HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
SUMMARY
17 NOVEMBER 2021

The legally binding text is the original French opinion version

azacitidine
ONUREG 200 mg film-coated tablets
ONUREG 300 mg film-coated tablets

First assessment

Key points

Favourable opinion for reimbursement as maintenance therapy in adult patients with acute myeloid leukaemia (AML) who achieved complete remission (CR) or complete remission with incomplete blood count recovery (CRi) following induction therapy with or without consolidation treatment and who are not candidates for, including those who choose not to proceed to, hematopoietic stem cell transplantation (HSCT).

What therapeutic improvement?

Therapeutic improvement compared to no therapy with monitoring.

Role in the care pathway?

For patients having obtained CR/CRi and not eligible for HSCT, maintenance therapy may be considered. This approach is aimed at delaying relapse and prolonging the duration of remission and survival, particularly in patients with intermediate or high risk.

Midostaurine (RYDAPT) is indicated in the treatment of AML with an indication restricted to patients with AML who are FLT3 mutation-positive in combination with standard induction chemotherapy and consolidation chemotherapy, followed by RYDAPT (midostaurine) single agent maintenance therapy, in the absence of HSCT. This FLT3 mutation concerns around 30% of AML cases.

In its opinion of 13/06/2018 relative to RYDAPT (midostaurine), the Transparency Committee nonetheless highlighted that it is impossible to determine the specific contribution of maintenance therapy with RYDAPT (midostaurine) in patients not having undergone allogeneic SCT in the absence of randomisation before the initiation of maintenance therapy, in view of the study design in the RATIFY pivotal study.

The current strategy in the maintenance therapy of AML consists of clinical and laboratory monitoring.

Role of ONUREG (azacitidine) in the care pathway?

ONUREG (azacitidine) is a maintenance therapy in adult patients with AML who achieved complete remission (CR) or complete remission with incomplete blood count recovery (CRi) following induction therapy with or without consolidation treatment and who are not candidates for hematopoietic stem cell transplantation (HSCT). Its superiority has been established versus placebo in terms of overall survival and relapse-free survival over a median follow-up period of 41.2 months.

In patients with an FLT3 mutation, in the absence of comparative data and given the impossibility of determining the specific contribution of maintenance therapy with RYDAPT (midostaurine) in patients not having undergone allogeneic SCT (see opinion of 13/06/2018 concerning RYDAPT), the role of ONUREG (azacitidine) compared to RYDAPT (midostaurine) cannot be determined.

COMMITTEE'S CONCLUSIONS

Considering all of this information and further to debate and voting, the Committee considers:

Clinical benefit

◗ Acute myeloid leukaemia (AML) is a serious, life-threatening disease.

◗ ONUREG (azacitidine) can be incorporated in the curative treatment of AML.

◗ The efficacy/adverse effects ratio is high.

◗ There are no alternatives recommended in the maintenance therapy of AML.

◗ ONUREG (azacitidine) is a maintenance therapy in adult patients with AML who achieved complete remission (CR) or complete remission with incomplete blood count recovery (CRi) following induction therapy with or without consolidation treatment and who are not candidates for hematopoietic stem cell transplantation.

Public health impact

Considering:

- the seriousness of AML and its low incidence (between 5 and 8 cases per 100,000 adults in Europe)
- the unmet medical need in the maintenance therapy of AML;
- the partial response to the identified need, due to:
    - the demonstrated additional impact on morbidity and mortality of ONUREG (azacitidine) compared to no therapy, in view of the overall survival data in the QUAZAR-AML 001 study (median increase in OS of 9.9 months) and relapse-free survival data (median increase in RFS of 5.3 months),
    - despite the absence of robust data on quality of life supporting maintenance or improvement in quality of life compared to no therapy with monitoring,
- a potentially negative impact on the organisation of care with the absence of data supporting the absence of a deterioration, at least, in the care and/or life pathway of patients treated with ONUREG (azacitidine) in comparison with no therapy with monitoring in view of the safety profile of ONUREG (azacitidine) marked by haematological and gastrointestinal adverse events,

ONUREG (azacitidine) is unlikely to have an additional impact on public health in this indication.

Considering all these elements, the Committee deems that the clinical benefit of ONUREG (azacitidine) 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 marketing authorisation indication and dosages.

◗ **Recommended reimbursement rate: 100%**

Clinical Added Value

Considering:

- **demonstration of the superiority of ONUREG (azacitidine) versus placebo in terms of overall survival, the primary endpoint, with an absolute increase of 9.9 months (HR = 0.69; $CI_{95\%}$ = [0.55; 0.86], p = 0.0009),**
- **demonstration of the superiority of ONUREG (azacitidine) versus placebo in terms of relapse-free survival (ranked secondary endpoint), with an absolute increase of 5.3 months (HR = 0.65; $CI_{95\%}$ = [0.52; 0.81], p = 0.0001),**
- **the safety profile of ONUREG (azacitidine) deemed to be acceptable but marked by the occurrence of adverse events, particularly haematological and gastrointestinal events,**
- **the unmet medical need in the maintenance therapy of AML,**

and despite:

- **the absence of robust quality of life data in comparison with no therapy with monitoring, in particular the absence of data supporting maintenance of quality of life in patients receiving long-term treatment with ONUREG (azacitidine) in view of its safety profile,**

the Committee considers that ONUREG (azacitidine) as maintenance therapy provides a moderate clinical added value (CAV III) compared to no therapy with monitoring, in adult patients with AML who achieved CR or CRi following intensive therapy and who are not candidates for hematopoietic stem cell transplantation.