OPINION ON MEDICINAL PRODUCTS

asciminib

SCEMBLIX 20 mg and 40 mg,

film-coated tablets

First assessment

Adopted by the Transparency Committee on 23 November 2022

SUMMARY

The legally binding text is the original French opinion version

Key points

Approval of reimbursement for “the treatment of adult patients with Philadelphia chromosome-positive chronic myeloid leukaemia in chronic phase (Ph+ CML-CP) previously treated with two or more tyrosine kinase inhibitors (see Section 5.1 of the SPC)”.

Note that, in this indication and at the marketing authorisation dosages, patients with a T315I mutation are not included within the scope of the current marketing authorisation.

Therapeutic improvement?

Therapeutic improvement with respect to bosutinib for the treatment of adult patients with Philadelphia chromosome-positive chronic myeloid leukaemia in chronic phase (Ph+ CML-CP) previously treated with two or more tyrosine kinase inhibitors.

Role in therapeutic strategy?

The treatment of Ph+ CML in chronic, accelerated or blast phase is essentially based on tyrosine kinase inhibitors (TKIs).

According to international guidelines, the TKIs indicated as a first-line treatment are first- and second-generation treatments (imatinib, dasatinib, bosutinib, and nilotinib), with dasatinib only being reimbursed in France from the second line of treatment. The choice of TKI must be made according to the treatment objectives, age and comorbidities and must account for the safety profile of the medicinal products available, Note that the NCCN guidelines recommend a preference for second-generation TKIs (dasatinib, bosutinib and nilotinib) for patients with an intermediate or high risk score.

TKIs authorised for first-line treatment may be used for second-line treatment, the choice being based on the same criteria as for the first-line approach, as well as on the toxicity of the TKI used as a first-line treatment and the patient's mutation status. Furthermore, ponatinib (a third-generation TKI) may also be used from the second line of treatment.

As a third and subsequent line of treatment, there are no specific guidelines as to the therapeutic strategy to adopt. In the absence of an alternative, the choice of a TKI must be guided by the BCR-ABL1 mutation sensitivity profile.

According to European guidelines, allogeneic haematopoietic stem cell (HSC) transplantation is a therapeutic option for patients with CML in chronic phase failing to respond (or with a suboptimal response) to two or more TKIs or potentially carrying the T315I mutation. Patients with a high conversion risk must also be envisaged for allogeneic transplantation. Furthermore, allogeneic HSC transplantation may also be a therapeutic option in patients developing an advanced phase during TKI treatment.

Role of the medicinal product

SCEMBLIX (asciminib) is a third-line or subsequent treatment for the treatment of adult patients with Philadelphia chromosome-positive chronic myeloid leukaemia in chronic phase (Ph+ CML-CP), with no T315I mutation and previously treated with two or more tyrosine kinase inhibitors. In the absence of comparative data, it is not possible to determine the role of SCEMBLIX (asciminib) with respect to ponatinib.

Committee's conclusions

Actual Clinical Benefit

Treatment of adult patients with Ph+ CML-CP previously treated with two or more TKIs

- Chronic myeloid leukaemia (CML) is life-threatening.
- The proprietary medicinal product SCEMBLIX (asciminib) is a curative medicinal product.
- The efficacy/adverse effect ratio is significant.
- Medicinal (bosutinib and ponatinib) and non-medicinal (allogeneic haematopoietic stem cell transplantation) alternatives are available.
- SCEMBLIX (asciminib) is a therapeutic alternative as a third-line and subsequent approach, in patients previously treated with two or more tyrosine kinase inhibitors. Given the lack of comparative data, it is not possible to specify the role of SCEMBLIX (asciminib) in relation to ponatinib.

Public health benefit

Considering:

- in terms of public health, despite the severity of this disease, the burden represented by chronic myeloid leukaemia (CML) is low considering the restricted number of patients concerned.
- in the light of the data from the comparative phase III study versus bosutinib, including patients with Ph+ CML-CP with no T315I mutation, having previously received 2 or more TKI treatment lines and failing to respond or intolerant to the most recent TKI received, no impact is expected in terms of morbidity-mortality and quality of life for the proprietary medicinal product SCEMBLIX (asciminib) with respect to the current treatment.
- SCEMBLIX (asciminib) could be an alternative for patients with Ph+ CML-CP, for whom treatments are limited. However, this proprietary medicinal product cannot meet the identified public health need.

SCEMBLIX (asciminib) is not likely to have an additional impact on public health.

Considering all of these elements, the Committee deems that the actual clinical benefit of SCEMBLIX (asciminib) is significant in the treatment of adult patients with Philadelphia chromosome-positive chronic myeloid leukaemia in chronic phase (Ph+ CML-CP) previously treated with two or more tyrosine kinase inhibitors.

Note that, in this indication and at the marketing authorisation dosages, patients with a T315I mutation are not included within the scope of the current marketing authorisation.

The Committee approves inclusion in the list of proprietary medicinal products qualifying for reimbursement under social security and in the list of proprietary products approved for community use for the treatment of adult patients with Philadelphia chromosome-positive chronic myeloid leukaemia in chronic phase (Ph+ CML-CP) previously treated with two or more tyrosine kinase inhibitors and at the marketing authorisation dosages.

Recommended reimbursement rate: 65%

Clinical Added Value

Considering:

- the evidence of the superiority of asciminib with respect to bosutinib in patients with CML-CP, having previously received 2 or more TKI treatment lines and failing to respond or intolerant to the most recent TKI received, on a major molecular response rate with no failure outcome measure at 24 weeks and at 96 weeks,
- methodological limitations limiting the interpretation of the effect size observed, namely:
  - the measurement bias considering the open-label study design and that the patients having discontinued their treatment, regardless of cause, were considered as non-responders in the primary outcome measure,
  - the BCR-ABL transcript threshold of >0.1% for patients intolerant to the most recent TKI received, with no amendment of the primary outcome measure for these patients,
- a more favourable safety profile than bosutinib,
- the medical need partially met by the alternatives available,
- the immaturity of the overall survival data,

the Transparency Committee deems that SCEMBLIX (asciminib) provides minor clinical added value (CAV IV) with respect to bosutinib in adult patients with Philadelphia chromosome-positive chronic myeloid leukaemia in chronic phase (Ph+ CML-CP) previously treated with two or more tyrosine kinase inhibitors.