HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
SUMMARY
16 DECEMBER 2020
The legally binding text is the original French opinion version

fostamatinib
TAVLESSE 100 mg, 150 mg film-coated tablets

First assessment

Key points

Favourable opinion for reimbursement in the treatment of chronic immune thrombocytopenia (ITP) in adult patients who are refractory to other treatments.

What therapeutic improvement?

No clinical added value in the therapeutic strategy for chronic ITP on the basis of currently available data.

Role in the care pathway?

Chronic ITP requires the initiation of specialised care, in liaison with the general practitioner.

In the absence of clinical or haematological signs of ITP severity and consequences on quality of life (asthenia, impact on schooling, etc.), no treatment or corticosteroid/Ig IV therapy (on demand or programmed) may be proposed.

In the event of chronic ITP, i.e., present for more than 12 months, several second-line treatments may be proposed in adults; few of these treatments have been evaluated in randomised controlled studies. Only thrombopoietin receptor agonists (romiplostim, eltrombopag) and azathioprine have an indication in ITP validated by an MA. Rituximab has a temporary recommendation for use (RTU) in this indication. According to the 2017 French national diagnostic and care protocol (PNDS), splenectomy is also one of the second-line therapeutic options in the event of chronic ITP. Despite the increased risks of serious infections and venous and/or arterial thrombosis in adults, splenectomy is the only treatment that has been established as being curative. There is no consensus with respect to its role in the hierarchical sequence of second-line treatments and it may be performed before or after rituximab and/or Thrombopoietin receptor agonists (TPO-RA).

In the absence of a consensus-based care pathway, the choice of treatment among the available options must remain personalised and be discussed on a case-by-case basis.

In accordance with the most recent Committee opinions relative to TPO-RA (eltrombopag and romiplostim), the occasional use of TPO-RA may be considered in the treatment of marked thrombocytopenia refractory to first-line treatments, in the event of severe bleeding syndrome, in the context of preparation for a surgical procedure or pending the effect of already initiated second-line therapy (depending on expert opinion). Outside these occasional uses, given the primarily suspensive effect and uncertainties with respect to the long-term safety data of these medicinal products, they may be considered in the treatment of chronic ITP refractory to first-line treatments (e.g. corticosteroids, immunoglobulins) and following the failure of one of the second-line treatments (immunosuppressant, rituximab or splenectomy) or as an alternative to these treatments when they are not considered to be appropriate.

Role of the medicinal product in the care pathway:

On the basis of currently available data and taking into account the identified medical need, the Committee considers that the use of TAVLESSE (fostamatinib) may be considered only as a last-resort treatment for multirefractory chronic ITP resistant to second-line treatments (which, according to the 2017 PNDS include splenectomy TPO-RA [switches included] and rituximab). In patients not having undergone splenectomy, multirefractory to medicinal treatments, TAVLESSE may be a treatment option when splenectomy is deemed to be inappropriate by reference or expert centres.

The Committee points out that this medicine is subject to hospital prescription only by certain specialist physicians (PRS). In addition, renewal of prescription is limited to certain healthcare professionals.

Given the specificities of treatment of this rare disease, the Committee recommends that decisions to initiate or discontinue fostamatinib treatment be taken after a documented proposal resulting from a multidisciplinary team meeting within a reference or expert centre for the treatment of ITP. Regular follow-up of patients within one of these centres is essential to ensure the efficacy of treatment and monitor its safety.

Special recommendations

Given the specificities of treatment of this rare disease, the Committee recommends that decisions to initiate or discontinue fostamatinib treatment be taken after a documented proposal resulting from a multidisciplinary team meeting within a reference or expert center for the treatment of ITP. Regular follow-up of patients within one of these centers is essential to ensure the efficacy of treatment and monitor its safety.

COMMITTEE'S CONCLUSIONS

Clinical benefit

◗ Immune thrombocytopenia is characterised by thrombocytopenia, generally combined with a bleeding syndrome, usually limited to purpura, ecchymoses, petechiae and/or mucous membrane bleeding (epistaxis, bleeding blisters inside the mouth, menorrhagia and metrorrhagia). Evolution towards chronicity (present for more than 12 months) is more common in adults than in children but spontaneous remissions remain possible, even after several years. In very rare cases of very severe thrombocytopenia (10 $x10^9$/l), visceral bleeding may occur. This disease can significantly affect quality of life. The prognosis is severe in chronic (diagnosed more than 12 months earlier) and multirefractory forms.
◗ Due to its suspensive mechanism of action fostamatinib can be considered as a symptomatic treatment.
◗ The efficacy/adverse effects ratio of fostamatinib is low given:
- its efficacy assessed only versus placebo, shown to be low in terms of short-term stable platelet response with a demonstrated superiority in only one of the two phase 3 studies, and no demonstrated impact on haemorrhagic scores,
- the short-term safety profile, marked by diarrhoea, an adverse effect liable to impact the quality of life of patients, and hypertension, and uncertainties with respect to the long-term safety, in particular regarding its potential effects on bone remodelling, particularly in the event of long-term use.

◗ In adults with chronic ITP refractory to other treatments, there are few therapeutic alternatives (see section 05 of the opinion).
◗ The use of TAVLESSE (fostamatinib) may be envisaged only as a last-resort treatment for multirefractory chronic ITP resistant to second-line treatments. In patients not having undergone splenectomy, multirefractory to medicinal treatments, TAVLESSE may be a treatment option when splenectomy is deemed to be inappropriate by reference or expert centers (see section 08).

Public health impact

Considering:
- the seriousness of chronic immune thrombocytopenic purpura,
- its prevalence in adults,
- the partially met medical need in multirefractory patients,
- the very partial response to the identified partially met medical need, given the expected additional impact on the morbidity of patients with multirefractory chronic ITP,
- the lack of demonstrated impact on the organisation of care and on quality of life,

TAVLESSE (fostamatinib) is unlikely to have an additional impact on public health.

Given all these elements, the Committee deems that the clinical benefit of TAVLESSE (fostamatinib) is low in the MA indication.

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

◗ **Recommended reimbursement rate: 15%**

Clinical Added Value

Considering:
- **the efficacy of fostamatinib, shown to be superior to placebo in terms of platelet response in one of the two phase 3 studies, with an absolute difference of 17.6% between the groups ($CI_{95\%}$ [7.2; 28.1]; p = 0.0261),**
- **the identified medical need in adult patients who are refractory to other treatments,**

but considering:
- **the low effect size compared to placebo, with no demonstrated impact on bleeding scores,**
- **the absence of comparison with the other available treatments,**
- **the short-term safety profile, marked in particular by diarrhoea and hypertension, and the uncertainties with respect to the long-term safety, in particular regarding its potential effects on bone remodelling,**

the Committee considers that TAVLESSE (fostamatinib) provides no clinical added value (CAV V) in the treatment of chronic immune thrombocytopenia (ITP) in adult patients who are refractory to other treatments.