SUMMARY

acalabrutinib
CALQUENCE 100 mg,

capsule

Reassessment

Original French opinion adopted by the Transparency Committee on 22 March 2023

The legally binding text is the original French opinion version

Key points

Favourable opinion on reimbursement in “the first-line treatment of chronic lymphocytic leukaemia (CLL), solely in monotherapy or in combination with obinutuzumab: in adult patients not presenting with a 17p deletion or a TP53 mutation and ineligible for treatment with full-dose fludarabine, or in adult patients presenting with a cytogenetic status with a poor prognosis (17p deletion or a TP53 mutation)”.

What therapeutic improvement?

Therapeutic improvement in the management strategy.

Role in the care pathway?

The new data are not of a nature to modify the previous conclusions of the TC (opinion of 05/05/2021).

Transparency Committee's Conclusions

Clinical Benefit

- Chronic lymphocytic leukaemia (Binet stages B and C), characterised by the proliferation and accumulation of a malignant mature B-cell clone in the bone marrow, the blood and the lymphatic organs, is life-threatening.
- CALQUENCE (acalabrutinib) in monotherapy or in combination with obinutuzumab is a specific curative treatment for CLL.
- The efficacy/adverse effect ratio is:
  - significant for patients with chronic lymphocytic leukaemia that has not been previously treated, in adult patients not presenting with a 17p deletion (del) or TP53 mutation and ineligible for treatment with full-dose fludarabine, or in adult patients presenting with a cytogenetic status with a poor prognosis (17p deletion or TP53 mutation);
  - poorly established in monotherapy or in combination with obinutuzumab, in patients eligible for treatment with full-dose fludarabine and not presenting with a 17p deletion (del) or TP53 mutation due to lack of data.
- There are medicinal alternatives (see section "2.3 Clinically relevant comparators and medical need").
- CALQUENCE (acalabrutinib) in monotherapy or in combination with obinutuzumab is a first-line treatment for CLL in adult patients not presenting with a 17p deletion (del) or TP53 mutation and ineligible for treatment with full-dose fludarabine, or in adult patients presenting with a cytogenetic status with a poor prognosis (17p deletion or TP53 mutation). In the other situations CALQUENCE (acalabrutinib) in monotherapy or in combination with obinutuzumab does not have a role in the treatment strategy.

Public health benefit

Considering:

- the gravity of the CLL (Binet stages B and C) which is life-threatening and of its incidence,
- the partially met medical need,
- the partial response to the need identified, with:
  - an additional impact on morbidity and mortality that is difficult to quantify with regard to the available alternatives;
  - the absence of demonstration of an impact on quality of life (exploratory data in an open study);
  - the absence of data allowing an assessment of the additional impact on the organisation of care;

CALQUENCE (acalabrutinib) in monotherapy or in combination with obinutuzumab is not liable to have an additional impact on public health.

Considering all these elements, the Committee considers that the actual benefit provided by CALQUENCE (acalabrutinib) in monotherapy or in combination with obinutuzumab is significant in the first-line treatment of chronic lymphocytic leukaemia (CLL) solely: in adult patients not presenting with a 17p deletion or a TP53 mutation and ineligible for treatment with full-dose fludarabine, or in adult patients presenting with a cytogenetic status with a poor prognosis (17p deletion or TP53 mutation).

The Committee gives a favourable opinion on inclusion on the list of medicinal products reimbursable to persons insured under social insurance schemes and on the list of medicinal products approved for the use of communities solely in monotherapy or in combination with obinutuzumab in the first-line treatment of chronic lymphocytic leukaemia (CLL) solely: in adult patients not presenting with a 17p deletion or a TP53 mutation and ineligible for treatment with full-dose fludarabine, or in adult patients presenting with a cytogenetic status with a poor prognosis (17p deletion or TP53 mutation) and at the MA doses.

Recommended reimbursement rate: 100 %

Clinical Added Value

Taking into account:

- the demonstration of the superiority of the combination acalabrutinib and obinutuzumab (AO) versus chlorambucil + obinutuzumab (O-Clb) (HR = 0.10; $_{95\%}$ CI, [0.06; 0.17], p<0.0001), and of acalabrutinib in monotherapy versus O-Clb (HR = 0.20; $_{95\%}$ CI, [0.13; 0.30], p<0.0001), with regard to progression-free survival (hierarchical primary or secondary endpoint) in patients with CLL not previously treated (9.2 % with a 17p del mutation and 11.4 % with a TP53 mutation),
- with a median progression-free survival not reached with the AO combination and acalabrutinib in monotherapy and a median of 22.6 months in the O-Clb group,

But in view of:

- the absence of a robust comparison with ibrutinib, a comparator judged more clinically relevant than the combination chlorambucil + obinutuzumab with regard to current practice and the development of therapeutic strategy, in particular in patients presenting with a 17p deletion or a TP53 mutation,
- the absence of robust data on overall survival, an endpoint that will remain exploratory due to the interruption of the hierarchical sequence upstream,
- the absence of a formal conclusion on quality of life (exploratory endpoint),
- the partially met medical need in first-line treatment with the available alternatives, particularly ibrutinib,

In the same way as VENCLYXTO (venetoclax) in combination with obinutuzumab, the Committee considers that CALQUENCE (acalabrutinib) in monotherapy or in combination with obinutuzumab provides minor clinical added value (CAV IV) compared to the combination chlorambucil + obinutuzumab in patients with CLL not previously treated and presenting with a 17p deletion or a TP53 mutation or in patients not presenting with a 17p deletion or a TP53 mutation and ineligible for treatment with fludarabine.