HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE

SUMMARY

30 JUNE 2021

The legally binding text is the original French opinion version

venetoclax

VENCLYXTO 10 mg film-coated tablets
VENCLYXTO 50 mg film-coated tablets
VENCLYXTO 100 mg film-coated tablets

New indication

Key points

Favourable opinion for reimbursement only in combination with azacitidine, for the treatment of adult patients with newly diagnosed acute myeloid leukaemia (AML) who are ineligible for intensive chemotherapy.

Unfavourable opinion for reimbursement in combination with a hypomethylating agent other than azacitidine.

What therapeutic improvement?

Therapeutic improvement compared to azacitidine.

Role in the care pathway?

The objective of treatment in patients with AML is to achieve complete remission via an induction treatment (to restore bone marrow function and thereby limit the risk of potentially life-threatening infection and/or bleeding), then to limit the risk and increase the time to relapse via consolidation therapy. The type of treatment is based on eligibility for intensive chemotherapy and potential allogeneic haematopoietic stem cell transplantation. Management is therefore determined by weighing up the objectives and risks, which themselves depend on the characteristics of the patient (general condition, age, comorbidities), the disease (cytogenetic risk group, treatment line) and the availability of a donor.

In subjects who are not eligible for induction chemotherapy, the use of hypomethylating agents (azacitidine and decitabine) or low-dose cytarabine is recommended.

Role of the medicinal product in the care pathway

Considering demonstration of a clinically relevant benefit compared to azacitidine as monotherapy in terms of overall survival, the Transparency Committee considers that VENCLYXTO (venetoclax) in combination with azacitidine is a first-line treatment in adult patients with newly diagnosed acute myeloid leukaemia (AML) who are ineligible for standard induction chemotherapy.

Given the lack of direct comparative data and the methodological limitations of indirect comparative data, the role of the venetoclax + azacitidine combination versus low-dose cytarabine cannot be determined.

In the absence of data, the combination of VENCLYXTO (venetoclax) with a hypomethylating agent other than azacitidine has no role in the care pathway.

COMMITTEE'S CONCLUSIONS

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

Clinical benefit

◗ Acute myeloid leukaemia (AML), particularly in patients who are ineligible for standard induction chemotherapy, is a serious disease that is life-threatening in the short term.

◗ The proprietary medicinal product VENCLYXTO (venetoclax) is a curative medicinal product.

◗ The efficacy/adverse effects ratio of VENCLYXTO (venetoclax), in combination with azacitidine, is high for the treatment of adult patients with newly diagnosed acute myeloid leukaemia (AML) who are ineligible for standard induction chemotherapy.

◗ There are medicinal alternatives, represented by hypomethylating agents (azacitidine and decitabine) or low-dose cytarabine.

◗ VENCLYXTO (venetoclax) in combination with azacitidine is a first-line treatment in adult patients with newly diagnosed acute myeloid leukaemia (AML) who are ineligible for standard induction chemotherapy.

Public health impact

Considering:

- the seriousness of the disease and its incidence,
- the medical need, which is considered to be partially met,
- the partial response provided by VENCLYXTO (venetoclax), in combination with azacitidine, to the partially met medical need,
    - with an impact on morbidity and mortality due to demonstration of its superiority compared to azacitidine alone, on overall survival,
    - but without a demonstrated impact on quality of life (interruption of the ranked analysis before the quality of life endpoints, meaning that these results cannot be taken into consideration),
- the absence of any demonstrated impact on the organisation of care,

VENCLYXTO (venetoclax) is unlikely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of VENCLYXTO (venetoclax) is:

- **substantial in combination with azacitidine for the treatment of adult patients with newly diagnosed acute myeloid leukaemia (AML) who are ineligible for standard induction chemotherapy;**
- **insufficient in combination with a hypomethylating agent other than azacitidine to justify public funding cover.**

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 indication "in combination with azacitidine high for the treatment of adult patients with newly diagnosed acute myeloid leukaemia (AML) who are ineligible for standard induction chemotherapy" and at the MA dosages.

The Committee issues an unfavourable opinion for inclusion in both the hospital formulary list and the retail formulary list of reimbursed proprietary medicinal products approved for use in combination with a hypomethylating agent other than azacitidine.

◗ **Recommended reimbursement rate: 100%**

Clinical Added Value

In combination with azacitidine:

Considering:

- **demonstration of the superiority of VENCLYXTO (venetoclax) compared to placebo, each in combination with azacitidine, in a randomised double-blind study, in terms of overall survival (joint primary endpoint) with an absolute increase of 5.1 months (considered to be clinically relevant), HR=0.66 [CI95%: 0.52-0.85] and in terms of composite complete remission rate according to the investigator (joint primary endpoint): 65% versus 25%;**
- **demonstration of the superiority of VENCLYXTO (venetoclax) compared to placebo, each in combination with azacitidine, in a randomised double-blind study, on ranked secondary endpoints of clinical interest in this indication (restoration of haematopoiesis): complete remission and transfusion independence;**
- **the need to have access to treatments improving the overall survival and quality of life of these patients;**

and despite:

- **the safety profile of VENCLYXTO (venetoclax) in combination with azacitidine, marked by myelotoxicity with, in particular, the occurrence of febrile neutropenia and serious infections;**
- **the lack of demonstrated impact on quality of life, with the ranked analysis having been discontinued before this endpoint, meaning that it is not possible to take these results into consideration;**

the Committee considers that VENCLYXTO (venetoclax) in combination with azacitidine provides a moderate clinical added value (CAV III) compared to azacitidine as monotherapy in the treatment of adult patients with newly diagnosed acute myeloid leukaemia (AML) who are ineligible for standard induction chemotherapy.