Conitec

Recomendation report

DRUGS

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Sibutramine for the treatment of obese patients

Brasília – DF
2020

Technology: Sibutramine hydrochloride monohydrate

Indication: Adjuvant therapy as part of a weight management program for obese patients with a body mass index (BMI) greater than or equal to 30 kg/m2

Applicant: Secretariat of Science, Technology and Strategic Inputs (SCTIE)/Ministry of Health of Brazil, and Brazilian Association for the Study of Obesity and Metabolic Syndrome (ABESO)

Question: Is sibutramine effective and safe for the treatment of obese adult patients, who do not respond to non-pharmacological treatment and do not have cardiovascular disease?

Scientific evidence: In the report prepared by SCTIE/Ministry of Health of Brazil, 14 studies were included: three systematic reviews, ten randomized controlled trials (RCTs), and one cohort study. The three systematic reviews were assessed as high risk of bias. The RCTs were assessed using the Cochrane risk of bias tool, most of which were classified as high risk or unclear risk, while the cohort study as low risk according to respective assessment tool. In the critical analysis of the Technical Dossier prepared by ABESO, 13 studies were included: ten RCTs, and three cohort studies. According to the evidence presented by both applicants, sibutramine has been shown to be effective in achieving clinically significant weight loss, as well as in reducing body mass index and waist circumference, especially compared with placebo, and in short and medium term. In the long term, there is evidence that indicates a weight regain and low persistence. In most studies, sibutramine was used in conjunction with the recommendation to change eating habits and behaviors. The main adverse events associated with the use of sibutramine were dry mouth, constipation and insomnia. Increased blood pressure and heart rate were also reported, but to a lesser extent. RCTs and cohort studies included in the critical analysis had a high risk or unclear risk of bias.

Economic evaluation: In SCTIE's report, the cost-effectiveness analysis was based on data from the Management System of the Table of Procedures, Medicines, Orthotics, Prosthetics and Special Materials (SIGTAP) of the Brazilian Public Health System (SUS), in order to estimate the costs of conventional treatment offered to obese adult patients. The annual cost of sibutramine per patient was estimated at BRL 532.10 considering the average treatment cost for different dosages. Procedures related to conventional treatment, diet and exercise were not found in SIGTAP, thus, these costs were set to zero. The effectiveness outcome was the proportion of patients achieving at least 10% body weight loss (clinically significant weight loss), obtained through the meta-analysis of proportion of the studies included in the review by Rucker et al., 2007, and in the study by Halpern et al., 2002. Thus, the incremental cost-effectiveness ratio was BRL 3,130.00 for a patient to achieve at least 10% body weight loss, compared with conventional treatment. In ABESO's Technical Dossier, the incremental cost-effectiveness ratio was shown to be favorable to the use of sibutramine compared with the non-pharmacological treatment available in SUS (a saving of BRL 602.35). After the sensitivity analysis, the 12-month treatment of obesity with sibutramine was the dominant strategy in 44.97% of the simulations (less costly and more effective). However, the results in the Technical Dossier may be under or overestimated, due to uncertainties and limitations in the parameters and assumptions used, as well as the impossibility of verifying and reproducing the calculations used in the analyses.

Budget impact analysis: In SCTIE's report, the pharmaceutical forms registered with the Brazilian National Health Surveillance Agency, sibutramine 10 and 15 mg capsules, were considered to estimate the cost of treatment. The costs were limited to the purchase price of medicines. As no data were found in the literature on the percentage of patients receiving daily doses of 10 and 15 mg, it was decided to develop six scenarios: a scenario where all patients receive daily doses of 10 mg; a scenario where all patients receive daily doses of 15 mg; a scenario where half of patients receive daily doses 10 mg; and other three scenarios where patient population would be excluded due to some contraindications (cardiovascular diseases; diabetes and arterial hypertension; and uncontrolled hypertension). The analysis was conducted over a five-year time horizon, assuming an initial market share of 30% for sibutramine, with annual increments of the same value, reaching 50% in the fifth year. Thus, in these six scenarios, the budget impact of incorporating sibutramine would range from BRL 3.3 to BRL 4.3 billion in the first year, and from BRL 22.7 to BRL 29.6 billion after five years. Based on the lowest price of public procurement during six months of the current year, recent data on the eligible population, and other premises of the previous scenarios, the budget impact of incorporating sibutramine was estimated to range from BRL 1.4 to BRL 1.7 billion in the first year, and from BRL 9.3 to BRL 11.8 billion after five years. Three other scenarios were developed, based on these updated price and population data, but excluding patients who underwent stomach reduction surgery, patients without significant weight loss, and patients with cardiovascular diseases (except hypertension), diabetes and arterial hypertension, or uncontrolled arterial hypertension, and considering persistence rate and market share of 100%. In these scenarios, the amount would be BRL 6.4, BRL 5.6 and BRL 5.8 billion, respectively. In ABESO's Technical Dossier, the budget impact over five years would range from BRL 542.3 to BRL 902.5 million, considering different values of effectiveness. Varying the market share and the highest and lowest effectiveness value, the amounts may reach BRL 1.8 billion. Considering the efficacy values of sibutramine, the reduction in the incidence of diabetes cases, and discounting the value of sibutramine, the budget impact would result in savings ranging from of BRL 769.5 million to BRL 2.9 billion. However, the results in the ABESO's Technical Dossier may be under or overestimated, due to uncertainties and limitations in the parameters and assumptions used in the budget impact analysis, as well as the impossibility of verifying and reproducing the calculations used, so compromising the understanding of the financial consequences of incorporating sibutramine in the scope of SUS.

International recommendations: The National Institute for Health and Care Excellence – NICE (United Kingdom), Pharmaceutical Benefits Advisory Committee – PBAC (Australia), and Pharmaceutical Management Agency – PHARMAC (New Zealand) do not recommend the use of sibutramine to obese patients. PBAC pointed out the high potential for use outside the restriction, and according to PHARMAC, treatment should address the causal factors of obesity, including changes in lifestyle and community's attitudes. As in the United Kingdom, sibutramine was withdrawn from the New Zealand market because it has shown only moderate effects, together with significant risks.

Considerations: The available evidence suggests that treatment with sibutramine for weight loss is clinically relevant for obese patients. However, there are uncertainties about the benefits of sibutramine due to factors such as low methodological quality of the studies, trend of weight regain over time, trend of publishing positive results, a significant number of adverse events, and persistence of use. Although available in Brazil, sibutramine has been withdrawn from the market in many countries.

Public consultation: A total of 1.421 contributions were received, 38 of which were technical-scientific contributions, and 1.383 were experience or opinion contributions. The majority disagreed with Conitec's recommendation, mainly pointing out the efficacy and safety of sibutramine, obesity as a disabling condition and a risk factor for other comorbidities, and the absence of alternatives for the pharmacological treatment of obese patients in SUS. ABESO and the Brazilian Society of Endocrinology and Metabolism (SBEM) took part in the public consultation, and their comments were properly considered.

Final Recommendation: The Conitec's members present at the 86th Ordinary Meeting decided not to recommend the incorporation of sibutramine for the treatment of obese patients. The Deliberation Record No. 513/2020 was signed.

Decision: Not to incorporate sibutramine for the treatment of obese patients, within the scope of SUS, according to Ordinance No. 15, published in the Official Gazette of the Federal Executive No. 78, Section 1, page 221, on April 24th, 2020.

Decision: Not to incorporate orlistat for weight loss in overweight or obese patients, within the scope of SUS, according to Ordinance No. 14, published in the Official Gazette of the Federal Executive No. 78, Section 1, page 221, on April 24th, 2020.