

A rapid and systematic review of the clinical effectiveness and cost-effectiveness of orlistat in the management of obesity

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Executive summary

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Executive summary

Background

The prevalence of obesity in developed societies is increasing. Obesity is associated with an increased risk of co-morbidity, including cardiovascular disease and diabetes. Following the withdrawal of fenfluramine and dexfenfluramine, interest has focused on a novel anti-obesity drug orlistat.

Objective

To systematically assess the clinical effectiveness and cost-effectiveness of orlistat in the management of obesity.

Methods

Search strategy

Nineteen electronic databases were searched from inception to June 2000. Additionally, Internet searches were carried out, bibliographies of retrieved articles were examined and submissions were received from the manufacturer of orlistat.

Inclusion and exclusion criteria

Randomised controlled trials (RCTs) evaluating the effectiveness of orlistat used for weight loss or maintenance of weight loss in overweight or obese patients were eligible for inclusion. Primary outcome measures were changes in body weight, fat content or fat distribution. Secondary outcomes were changes in obesity-related risk-factor profiles, such as lipid levels, indicators of glycaemic control and blood pressure. Studies recruiting people with eating disorders such as anorexia nervosa and bulimia nervosa were excluded.

Process of study selection

Assessment of titles and abstracts was performed independently by two reviewers. If either reviewer considered a reference to be relevant, the full paper was retrieved. Full papers were assessed against the review selection criteria by two independent reviewers, and disagreements were resolved through discussion.

Data extraction

Data were extracted by one reviewer into structured summary tables and checked by a second reviewer.

Any disagreements about data were resolved by discussion.

Quality assessment

Each included trial was assessed against a comprehensive checklist for methodological quality. Quality assessment was performed independently by two reviewers with disagreements resolved by discussion.

Methods of analysis/synthesis

This report is a narrative summary, with results grouped according to study endpoint. Statistical pooling was undertaken in groups of trials that were considered to be sufficiently similar.

Estimation of quality of life, costs and cost-effectiveness and/or cost per quality-adjusted life-year

Relevant economic evaluations were identified from the search strategy described above. Assessment of methodological quality was undertaken using principles outlined in published guidelines.

Company submissions

Data from company submissions were subject to the same selection and appraisal processes as other studies considered for inclusion in the review, except that only RCTs with a duration of at least 1 year were selected.

Results

Results of the search strategy

Fourteen RCTs (including three company submissions) and two economic evaluations (including one company submission) were included in the review.

Results of the quality assessment

Methodological quality of trials was moderate to good. The main problems were lack of detail on methods used to produce true randomisation, small sample sizes in some cases and failure to use intention-to-treat analysis. It is likely that maintenance of blinding was difficult due to adverse effects associated with the study medication.

Evidence of clinical effectiveness and cost-effectiveness

Most of the trials showed greater weight loss and better weight maintenance with orlistat compared to placebo at all endpoints (statistically significant differences for both outcomes). Orlistat 120 mg three times daily was the optimum regimen in terms of weight loss. Most trials showed significant improvement in at least some lipid concentration parameters, and, in three RCTs, orlistat produced statistically significant reductions in blood pressure relative to placebo. In obese patients with type 2 diabetes, orlistat resulted in a significantly greater weight loss at 1 year compared with placebo, and some parameters of glycaemic control and lipid concentration also showed significantly greater improvements compared with placebo. The incidence of gastrointestinal adverse events was consistently higher in orlistat groups compared with placebo, and orlistat use was associated with lower serum levels of fat-soluble vitamins. The cost per quality-adjusted life-year for orlistat was £45,881.

Conclusions

Implications for clinical practice

Although many trials have demonstrated statistically significant differences between groups in

terms of weight loss in favour of orlistat versus placebo, the differences may not always be of clinical significance. The clinical significance of between-group differences for secondary outcomes may also be debatable. Possible adverse effects should be taken into account when prescribing orlistat, particularly gastrointestinal effects.

Implications for future research

Future trials should ensure good methodological quality. Further research is required to determine the effects of orlistat in different patient groups according to gender, age, ethnicity and social class. Clinical trials should be designed to match protocols observed in clinical practice with regard to patient selection and treatment.

Publication

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