HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
OPINION
24 JUNE 2020

gilteritinib
XOSPATA 40 mg film-coated tablets

First assessment

Key points

Favourable opinion for reimbursement in the treatment of adult patients who have relapsed or refractory acute myeloid leukaemia (AML) with a FLT3 mutation.

What therapeutic improvement?

Improvement in the therapeutic strategy.

Role in the care pathway?

According to the recommendations, the objectives of treatment in patients with AML are, firstly, to obtain complete remission enabling recovery of bone marrow function and, secondly, to limit the risk of and time to relapse, generally associated with a poor prognosis. The type of treatment is based on eligibility for intensive chemotherapy and allogeneic haematopoietic stem cell transplantation (HSCT). Management is therefore determined by weighing up the objectives and risks, which depend on the characteristics of the patient (general condition, age, comorbidities), the disease (genetic risk group, treatment line) and the availability of an HSCT donor.

In patients with relapsed or refractory AML (from the second line of treatment), the therapeutic strategy depends on the time to relapse and the characteristics relative to the patient, the disease and the possibility of performing allogeneic HSCT. The options are based on intensive salvage chemotherapy

with cytarabine combined with anthracycline in patients eligible for intensive chemotherapy, or with azacitidine (VIDAZA), low-dose cytarabine or supportive care for patients ineligible for intensive chemotherapy. In the event of complete remission, allogeneic HSCT may be envisaged.

Role of the medicinal product in the care pathway

Given the demonstrated superiority in terms of overall survival of a therapeutic strategy including oral XOSPATA (gilteritinib) as monotherapy compared to a therapeutic strategy based on salvage chemotherapy, XOSPATA (gilteritinib) is a first-line treatment to be used in patients who have relapsed or refractory AML with a FLT3 mutation.

The Committee nonetheless highlights the fact that there are insufficient data in patients in third or later-line therapy and that the data are limited in patients with a FLT3-TKD mutation, in patients with an ECOG score > 1 and in patients treated with a FLT3 inhibitor as first-line therapy. In addition, it is not possible to assess the specific utility of post-transplant maintenance treatment with XOSPATA (gilteritinib).

01 COMMITTEE'S CONCLUSIONS

01.1 Clinical benefit

◗ Acute myeloid leukaemias (AML) include various malignant blood diseases characterised by the clonal proliferation of abnormal myeloid precursors and impairment of normal haematopoiesis. It is a life-threatening disease;
◗ This is a curative treatment.
◗ The efficacy/adverse effects ratio is high.
◗ There are medicinal alternatives, represented by cytotoxic-based chemotherapy and allogeneic hematopoietic stem cell transplantation (HSCT) (see paragraph 04 of the present opinion)
◗ XOSPATA (gilteritinib) is a first-line treatment to be used in patients who have relapsed or refractory AML with a FLT3 mutation (see paragraph 08 of the present opinion).

Public health impact

Considering:

- the seriousness of the disease and its low incidence, particularly in relapsed or refractory patients with a FLT3 mutation,
- the medical need considered to be partially met by chemotherapies and allogeneic HSCT,
- the demonstrated impact of XOSPATA (gilteritinib) on the mortality of patients with relapsed or refractory AML with a FLT3 mutation compared to chemotherapy and the methodological limitations of this demonstration,
- the absence of a demonstrated impact on patients' quality of life,
- the partial response to the identified medical need,
- the expected additional impact on the organisation of care and patient pathway given the oral administration method relative to the comparators administered by IV,

XOSPATA (gilteritinib) is likely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of XOSPATA (gilteritinib) is substantial in the MA indication.

The Committee issues a favourable opinion for inclusion in both the hospital formulary list and the retail formulary list of reimbursed proprietary medicinal products approved for use in the MA indication and dosages.

01.2 Clinical Added Value

Considering:

- **demonstration of the superiority of a therapeutic strategy including XOSPATA (gilteritinib) as monotherapy compared to a therapeutic strategy based on salvage chemotherapy chosen by the investigator, in terms of overall survival (primary endpoint) with a median improvement of 3.7 months (HR = 0.637; $CI_{95\%}$ [0.490; 0.830]; $p_{one\text{-}sided}$= 0.0004),**
- **the medical need partially met by chemotherapy protocols and allogeneic HSCT,**

and despite,

- **uncertainties with respect to the specific effect size of XOSPATA (gilteritinib) insofar as patients in both groups could benefit from allogeneic HSCT,**
- **the fact that it is impossible to robustly determine the impact of a strategy with XOSPATA (gilteritinib) compared to a salvage chemotherapy-based strategy in terms of the proportion of patients able to receive allogeneic HCST (the only potentially curative treatment),**
- **the absence of robust data on quality of life (exploratory endpoint in an open-label study),**

XOSPATA (gilteritinib) provides a minor clinical added value (CAV IV) in the therapeutic strategy for patients who have relapsed or refractory AML with a FLT3 mutation.