HAUTE AUTORITÉ DE SANTÉ

ONCOLOGY
New indication
June 2017

BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

VIDAZA (azacitidine), antimetabolite

Insufficient clinical benefit in the treatment of acute myeloblastic leukaemia with more than 30% marrow blasts in adults ineligible for haematopoietic stem cell transplantation

Main points

- VIDAZA already has marketing authorisation in the treatment of acute myeloblastic leukaemia (AML) with more than 30% marrow blasts in adults ineligible for haematopoietic stem cell transplantation (HSCT).
- The pivotal study did not demonstrate any difference between VIDAZA and conventional treatments on overall survival (primary endpoint) or on quality of life. Its role has therefore not been established compared with the current therapeutic strategies.

Pre-existing indications*

VIDAZA already has marketing authorisation in the treatment of adults ineligible for haematopoietic stem cell transplantation (HSCT) and with a myelodysplastic syndrome (MDS) of intermediate risk 2 or higher according to the International Prognostic Scoring System (IPSS), a chronic myelomonocytic leukaemia with 10 to 29% marrow blasts without myeloproliferative syndrome or an AML with 20 to 30% blasts and multilineage dysplasia.

Therapeutic strategy

- Treatment of AML, with more than 30% marrow blasts, differs depending on whether or not the patient is eligible for induction chemotherapy combining cytarabine and an anthracycline.
  - In subjects who are candidates for induction chemotherapy, eligibility for allotransplantation cannot be completely determined from the outset. Indeed, other than the availability of a graft, it depends in particular on obtaining a complete remission following the induction chemotherapy.
  - In subjects who are not candidates for induction chemotherapy, in particular in subjects with a worse predictable prognosis (age > 75 years, poor general condition, comorbidities, pejorative karyotype and/or prior myelodysplasia), symptomatic treatment (transfusions, anti-infectious agents) and a palliative approach or a less intensive treatment, for example with low doses of subcutaneous aracytine, are preferred. The therapeutic attitude notably takes into account the treatments previously received in the case of AML secondary to an MDS.
- **Role of the medicinal product in the therapeutic strategy**
  The available data do not allow the role of VIDAZA to be established in the current management of AML with more than 30% marrow blasts in adults ineligible for haematopoietic stem cell transplantation.

* This summary does not cover these indications.

Clinical data

- A study conducted in patients aged 65 years or more with a newly diagnosed AML, de novo or secondary, compared the efficacy and safety of azacitidine (n=241) versus a conventional treatment (n=247) with 3 options that were left to the discretion of the physician prior to randomisation:
  - either a chemotherapy protocol (n=44) including an induction cycle combining cytarabine and an anthracycline according to a “7+3” regimen followed by one or two consolidation cycles combining cytarabine and the anthracycline administered in induction,
  - or treatment with low-dose cytarabine (n=158): 20 mg/m^2 SC twice daily for 10 days per 28-day cycle,
  - or no active treatment (n=45).

  During the final analysis of overall survival, after a median follow-up of 24.4 months, no statistically significant difference was observed between the two treatment groups for the primary endpoint: the median overall survival was 10.4 months in the azacitidine group and 6.5 months in the conventional treatment group.
- The percentage of patients who stopped treatment due to adverse events was 46.6% (110/236) in the azacitidine group and variable according to the conventional treatment: 0% with optimal symptomatic treatment, 44.4% (68/153) with cytarabine and 26.2% (11/42) with the chemotherapy protocol. The percentage of patients who had at least one grade 3 or 4 adverse event was 87.7% (207/236) in the azacitidine group and according to the conventional treatment: 65% (26/40) with optimal symptomatic treatment, 92.2% (141/153) with cytarabine and 88.1% (37/42) with the chemotherapy protocol. In the azacitidine group, the most common grade 3 or 4 adverse events were: febrile neutropenia (28%), non-febrile neutropenia (26.3%) and thrombocytopenia (23.7%). These events were reported with similar percentages in the cytarabine and chemotherapy protocol sub-groups.
  Respectively 70% and 67% of patients from the azacitidine and conventional treatment arms were hospitalised because of an adverse event.

Special prescribing conditions

- Medicinal product for hospital prescription, restricted to oncology or haematology specialists or doctors with cancer training
- Medicinal product requiring special monitoring during treatment

Benefit of the medicinal product

- The actual clinical benefit* of VIDAZA is insufficient to justify reimbursement by National Health Insurance in this extension of indication of marketing authorisation. .
- Does not recommend inclusion on the list of reimbursable products for hospital use in the treatment of acute myeloblastic leukaemia (AML) with more than 30% marrow blasts in adults ineligible for haematopoietic stem cell transplantation (HSCT), according to the WHO classification.

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This document was created on the basis of the Transparency Committee Opinion of 21 June 2017 (CT-15700) and is available at **www.has-sante.fr**

* The actual clinical benefit (ACB) of a medicinal product describes its benefit primarily in terms of its clinical efficacy and the seriousness of the condition being treated. The HAS Transparency Committee assesses the ACB, which can be substantial, moderate, low or insufficient for reimbursement of the medicinal product for hospital use.

** The clinical added value (CAV) describes the improvement in treatment provided by a medicinal product compared with existing treatments. The HAS Transparency Committee assesses the degree of CAV on a scale from I (major) to IV (minor). A level V CAV (equivalent to “no CAV”) means “no clinical added value”.