Conitec

Recomendation report

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Cytoreductive surgery with hyperthermic chemotherapy in patients with malignant peritoneal mesothelioma

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Technology: Cytoreductive surgery (peritonectomy) with Hyperthermic Intraperitoneal Chemotherapy (HIPEC).

Indication: Treatment of Malignant Peritoneal Mesothelioma (MPM).

Applicant: Secretariat of Science, Technology and Strategic Inputs (Ministry of Health of Brazil).

Background: The combination of cytoreductive surgery with intraoperative perfusion of the peritoneal cavity, and hyperthermic chemotherapeutic agents, represents a new and promising therapeutic strategy for MPM. Its incidence varies across the world with the highest reported rate in Australia, Belgium and Great Britain. MPM is associated with exposure to asbestos. Given its long latency period (15 to 60 years), an increasing incidence of MPM is expected in the coming decades. In Brazil, an increase in mortality from this neoplasia is also expected in the coming years.

Question: Is treatment with cytoreductive surgery with hyperthermic chemotherapy more effective and cost-effective than systemic chemotherapy for patients with diffuse malignant peritoneal mesothelioma?

Scientific evidence: Clinical trials on cytoreductive surgery with HIPEC specifically for patients with MPM were not found. As HIPEC was the intervention of interest, studies on normothermic intraperitoneal chemotherapy were not considered. Eleven observational studies were selected, which had used a database of patients from one or more health centres. The number of patients evaluated in these studies ranged from 11 to 401, and the data collection period ranged from 3 to 26 years. The HIPEC techniques used were: in 4 studies, open abdomen (or Coliseum technique); in another 4 studies, closed abdomen; in 2 multicentre studies, the (open or closed) surgical procedures varied among the participating centres; and in one study, details of the technique were not reported. The temperature of HIPEC ranged from 40 to 43 ºC, and the duration ranged from 60 to 120 minutes, and mitomycin C alone or in combination with a platinum-based drug was used in most studies. Most studies reported an overall 5-year survival rate ranging from 27% to 80.8%.

Economic evaluation: Markov chain simulations were performed, with 24 patients, over a lifetime horizon, from the perspective of the Brazilian Public Health System (SUS), using a discount rate of 5%. The incremental cost-effectiveness ratio (ICER) of the procedure was estimated at BRL 56,929.28/life-year gained. In none of the simulations, ICER was estimated below 1 GDP per capita. When the value of the surgery was limited to BRL 34,621.00, ICER was equal to this threshold.

Budget impact analysis: The incremental value per health centre was assessed considering it would perform 24 procedures per year. A dynamic microsimulation model was developed, over a five-year time horizon. According to the Brazilian Society of Surgical Oncology (SBCO in Portuguese), 120-200 cases per year of pseudomyxoma peritonei and peritoneal mesothelioma would be eligible for the procedure. The average annual budget impact for the 24 patients was estimated to be BRL 1,692,864.36. For the entire population, the values per year ranged from BRL 8,661,117.15 to BRL 14,657,044.06.

Initial Recommendation: Conitec's plenary session, at the meeting on December 4th, 2019, considered that, despite the limited scientific evidence, the results indicated greater efficacy of the treatment with cytoreductive surgery with HIPEC in patients with peritoneal mesothelioma. The economic evaluation estimated the incremental cost-effectiveness ratio with a value close to 2 GDP per capita per life-year gained, which was considered acceptable for rare clinical condition. Therefore, the preliminary recommendation was to incorporate cytoreductive surgery (peritonectomy) with Hyperthermic Intraperitoneal Chemotherapy (HIPEC) into SUS, for the treatment of peritoneal mesothelioma. This

incorporation should be implemented in health centres with professionals trained to perform this complex procedure.

Competing interests: The authors declare that they have no competing interests.

Public consultation: A total of 45 technical-scientific contributions and 13 experience or opinion contributions were received, most of which agreed with the favourable preliminary recommendation to the incorporation of cytoreductive surgery with HIPEC for the treatment of peritoneal mesothelioma. Only one contribution neither agreed or disagreed with this recommendation, but it reported having no experience with the topic. There was not sufficient reason to change the preliminary recommendation.

Final Recommendation: The Conitec's members present at the 86th Ordinary Meeting, on March 4th and 5th, 2020, unanimously decided to recommend the incorporation of cytoreductive surgery with HIPEC for the treatment of peritoneal mesothelioma, in the scope of SUS, in accordance with a protocol to be developed by the Ministry of Health.

Decision: To incorporate cytoreductive surgery with hyperthermic chemotherapy in patients with malignant peritoneal mesothelioma, in the scope of SUS, as established by the Ministry of Health of Brazil, according to Ordinance No. 12, published in the Official Gazette of the Federal Executive No. 64, Section 1, page 91, on April 2nd, 2020.