HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE

SUMMARY

17 FEBRUARY 2021

The legally binding text is the original French opinion version

midostaurin

RYDAPT 25 mg soft capsules

Re-evaluation

Key points

Favourable opinion for maintenance of reimbursement, as monotherapy, for the treatment of adult patients with aggressive systemic mastocytosis (ASM), systemic mastocytosis with associated haematological neoplasm (SM-AHN), or mast cell leukaemia (MCL).

What therapeutic improvement?

No clinical added value in the therapeutic strategy.

◗ Role in the care pathway?

The treatment of aggressive systemic mastocytosis (ASM), systemic mastocytosis with associated haematological neoplasm (SM-AHN), or mast cell leukaemia (MCL) is complex given the heterogeneity of the disease and the different therapeutic needs, depending on the patient.

Specific cytoreductive treatments (off-label), such as interferon alpha, cladribine, rapamycin or tyrosine kinase inhibitors, and symptomatic treatments, in particular antihistamines, corticosteroids or sodium cromoglycate, are used in clinical practice to improve symptoms and prolong patients' survival.

Role of the medicinal product in the care pathway

Despite the low level of evidence of the data supplied and although it is regrettable, in particular, that data from the already existing CEREMAST registry were not supplied, but taking into account the medical need in these serious and heterogeneous rare diseases, requiring complex management, the Transparency Committee considers that RYDAPT (midostaurin), as monotherapy, currently remains a treatment for aggressive systemic mastocytosis (ASM), associated or not with haematological neoplasm, or mast cell leukaemia (MCL).

In the absence of any comparative efficacy data versus available alternatives, in particular cladribine (off-label) in patients eligible for this treatment (symptomatic forms of ASM without associated haematological neoplasm), the place of RYDAPT (midostaurin) relative to cladribine is still unknown.

The Committee will be attentive to the evolution of the care pathway in the treatment of aggressive systemic mastocytosis (ASM), systemic mastocytosis with associated haematological neoplasm (SM-AHN) and mast cell leukaemia (MCL). Any change in this strategy could lead the Committee to re-evaluate RYDAPT (midostaurin), in this indication.

COMMITTEE'S CONCLUSIONS

Clinical benefit

◗ Aggressive forms of systemic mastocytosis (aggressive systemic mastocytosis (ASM), systemic mastocytosis with associated haematological neoplasm (SM-AHN), and mast cell leukaemia (MCL)) are serious diseases that are life-threatening.

◗ This is a curative treatment.

◗ The efficacy/adverse effects ratio remains low.

◗ There are therapeutic alternatives, none of which have an MA.

◗ **RYDAPT, as monotherapy, is a treatment for aggressive systemic mastocytosis (ASM), associated or not with haematological neoplasm, or mast cell leukaemia (MCL).** Its role compared to the **available alternatives, in particular cladribine,** cannot be determined due to a lack of comparative data (see section 9).

Public health impact

Considering:

- the seriousness of the disease and its low incidence (estimated to be between 15 and 30 patients per year in France),
- the substantial medical need,
- the lack of response provided by RYDAPT (midostaurin) to the identified medical need in view of the limited data available,
- the absence of an impact on the organisation of care,

RYDAPT (midostaurin) is unlikely to have an additional impact on public health.

The Committee regrets that data from the already existing CEREMAST registry were not supplied for this reevaluation. However, considering the substantial medical need in this rare disease, and given the complexity of treatment of these patients, the Committee maintains its initial opinion and considers that the clinical benefit of RYDAPT (midostaurin) remains low in the MA indication.

The Committee issues a favourable opinion for maintenance of inclusion in both the hospital formulary list and the retail formulary list of reimbursed proprietary medicinal products approved for use in the MA indication and dosages.

Clinical Added Value

Considering:

- **limited efficacy data from a phase 2 non-comparative study demonstrating an overall response rate of close to 60%,**
- **the absence of any conclusive data demonstrating an improvement in overall survival and quality of life in this study,**
- **the methodological limitations of the use data supplied in the context of this reevaluation (non-exhaustive, selection bias, etc.) not addressing, in particular, the Committee's request to have access to exhaustive follow-up data for patients treated with RYDAPT (midostaurin) in France,**

But taking into account:

- **the difficulty of conducting a comparison with a single treatment recommended in the same study for all the patients in the indication given the heterogeneity of the disease and its management and, in particular, its association or otherwise with a haematological neoplasm,**
- **the substantial medical need in these rare and serious diseases in the absence of any other medicinal products with an MA at present,**

the Committee considers that RYDAPT, as monotherapy, provides no clinical added value (CAV V) in the care pathway for the treatment of aggressive systemic mastocytosis (ASM), systemic mastocytosis with associated haematological neoplasm (SM-AHN), or mast cell leukaemia (MCL).