REPORT 149

Pegvisomant for the treatment of acromegaly

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EXECUTIVE SUMMARY

Technology: Pegvisomant (Somavert®).

Indication: Acromegaly.

Applicant: Laboratórios Pfizer LTDA.

Context: Acromegaly is a chronic systemic disease characterized by excessive growth hormone (GH) production after epiphyseal closure and that may be caused by different clinical conditions. The Ministry of Health has prepared and made available, by means of Ordinance no. 199, dated February 25, 2013, the Clinical Protocol and Therapeutic Guidelines for treating the disease, and SUS offers the entire line of care provided for in the mentioned protocol, which includes, in addition to surgical and radiological procedure, the treatment using drugs, such as somatostatin analogues (octreotide and lanreotide) and dopamine antagonists. The drug pegvisomant is currently indicated in the package insert for patients with acromegaly who had an inadequate response to surgery and/or radiotherapy, and for patients whose medical treatment with somatostatin analogues did not normalize serum IGF-I concentrations or was not tolerated.

Question: “Which are the benefits of using the Somavert® (pegvisomant) technology compared to dose escalation of somatostatin analogues (SA), whether in combination or as monotherapy, for the treatment of patients with inadequate response to SA?”.

Scientific evidence: Four interventional and three observational studies have been analyzed, by means of which the intervention with pegvisomant was assessed regarding biochemical parameters of a heterogeneous population of patients with acromegaly with different histories and responses to previous treatments. In addition, the influence of the treatment with pegvisomant on clinical signs and symptoms of acromegaly, such as arthralgia, blood pressure and some cardiovascular parameters was also assessed. By analyzing the interventional studies, pegvisomant has been seen to normalize age-appropriate blood IGF-1 levels in 56 to 80% of patients treated at different dosage schedules of the drug as monotherapy and in combination. Treatment influence on disease signs and symptoms was little expressive and very heterogeneous among patients recruited to participate in the studies. In the same way, a small change in quality of life of patients treated in the period from 7 to 27 months was observed. In an observational study used to follow up the clinical evolution of 1,288 patients with acromegaly and on treatment with pegvisomant for five years, the normalization rate for blood IGF-1 levels was seen in a little more than 63% in the group of followed-up patients.
**Economic assessment:** The applicant presented a cost-effectiveness analysis from the perspective of SUS through a Markov model, in which the evolutions of two hypothetical cohorts of patients with acromegaly for 35 years treated with pegvisomant or octreotide LAR at doses higher than 40 mg every 28 days were compared. The parameters assessed were life years gained and normalization of serum IGF-1 and GH levels. According to the model results, the treatment with pegvisomant would be, on average, BRL 313,599.84 less expensive per patient and would result in an increment of 1.37 life years with disease control, and of 0.46 years in life expectancy for each patient. Therefore, treatment with pegvisomant would be cost-saving, i.e., more effective and with a lower associated cost. A sensitivity analysis on select parameters did not demonstrate a change in main analysis results.

**Budget Impact Assessment:** The applicant presented a budget impact analysis, by means of which the incremental impact generated by a possible incorporation of pegvisomant as monotherapy into SUS was determined. The eligible population considered to receive the treatments was that of patients with acromegaly without an adequate response to treatment with somatostatin analogue and on dose escalation of octreotide LAR above 40 mg every 28 days. The considered costs were those concerning drug acquisition and the performance of supplementary tests required to the follow-up of patients on treatment with octreotide LAR and pegvisomant. Three hypothetical scenarios have been outlined, in which pegvisomant was used at different dosages and for different proportions of the population eligible to receive the treatment. According to the scenario assessed, the impact of a possible pegvisomant incorporation into SUS varied between 38 and 45 million Brazilian reais. The fact of considering a target population that is using a dose higher than 40 mg/28 days (not recommended in the treatment protocol for the disease) directly affects the results, since most of the expenses comprised in the analysis are derived from drug acquisition.

**International Experience:** Countries having public health systems, such as Canada, United Kingdom and Australia, do not recommend public funding for pegvisomant because they do not consider it to be cost-effective.

**Recommendation made by CONITEC:** CONITEC members attending the 33rd plenary session meeting held on 03/04/2015 and 03/05/2015 unanimously decided not to incorporate pegvisomant (Somavert®) for acromegaly treatment into SUS.

**Public consultation:** 24 contributions have been received for the public consultation, which included 15 technical-scientific contributions and 9 originating from patients and/or caregivers. All of the contributions received took a stand in favor of pegvisomant incorporation. Patients using the drug have identified as positive points of treatment the normalization of blood IGF-1 levels, quality of life improvement, and joint pain minimization, while commenting that the use of daily injections and liver hepatotoxicity are negative points of treatment. Several institutions brought information that the technology is effective, reduces disease-related morbidity and mortality, and is safe in long term. All of this information had already been assessed, both in the
preparation of reports by CONITEC, and in the preparation of the Clinical Protocol and Therapeutic Guidelines for disease treatment. They have also proposed that drug incorporation is restricted to sites that are able to fully assist the patient with acromegaly, and that such sites also have surgeons who are experienced in transsphenoidal surgery for resection of pituitary adenomas.

**Final deliberation:** CONITEC members attending the plenary session meeting on 05/06/2015 unanimously deliberated in favor of recommending not to incorporate pegvisomant as monotherapy for acromegaly treatment. Deliberation Record no. 120/2015 was signed.