Conitec

Recomendation report

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Ranibizumab for the treatment of diabetic macular edema (DME)

Brasília – DF
2020

Technology: Ranibizumab (Lucentis®).

Indication: Diabetic macular edema (DME).

Applicant: Novartis Biociências S.A. (Brazil).

Background: Diabetic macular edema (DME) is a major cause of vision loss associated with diabetic retinopathy, which is one of the most common complications of diabetes mellitus. DME is characterized by thickening of the tissue in the macula due to leakage of fluid from blood vessels or the presence of hard exudates in the centre of the macula. The main therapies for DME available in the Brazilian Public Health System - SUS are laser treatment (photocoagulation and panphotocoagulation), vitrectomy surgery, and aflibercept, an antiangiogenic agent recently incorporated in Brazilian Public Health System (SUS).

Question: Is ranibizumab effective and safe as an anti-VEGF drug for the treatment of diabetic macular edema when compared with the treatments available in SUS (laser photocoagulation and aflibercept)?

Scientific evidence: The applicant presented 12 studies: three systematic reviews, and nine clinical trials that evaluated ranibizumab. Two meta-analyses that the applicant had excluded from his analysis were also included. All primary studies compared ranibizumab with laser treatment and showed significant superiority results of the efficacy of ranibizumab in improving visual acuity in patients with DME. The systematic reviews that compare ranibizumab with other anti-VEGF showed that they have similar efficacy, with some studies suggesting superiority of aflibercept. According to updated results from the meta-analysis by Virgilli and colleagues, aflibercept and ranibizumab were more effective than laser, demonstrating an improvement in vision of two lines or more after one year of treatment (high quality). The relative risk (RR) versus laser was 3.66 (95% CI 2.79 to 4.79) for aflibercept, and RR 2.76 (95% CI 2.12 to 3.59) for ranibizumab. People with DME receiving ranibizumab were less likely to gain three or more lines of visual acuity in one year compared with aflibercept - RR 0.75 (95% CI 0.60 to 0.94). There was no difference between aflibercept and ranibizumab with regard to serious systemic adverse events. A network meta-analysis developed by Zhang and colleagues showed that ranibizumab had better results than aflibercept in improving the best corrected visual acuity (BCVA) at 6 months with an odds ratio (OR) of 7.01 (95% CI 2.56 to 11.39), but aflibercept showed better efficacy at 12 months of treatment with OR of 8.19 (95% CI 5.07 to 11.96). These results demonstrate that both ranibizumab and aflibercept have similar efficacy for DME.

Economic evaluation: The applicant submitted a cost-minimization analysis using aflibercept as a comparator. Ranibizumab is a resource-saving alternative to aflibercept for the treatment of adult patients with DME. The total cost of treatment with ranibizumab for three years was estimated to be BRL 18,171.48, and with aflibercept BRL 21,629.11, resulting in savings of approximately 16%. The analysis evaluated the treatment costs per patient related to acquisition, administration, follow-up and monitoring of treatment, but not costs associated with safety. Despite costs of complications and adverse events may impact the economic outcome of the treatment, the evaluation of these costs was absent from the sensitivity analysis.

Budget impact analysis: The budget impact analysis considered a population of patients with diabetic retinopathy and DME, with a prevalence rate of 11.7% according to a study carried out in Brazil. In the proposed scenario with ranibizumab, the annual cost of treatment was estimated to be BRL 79,266,917.64 in the first year of incorporation, and BRL 181,283,719.49 in the fifth year, comparing with aflibercept, which was estimated to be BRL 69,312,302.72 and BRL 154,658,419.96, respectively. The budget impact analysis demonstrated that the incorporation of ranibizumab in the treatment of DME as an alternative to aflibercept could result in cost savings up to over BRL 104.1 million in five years, considering a market share of 50%. In all scenarios in the sensitivity analysis, the incorporation of ranibizumab for DME in SUS would result in cost savings. There were some limitations in the analysis, such as uncertainty about the size of the market share of ranibizumab (considered at 50%); uncertainty that this treatment would only be indicated for patients with retinal thickness greater than

400 micrometres; and uncertainty about the source of the estimates of the market share, which may compromise the results.

International recommendations: The Canadian Agency for Drugs and Technologies in Health - CADTH (Canada), Scottish Medicines Consortium - SMC (Scotland), National Institute for Health and Care Excellence - NICE (England), and Pharmaceutical Benefits Advisory Committee - PBAC (Australia) recommend the use of ranibizumab for the treatment of DME, but some agencies have restricted its use considering the glycated haemoglobin control.

Technology horizon scanning: Two new drugs were identified for the treatment of DME: brolucizumab (VEGF-A inhibitor) and faricizumab (VEGF-A inhibitor and angiopoietin-2 inhibitor) in an ongoing phase 3 clinical trial. Biosimilars of aflibercept and ranibizumab were also identified.

Initial Recommendation: CONITEC, at its 86th Ordinary Meeting, on March 4th and 5th, 2020, decided that the subject matter should be made available in a public consultation with a preliminary recommendation in favour of the incorporation of ranibizumab for the treatment of adult patients with diabetic macular edema (DME), in the scope of SUS.

Public consultation: The CONITEC's preliminary recommendation report was made available through the Public Consultation No. 16/2020 between March 30th and April 20th, 2020. A total of 978 contributions were received, 156 of which were technical-scientific contributions, and 822 were experience or opinion contributions; 95.5% and 92.3%, respectively, agreed with the CONITEC's preliminary recommendation.

Final Recommendation: The CONITEC's members present at the 89th Ordinary Meeting, on August 5th, 2020, unanimously decided to recommend the incorporation of ranibizumab for the treatment of diabetic macular edema, according to the protocol of the Ministry of Health and the ophtalmological assistance in SUS.

Decision: To incorporate ranibizumab for the treatment of diabetic macular edema (DME), in the scope of SUS, according to the protocol of the Ministry of Health of Brazil and the ophtalmological assistance in SUS, according to Ordinance No. 39, published in the Official Gazette of the Federal Executive No. 181, Section 1, page 235, on September 21st, 2020.