REPORT 119
Ranibizumab for exudative age-related Macular Degeneration

Ordinance n° 16/2015 published on 04/10/2015
EXECUTIVE SUMMARY

**Technology:** Ranibizumab (Lucentis®)

**Indication:** Neovascular (exudative or wet) Age-Related Macular Degeneration.

**Applicant:** Novartis Biociências SA.

**Context:** Age-Related Macular Degeneration (AMD) is a degenerative disorder of the macula, the central area of retina, in which images are formed. AMD is the main cause of legal blindness in subjects aged over 50 years old. The prevalence of blindness is 8.7% among subjects affected by the disease. AMD occurs in approximately 10% (1,081,831) of the population aged over 65 years old. Out of these, only 10% (108,183) would develop the wet or exudative form, for which therapy with antiangiogenics is indicated.

**Question:** Is the use of ranibizumab effective, safe and cost-effective in patients with exudative (or wet) age-related macular degeneration when compared to bevacizumab or placebo?

**Scientific evidence:** The evidence currently available on the efficacy and safety of ranibizumab for the treatment of exudative AMD is based on studies of good methodological quality and degree of recommendation A, based on 6 systematic reviews and 9 clinical trials (MARINA, SAILOR, PIER, EXCITE, CATT, IVAN, HARBOR, GEFAL, MANTA). In this sense, the results presented suggest that the treatment of AMD with ranibizumab is more effective than placebo in delaying disease progression (Loss ≥ 15 letters: RR 0.14 (0.08-0.25); Loss ≥ 30 letters: RR 0.09 (0.03-0.28)); effect that may be associated with blindness prevention (Blindness: RR 0.27 (0.19-0.40)), and also in causing an improvement in VA of patients (Gain ≥ 15 letters: RR 6.69 (3.75-11.94)). Comparative studies between ranibizumab and bevacizumab have considered that bevacizumab (comparator) is non-inferior to ranibizumab in the treatment of AMD; however, regarding long-term maintenance of results, this is more significant with ranibizumab.

**Economic assessment:** A cost-utility analysis of ranibizumab compared to bevacizumab for exudative AMD was performed from the perspective of the Sistema Único de Saúde, in a 10-year time horizon, using a Markov model. In the analysis result, ranibizumab was shown to be dominant (Δcost = -2,158.95; Δutility = 0.0439).

**Budget Impact Assessment:** The budget impact analysis performed by the applicant used the price proposed for the incorporation into SUS with no negotiation (BRL 777.00). The impact result after 5 years from incorporation was BRL 377,146,478.00 (only for the SUS population) and BRL 508,337,168.00 for 95% of the target population in Brazil. The Executive Secretariat of CONITEC also conducted a budget impact analysis using the price proposed by the manufacturing company to the Ministry of Health subsequently to submission. The budget impact, in the
five-year scenario for 100% of the population, and considering the fractioning of 4 doses per 0.3-ml vial of ranibizumab with the new proposed value (BRL 507.50) and of 40 doses per 40-ml vial of bevacizumab (BRL 847.16), without the application and follow-up costs, which are identical between both, would generate an expense of BRL 300,949,504.64 for ranibizumab and BRL 50,236,922.63 for bevacizumab, and a value per dose of BRL 126.88 and BRL 21.18, respectively.

**Recommendation made by CONITEC:** At the 22nd ordinary meeting, the plenary session members of CONITEC recommended not to incorporate into SUS ranibizumab for exudative AMD. The drug was considered to be effective and safe, but it is equivalent in efficacy and safety to bevacizumab, which represents the treatment alternative. In addition, the latter has a much lower cost per dose: BRL 21.18, while the cost per dose for ranibizumab may get to approximately six times more, BRL 126.88. This means that, in case ranibizumab was incorporated, the Ministry of Health would be leaving 5 patients untreated for each 1 treated.

**Public consultation:** The public consultation was conducted between 04/08/2014 and 04/28/2014. 153 contributions have been received during public consultation. Of the total contributions sent on ranibizumab incorporation proposal, 101 were not related to the topic proposed. 52 contributions in favor of incorporating ranibizumab have been received, which presented rationales such as: drug of efficacy and safety proven by several clinical studies, conducted with the same population as that of the indication, in a presentation that is appropriate for intravitreal use, with no need for fractioning or fractioning into much less doses, which would decrease the risk of contamination.

**Final deliberation:** CONITEC members attending the 25th ordinary plenary session meeting on 05/08/2014 unanimously deliberated in favor of not recommending the incorporation of the drug ranibizumab for the treatment of Age-Related Macular Degeneration due to its unfavorable cost-effectiveness ratio.

**Decision:** Ordinance nº 16, dated april 9, 2015: It makes public the decision of not incorporating ranibizumab for exudative age-related macular degeneration within the scope of the Sistema Único de Saúde - SUS.