SUMMARY

zanubrutinib

BRUKINSA 80 mg,

hard capsule

Initial inclusion

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

The legally binding text is the original French opinion version

Transparency Committee's Conclusions

Clinical Benefit

- Waldenstrom macroglobulinaemia (WM) is a rare and life-threatening condition, in particular after failure to respond to several lines of treatment.
- This is a curative medicinal product.
- On account of the lack of evidence of superiority of BRUKINSA (zanubrutinib) in relation to IMBRUVICA (ibrutinib) in terms of complete response or very good partial response (primary outcome measure) during the primary analysis, the descriptive findings of the final analysis with a longer follow-up period do not provide more robust findings in favour of BRUKINSA (zanubrutinib) on these outcome measures, without however suggesting a loss of chance for the patient from receiving zanubrutinib. In view of the longer follow-up period in terms of safety suggesting a different safety profile of BRUKINSA (zanubrutinib) compared to IMBRUVICA (ibrutinib), the efficacy/adverse effects ratio of BRUKINSA (zanubrutinib) is low for patients who have received at least one prior treatment. As a first-line approach, in view of the insufficiency of the data available, the efficacy/adverse effects ratio of BRUKINSA (zanubrutinib) remains poorly defined.
- As a first-line treatment, there are recommended alternatives used off-label. As a second-line or further-line treatment, there is one alternative that has been granted a marketing authorisation, IMBRUVICA (ibrutinib), and there are recommended alternatives used off-label.
- BRUKINSA (zanubrutinib) has no role as monotherapy in the therapeutic strategy of the treatment of adult Waldenstrom macroglobulinaemia patients, as a first-line treatment for patients ineligible for chemo-immunotherapy. BRUKINSA (zanubrutinib) has a role in the therapeutic strategy as monotherapy for adult Waldenstrom macroglobulinaemia patients who have received at least one prior treatment.

➔ **Public health benefit**

In view of:

- the seriousness of Waldenstrom macroglobulinaemia,
- the low incidence of this condition,
- the partially met medical need,
- the lack of response to the identified need with the lack of evidence of an additional impact of BRUKINSA (zanubrutinib) on morbidity-mortality or on quality of life, considering the exploratory nature of the findings on these outcome measures in the phase III study (ASPEN),
- the lack of evidence of an additional impact on delivery of care in the absence of data,

BRUKINSA (zanubrutinib) is unlikely to have an additional impact on public health.

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

- **low only for the indication "as monotherapy for the treatment of adult Waldenstrom macroglobulinaemia (WM) patients who have received at least one prior treatment",**
- **insufficient to justify public funding for the indication "as monotherapy as a first-line approach for the treatment of adult Waldenstrom macroglobulinaemia (WM) patients ineligible for chemo-immunotherapy".**

The Committee:

- **approves inclusion in the list of covered drugs for outpatients and in the list of covered drugs for outpatients only for the indication "as monotherapy for the treatment of adult Waldenstrom macroglobulinaemia (WM) patients who have received at least one prior treatment" and at the marketing authorisation dosages,**
- **disapproves inclusion in the list of covered drugs for outpatients and in the list of covered drugs for inpatients only for the indication "as monotherapy as a first-line approach for the treatment of adult Waldenstrom macroglobulinaemia (WM) patients ineligible for chemo-immunotherapy".**

Recommended reimbursement rate for inclusion in the list of covered drugs for outpatients: 15%

Clinical Added Value

➔ **As monotherapy, for adult Waldenstrom macroglobulinaemia (WM) patients who have received at least one prior treatment:**

In view of:

- the lack of evidence of superiority in relation to IMBRUVICA (ibrutinib) and the uncertainties on the specific effect size of BRUKINSA (zanubrutinib), considering the methodological weaknesses of the ASPEN clinical study;
- the longer follow-up period provided by the final findings of the ASPEN study, which do not suggest loss of chance for patients in terms of efficacy from receiving BRUKINSA (zanubrutinib);

- the safety profile of BRUKINSA (zanubrutinib) benefitting from a longer follow-up period marked in particular by neutropenia, whereas the safety profile of the proprietary medicinal product IMBRUVICA (ibrutinib) includes signals of cardiac toxicity;
- the benefit of having an additional alternative for relapsed or refractory patients after at least one line of treatment considering the profile of older patients at a cardiovascular risk or who already have cardiac comorbidities;

the Committee deems that BRUKINSA (zanubrutinib) provides no clinical added value (CAV V) in relation to IMBRUVICA (ibrutinib) as monotherapy for the treatment of adult Waldenstrom macroglobulinaemia (WM) patients who have received at least one prior treatment.

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