REPORT 123
Risperidone in Autism Spectrum Disorder (ASD)

Ordinance nº 32/2014 published on 09/18/2014
EXECUTIVE SUMMARY

**Technology:** Risperidone is an antipsychotic that acts as antagonist of dopamine and serotonin receptors. It is part of the group of antipsychotics usually called atypical or second generation, which are known for the lower risk of incidence of extrapyramidal effects compared to first generation antipsychotics.

**Indication:** Treatment of Autism Spectrum Disorder symptoms.

**Applicant:** 1ª Vara Federal de Porto Alegre [1st Federal Court of Porto Alegre].

**Scientific evidence:** To search for evidence, the Systematic Reviews of Randomized Clinical Trials (RCT) were selected. Of the 21 references selected, a total of 16 reviews had their study focus on the efficacy of using risperidone in subjects with ASD, where, in accessory symptoms of hyperactivity, irritability and aggressiveness, risperidone was consistently effective when compared to placebo. When compared to haloperidol, the total results of symptom scales had a significant difference, but with difficult interpretation without its domains being separated. As to the other symptoms studied, such as restricted interests, emotional interaction and verbal communication, the studies converged in not demonstrating statistical significance. A total of 5 reviews focused on the associated adverse events, where the use of risperidone may be accompanied by the common events: sedation, enuresis, constipation, salivation, fatigue, tremors, tachycardia, appetite increase, weight gain, vomiting, apathy and dyskinesia. Special attention should be given to increase in (sic), increase in transaminases, abnormal heart conduction, weight gain and tardive dyskinesia with the prolonged use of risperidone.

**Budget impact:** Based on the assumptions and available data, the base case estimates an annual impact of BRL 334,274.69 with oral solution inclusion; BRL 724,535.17 with 0.25-mg and 0.5-mg tablet inclusion and BRL 526,547.28 with the inclusion of both oral solution and 0.25-mg and 0.5-mg tablets. That is, the base case demonstrates that including only the oral solution may translate into a saving of up to BRL 390,260.49. By applying variations of coverage rates and aggressiveness incidence, the conclusion that including solely the oral solution would be the less expensive proposal is kept, with the saving of at least BRL 384,545.00.

**Discussion:** When considered together, the results presented suggest that risperidone is effective, although it is not proven to be superior to other antipsychotics available in SUS, and is associated with significant side effects, which limit its use in patients with important irritability- and aggressiveness-related incapacitation, where the benefits of risperidone may overcome its risks, provided that duly monitored.
Recommendation made by CONITEC: At the 24th meeting held on 04/09 and 04/10/2014, the recommendation was to expand the use of risperidone for the treatment of autism spectrum disorder, according to the criteria to be established in a specific Clinical Protocol and Therapeutic Guidelines.

Public Consultation: The contributions from the laboratory that manufactures the reference drug have been received and the report text has been punctually reviewed, with a new budget impact prepared. However, despite grounded, the proposal presented by the contribution needs to consider the aspects of: monopoly of the mentioned presentations, which may imply difficulties in acquiring and distributing the drug; higher costs compared to the oral solution; disadvantages of administering in children compared to the oral solution.

Final Deliberation: At the 26th Meeting of CONITEC held on June 9, 2014, the plenary session members unanimously deliberated in favor of recommending the extension of risperidone use to control the irritability and aggressiveness that may arise with autism spectrum disorder, according to the criteria to be established in a specific Clinical Protocol and Therapeutic Guidelines. Deliberation Record nº 90/2014 was signed.