. A 13-week multicentre trial with 762 patients found that zafirlukast (20 mg twice daily) significantly decreased daytime asthma symptom scores, night-time awakenings, mornings with asthma, and beta-agonist use, and improved morning peak expiratory flow rates.

A multicentre trial found that both zafirlukast and cromolyn were significantly more effective than placebo \( p<0.05 \), with the two drug treatments exhibiting comparable efficacy.

The available data indicated that zafirlukast was well tolerated. Greater efficacy was noted following oral administration than with aerosol dosing, presumably because of the enhanced delivery of an ingested drug compared with an inhaled one.

**Authors’ conclusions**
Clinical trials have demonstrated that zafirlukast reduces asthma symptoms and concomitant beta-agonist use, improves pulmonary function, and has a safety profile comparable with placebo. However, its effectiveness relative to other anti-asthma medications still needs confirmation. Further research is needed to establish its role as an add-on agent for patients with severe asthma, aspirin-sensitive asthma, and both allergies and asthma. Zafirlukast has the advantage of being an oral agent with twice-daily dosing; these attributes offer the potential for greater patient adherence to pharmacotherapy.

**CRD commentary**
Details of the inclusion criteria were presented. The literature search was limited to only one database (MEDLINE), and details of the search strategy were unavailable. The author’s conclusions seem appropriate. It is important to stress that zafirlukast should be compared with other anti-asthma medications in further research.

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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.