OPINION ON MEDICINAL PRODUCTS

avapritinib
AYVAKYT 25, 50, 100, 200 mg,

film-coated tablet

New indication

Adopted by the Transparency Committee on 21 September 2022

SUMMARY

The legally binding text is the original French opinion version

Key points

Opinion in favour of reimbursement for the following indication:

AYVAKYT is indicated as monotherapy for the treatment of adult patients with aggressive systemic mastocytosis (ASM), systemic mastocytosis with an associated haematological neoplasm (SM-AHN) or mast cell leukaemia (MCL), after at least one systemic treatment.

Therapeutic improvement?

Therapeutic improvement in the care pathway.

Role in therapeutic strategy?

Patients with advanced systemic mastocytosis usually require antitumour therapy to reduce mastocytic infiltration and improve disease-related organ dysfunction, particularly of the bone marrow.

Currently recommended treatments for advanced systemic mastocytosis include midostaurin (approved in the US and EU for all advanced systemic mastocytosis subtypes), cladribine, interferon-alfa (both used off-label) and imatinib (approved in the US only for a subset of patients with aggressive systemic mastocytosis). Despite the marketing authorisation of midostaurin for the treatment of advanced systemic mastocytosis in 2017, cladribine is still recommended for patients requiring rapid debulking, or for patients who need to stop midostaurin due to toxicity, and interferon is recommended for patients with slow disease progression without the need for rapid cytoreduction. In addition to basic treatment, supportive care including symptomatic treatments (antihistamines, sodium cromoglycate, antacids, glucocorticoids, epinephrine, antileukotriene) is given on a long-term basis. The aim is to limit the symptoms of the disease due to the release of substances contained in the mast cells.

Role of AYVAKYT (avapritinib) in the therapeutic strategy:

AYVAKYT (avapritinib) is a second- and further-line treatment for advanced systemic mastocytosis (aggressive systemic mastocytosis, systemic mastocytosis associated with haematological neoplasm or mast cell leukaemia).

Committee’s conclusions

Clinical Benefit

- Advanced systemic mastocytosis is a severe, life-threatening disease.
- The proprietary medicinal product AYVAKYT (avapritinib) is a curative medicinal product.
- The efficacy/adverse effect ratio is moderate.
- There is a low level of evidence associated with the limited number of available alternative medicinal products (see chapter on comparator drugs).
- It is a second- and further-line treatment and more.

Public health benefit

Considering:

- the severity of the disease and its low prevalence,
- the medical need, which is considered as not covered in the light of the level of evidence for the available alternatives,
- the partial response to the identified medical need based on an objective response rate,
- the lack of a demonstrated impact on morbidity-mortality or quality of life in the absence of comparative data associated with the optimal level of evidence,
- the lack of data supporting a potential additional impact on the care and/or life pathway,

AYVAKYT (avapritinib) is not likely to have a public health benefit.

Considering all these elements, the Committee deems that the actual clinical benefit of AYVAKYT (avapritinib) is LOW in an extension of indication "as monotherapy for the treatment of adult patients with aggressive systemic mastocytosis (ASM), systemic mastocytosis with an associated haematological neoplasm (SM-AHN) or mast cell leukaemia (MCL), after at least one systemic treatment."

The Committee approves inclusion in the list of proprietary medicinal products qualifying for reimbursement under social security and in the list of proprietary medicinal products approved for community use in this extension of the marketing authorisation indication and at the marketing authorisation dosages.

Recommended reimbursement rate: 100%

Clinical Added Value

Considering:

- data from the pivotal non-comparative phase II study which showed an overall response rate of 59.6% in a cohort of patients for whom midostaurin had mostly failed,
- the medical need for this line of treatment (low level of evidence for the available alternatives),
- the indirect comparative data suggesting that the treatment is superior to the available alternatives despite the methodological limitations noted,

The Committee deems that AYVAKYT (avapritinib) provides minor clinical added value (CAV IV) in the management of adult patients with aggressive systemic mastocytosis (ASM), systemic mastocytosis associated with haematological neoplasm (SM-AHN) or mast cell leukaemia (MCL), after at least one systemic treatment.