REPORT 129

Arsenic trioxide for the treatment of Acute Promyelocytic Leukemia (APL)

Ordinance n° 46/2014 published on 12/17/2014
EXECUTIVE SUMMARY

Technology: Arsenic trioxide (Trisenox®).

Indication: Acute promyelocytic leukemia.

Applicant: Judicial Branch/Judicial Section of the State of Minas Gerais

Context: Acute promyelocytic leukemia (APML) is a subtype of acute myeloid leukemia (AML) associated with translocation between chromosomes 15 and 17 – t (15;17), comprising approximately 10% of AML cases. The treatment consists of administration of anthracyclines combined with trans-retinoic acid (ATRA), thus achieving molecular remission in up to 99% of patients, with a 90% disease-free survival at five years from diagnosis. The treatment is provided by SUS and the cost is reimbursement via APAC (Autorização de procedimentos de alta complexidade – Authorization of high-complexity procedures) procedure. The Oncology drugs and treatment schedules are defined by licensed hospitals.

Question: Is the use of arsenic trioxide effective and safe in patients with Acute Promyelocytic Leukemia (APML) previously treated with ATRA combined with chemotherapy, after hematologic or molecular relapse, as induction and consolidation therapy of the new treatment?

Scientific evidence: The evidence found is limited to non-randomized, non-comparative and open-label studies, which have results that are little representative. The number of patients included in the studies is small, and the lack of a comparator makes concluding that the assessed technology is superior, inferior or even similar to standard treatment unfeasible.

Budget impact: A cost comparison between arsenic trioxide and ATRA has been performed for the purpose of estimating treatment costs and budget impact.

Discussion: The evidence demonstrated concerning the proposed technology has a high degree of uncertainty. Therapeutic options for APML are available in SUS by means of APAC procedures covering up to the 4th line of treatment, in addition to bone marrow transplantation, when indicated. The disease, which used to have a serious profile with high mortality from the standard treatment (ATRA + anthracyclines) instituted in the ’90s, has become a curable disease in approximately 90% of cases. Studies have been conducted to clarify the gaps of knowledge on the best therapeutic approach in patients with APML who are refractory and relapsing. Recommendation made by CONITEC: CONITEC members, at the 25th ordinary meeting held on 05/07 and 05/08/2014, deliberated, after discussion, in favor of not incorporating the drug arsenic trioxide for the treatment of promyelocytic leukemia (ICD C92.4).
Public Consultation: The public consultation was performed from 07/24/2014 to 08/12/2014. After the initial recommendation made by CONITEC of not incorporating arsenic trioxide for APML, the report was submitted to public consultation and has received four contributions, made by a health institution/hospital (1), a medical society (1) and the company that manufactures the technology (2). The contributions brought no new evidence supporting the considerations made by the plenary session members of CONITEC.

Final Deliberation: After analysis of the contributions, the recommendation of not incorporating was kept. The drug has a high cost and was demonstrated to be non-inferior to ATRA, which has a high cure rate. There are options available for the treatment of APML in SUS via APAC procedures. As per treatment guidelines and manuals, arsenic trioxide has been used to treat refractory patients or disease relapse after initial therapy with anthracyclines and ATRA. CONITEC members attending the plenary session meeting on 09/04/2014 unanimously deliberated in favor of not recommending the incorporation of arsenic trioxide as a specific procedure for the treatment of Acute Promyelocytic Leukemia (APML). Deliberation Record nº 97/2014 was signed.