

# The clinical effectiveness and cost-effectiveness of sibutramine in the management of obesity: a technology assessment

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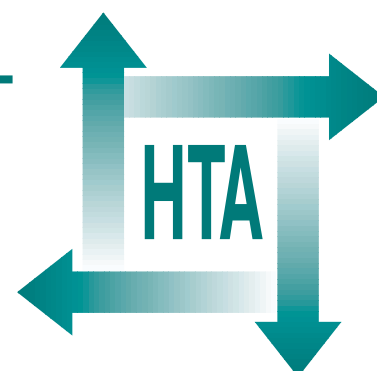
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## *Executive summary*

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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 in 1997, interest has focused on a novel anti-obesity drug: sibutramine. (Note: since the completion of this review, phentermine has been withdrawn from the market – May 2001.)

### Aims of the review

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

### Methods

#### Search strategy

A total of 19 electronic databases were searched from inception to June 2000. Additionally, Internet searches were carried out, bibliographies of retrieved articles were examined, and a submission was received from the manufacturer of sibutramine.

#### Inclusion and exclusion criteria

Randomised controlled trials (RCTs) evaluating the effectiveness of sibutramine 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

The 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. Two independent reviewers assessed full papers against the review selection criteria. 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 (QALY)

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

#### Company submission

Data provided by the manufacturer of sibutramine 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

A total of 16 RCTs (11 published and five submitted by the manufacturer) and one economic evaluation (submitted by the manufacturer) were included in the review. (Note: since the completion of this review, two of the RCTs submitted by the manufacturer have been published.)

#### Results of the quality assessment

The 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, and failure to use intention-to-treat analysis.

### **Evidence of clinical effectiveness and cost-effectiveness**

Most of the individual placebo-controlled trials and pooled estimates suggested that sibutramine produced statistically significant greater weight loss than placebo at all observed endpoints (weighted mean difference for weight change at 8 weeks: -3.4 kg; mean difference range for weight change at 6 months: -4.0 to -9.1 kg; and at 1 year: -4.1 to -4.8 kg). The most frequent dosing regimen was 10–20 mg daily. Findings suggested a dose–effect relationship in terms of weight loss. Sibutramine was also associated with better weight maintenance relative to placebo (statistically significant difference). Results from mainly small trials showed that sibutramine produced more favourable outcomes in terms of loss of fat mass, reduction in body mass index and loss of at least 5% and 10% of initial body weight. Between-group differences for waist circumference, hip circumference and waist–hip ratio did not reach statistical significance in most trials. Similar results for weight loss were found in trials recruiting solely patients with type-2 diabetes; between-group differences for changes in indicators of glycaemic control were not usually statistically significant. Sibutramine use was associated with small, statistically significant increases in pulse rate, heart rate and blood pressure. The cost per QALY was estimated as £10,500.

## **Conclusions**

### **Implications for clinical practice**

Although many trials demonstrated statistically significant differences between groups in terms of weight loss in favour of sibutramine 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 sibutramine.

### **Recommendations for future research**

Future trials should ensure good methodological quality, including adequate statistical power and analysis by intention-to-treat. Further research is required to determine the effects of sibutramine 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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