Conitec

Recomendation report

DRUGS

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Mirabegron for the treatment of storage dysfunction in patients with Neurogenic Bladder

Brasília – DF
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Technology: Mirabegron

Indication: Storage dysfunction in adult patients with neurogenic bladder

Background: Neurogenic bladder is a term applied to a malfunctioning urinary bladder and urinary sphincter, due to neurologic dysfunction emanating from internal or external trauma, disease or injury. Some patients with neurogenic lower urinary tract dysfunction experience symptoms that relate to impaired urine storage, such as increased frequency of micturition, urinary urgency and urinary incontinence.

Question: What is the efficacy and safety of mirabegron for storage dysfunction in adult patients with neurogenic bladder?

Scientific evidence: In the search for evidence, 121 references were retrieved, of which three studies were selected, one randomized controlled trial (RCT) and two case series. Concerning the methodological quality, the case series presented a high risk of bias, while the RCT presented an unclear risk of bias since it did not report how allocation and blinding of the participants and assessors had been carried out. The main efficacy outcomes were cystometric volume, residual volume, urgency episodes, incontinence episodes, number of pads, Incontinence Quality of Life (I-QoL) and Patient Perception of Bladder Condition (PPBC) scores. Moreover, these studies also reported adverse events. In regard to the cystometric volume, mirabegron 50 mg / day led to an increase from 183.50 (standard deviation [SD] = 121.60) mL at baseline to 238.81 (SD = 150.56) mL after four weeks of treatment; in the group of patients receiving placebo, there was a reduction of 210.44 (SD = 135.34) mL at baseline to 167.56 (SD = 102.96) mL after four weeks of treatment (p = 0.016). The two case series reported this outcome without a comparison group, and there were no significant differences before and after the intervention. In regard to the residual volume, only one case series evaluated this outcome: the residual volume was 83.4 (SD = 92.2) mL at baseline; 56.8 (SD = 61.4) mL in four weeks; and 78.8 (SD = 113.3) mL in 12 weeks. There were no differences between follow-up and baseline values. Compared with placebo, mirabegron yielded significant improvements in quality of life and functionality, after four weeks of study (p = 0.0013 and p = 0.0001, respectively, for I-QoL and PPBC scores). Adverse events were more frequent in the group receiving mirabegron, but the studies did not provide detailed information on the difference between the groups.

Economic evaluation: Considering the costs of mirabegron, the result of quality of life reported by one of the selected studies, and data on the overall life expectancy of patients with spine trauma, the Quality Adjusted Life Years (QALY) was estimated for the population in question. A deterministic model was developed comparing mirabegron and placebo. It was observed that mirabegron, at a dose of 50 mg, was the dominated strategy, with an incremental cost-effectiveness ratio of BRL 471.89/QALY/month. In the sensitivity analysis, it was observed that, regardless of the utility gain obtained by mirabegron, it was the dominated strategy.

Budget impact analysis: The budget impact analysis was conducted from the perspective of the Brazilian Public Health System (SUS), over a five-year time horizon (2020-2024). The treatment cost was limited to the purchase price of medicines according to the Health Price Database. Given the absence of specific data on individuals with neurogenic bladder, the four main causes of neurogenic bladder were considered: Parkinson's disease, multiple sclerosis, stroke and spinal damage. In the baseline scenario, it was considered the incorporation of mirabegron, and its budget impact over five

years was estimated to be BRL 11,273,255,511.53. An alternative scenario was developed taking into consideration the percentages of use of antimuscarinic agents based on a publication of the National Health Service (NHS) of the United Kingdom (UK). Thus, the budget impact of incorporating both antimuscarinics and mirabegron was estimated to be BRL 2,095,249,966.02, in the first year, and after five years, this amount would be BRL 10,679,375,762.42.

International recommendations: The Canadian Agency for Drugs and Technologies in Health (CADTH) recommends mirabegron only for the treatment of overactive bladder, and has not made a recommendation for storage dysfunction in adult patients with neurogenic bladder. The UK's National Institute for Health and Care Excellence (NICE) does not recommend the use of mirabegron.

Technology horizon scanning: Searches were carried out on ClinicalTrials.gov and Cortellis ™, in order to identify potential drugs for the treatment of adult patients with neurogenic bladder. No drugs were found as part of clinical trials, but it was identified fesoterodine in a study of pediatric patients with urinary incontinence related to neurological conditions.

Considerations: The studies have shown the efficacy of mirabegron in the treatment of incontinence symptoms, especially increase in the cystometric volume, quality of life (I-QoL) and functionality (PPBC) in patients with permanent spinal damage and multiple sclerosis. However, it should be noted that the two case series reported the outcome without a comparison group, and the RCT had a small sample size and an unclear risk of bias. Moreover, the estimated budget impact was over ten billion reais after five years of incorporation. Therefore, there is still insufficient evidence to allow the recommendation of mirabegron for patients with neurogenic bladder.

Initial Recommendation: Conitec, at its 82nd Ordinary Meeting, on October 9th, 2019, decided not to recommend the incorporation of mirabegron in the scope of SUS, for the treatment of neurogenic bladder. Apart from the financial aspect, it was considered, primarily, the absence of significant clinical benefit, as well as the low methodological quality of the studies analyzed.

Public consultation: Five contributions were received, three of which were experience and opinion, and two technical-scientific contributions. Among the experience and opinion contributions, two disagreed with the preliminary recommendation, and one neither agreed or disagreed, and the two technical-scientific contributions disagreed. Conitec decided that there was no sufficient reason to change the preliminary recommendation.

Final Recommendation: The Conitec's members present at the 85th Ordinary Meeting, on February 4th, 2020, unanimously decided not to recommend the incorporation of mirabegron in the scope of SUS, for the treatment of storage dysfunction in patients with neurogenic bladder.

Decision: Not to incorporate mirabegron for the treatment of storage dysfunction in patients with neurogenic bladder, in the scope of SUS, according to Ordinance No. 9, published in the Official Gazette of the Federal Executive No. 49, Section 1, pages 187 and 188, on March 12th, 2020.