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Recomendation report

DRUGS

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Bortezomib for the treatment of adult patients with previously treated multiple myeloma

Brasília – DF
2020

Technology: Bortezomib (VELCADE®).

Indication: Previously treated patients with relapsed or refractory multiple myeloma.

Applicant: Brazilian Association of Hematology, Hemotherapy, and Cellular Therapy (ABHH in Portuguese).

Background: Multiple myeloma (MM) is a hematologic malignancy characterized by the proliferation of malignant plasma cells in the bone marrow. It accounts for 1% of all malignancies and 10 to 15% of hematologic malignancies. MM is an incurable disease, its course is highly variable with a median survival of about 5 years, and significant morbidity associated with bone pain, kidney damage and anaemia. For eligible symptomatic MM patients, standard treatment is induction chemotherapy followed by high-dose chemotherapy with autologous haematopoietic stem cell transplantation (AHSCT). However, MM remains incurable, and the majority of patients eventually relapse with increasingly refractory disease after a variable period of time. In these cases, patients are reassessed for eligibility for additional treatments, and most of them will be treated with a new course of chemotherapy, which may include bortezomib.

Question: Is the use of bortezomib as a component of chemotherapy effective, safe and cost-effective in patients with relapsed or refractory MM, when compared with other chemotherapy regimens recommended by the diagnostic and therapeutic guidelines of the Ministry of Health of Brazil?

Scientific evidence: In a systematic review of the literature, the applicant selected four meta-analyses that compared bortezomib-containing chemotherapy regimens with non-bortezomib regimens in patients with relapsed or refractory MM. In the methodological quality evaluation, one study was rated as low, two studies as moderate and one as high quality. The finding of improvement of progression-free survival, complete remission, and overall response with the use of bortezomib was considered reasonably consistent. The hazard ratio/odds ratio for progression-free survival ranged from 0.26 (95%CI 0.11-0.63) to 0.75 (95%CI 0.53-1.06); and for complete remission, odds ratio was 3.35 (95%CI 2.06-5.43). Regarding safety, there was an increased risk of general adverse events, especially neurological side effects.

Economic evaluation: A cost-effectiveness analysis was conducted using a partitioned survival model, over a 10-year time horizon. The main result was an incremental cost-effectiveness ratio (ICER) estimated at BRL 65,212.78/life-year gained. In the sensitivity analysis, the model was sensitive to the cost of bortezomib and the magnitude of survival/progression-free survival gain. The model had potentially serious methodological limitations, with a tendency to underestimate the cost of the intervention and to produce more favourable ICER, such as not using utility or adverse effects data, and not considering cost of High Complexity Procedures Authorization (APAC in Portuguese) during therapy with bortezomib, or wastage in the administration of doses. Moreover, there should be more extensive sensitivity analyses, as well as alternative scenario analyses.

Budget impact analysis: In the applicant's budget impact analysis, the population eligible for treatment was estimated to be 5,143 patients in the first year, and 237 patients in the subsequent 4 years, with a market share between 15% and 70%, resulting in a budget impact of around BRL 23 million in 5 years. There were significant limitations in the analysis, in particular, unclear criteria used to define the target population, and only incident cases were considered for treatment from the second year, resulting in a population estimate that was much lower than expected, taking into account the epidemiological data. Finally, analysis of alternative scenarios was not reported.

International recommendations: The Scottish Medicines Consortium – SMC (Scotland) recommends bortezomib as part of the chemotherapy regimen as first-line treatment for patients with MM ineligible for AHSCT. The UK's National Institute for Health and Care Excellence (NICE) approved the use of

bortezomib in this setting, under a risk sharing scheme, with full reimbursement of its cost in case of non-response after two cycles. The Canadian Agency for Drugs and Technologies in Health – CADTH (Canada) has not carried out a specific review for this indication, but bortezomib regimens are currently reimbursed in some Canadian jurisdictions.

Considerations: The literature review provided consistent data regarding the efficacy of bortezomib in the proposed indication. The cost-effectiveness and budget impact analyses submitted by the applicant had methodological limitations that limited the conclusions about the economic impact of the technology.

Initial Recommendation: It was taken into consideration the benefits of bortezomib in the global survival, progression-free survival, response rate, and disease remission, and also other aspects such as the fact that bortezomib is available as a generic drug, it is cost-effective, and does not have a high budget impact. Therefore, the members of CONITEC's plenary session present at the 88th Ordinary Meeting, on July 9th, 2020, unanimously decided to make a preliminary recommendation in favour of the incorporation of bortezomib in the scope of the Brazilian Public Health System - SUS, for the treatment of previously treated patients with relapsed or refractory multiple myeloma, according to the oncological assistance in SUS.

Public consultation: The CONITEC's preliminary recommendation report was made available through the Public Consultation No. 31/2020 between July 27th and August 17th, 2020. A total of 245 contributions were received, 42 of which were technical-scientific contributions, and 203 were experience or opinion contributions; 100% and 98%, respectively, agreed with the CONITEC's preliminary recommendation.

Final Recommendation: The CONITEC's members present at the 90th Ordinary Meeting, on September 3rd, 2020, unanimously decided to recommend the incorporation of bortezomib for the treatment of previously treated adult patients with relapsed or refractory multiple myeloma, according to the protocol established by the Ministry of Health of Brazil and the oncological assistance in SUS.

Decision: To incorporate bortezomib for the treatment of adult patients with previously treated multiple myeloma, in the scope of SUS, according to Ordinance No. 44, published in the Official Gazette of the Federal Executive No. 186, Section 1, page 453, on September 28th, 2020.