HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
OPINION
05 FEBRUARY 2020

eltrombopag
REVOLADE 25 mg, 50 mg and 75 mg film-coated tablets
REVOLADE 25 mg powder for oral solution

MA amendments

Key points

Favourable opinion for maintenance of reimbursement in primary immune thrombocytopenia (ITP) lasting 6 months or longer from diagnosis and refractory to other treatments (e.g. corticosteroids, immunoglobulins).

What therapeutic improvement?

In the same way as NPLATE (romiplostim), REVOLADE (eltrombopag) represents a slight therapeutic improvement in the treatment of primary ITP lasting 12 months or longer from diagnosis of patients aged 1 year and above who are refractory to first-line treatments (e.g. corticosteroids, immunoglobulins) and who have not responded to one of the second-line treatments (immunosuppressant, rituximab or splenectomy).
REVOLADE (eltrombopag) represents a slight therapeutic improvement in the treatment of primary ITP lasting 6 to 12 months from diagnosis of patients aged 1 year and above who are refractory to first-line treatments (corticosteroids, immunoglobulins) and who have not responded to one of the second-line treatments (immunosuppressant, rituximab or splenectomy).
However, the clinical relevance of making a distinction between ITP lasting 12 months or longer from diagnosis and ITP lasting 6 to 12 months from diagnosis is low.

Role in the care pathway?

Immune thrombocytopenia (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, no treatment or corticosteroid/IgIV therapy (on demand or programmed) may be proposed.

According to the expert opinion, the occasional use of TPO-R agonists (romiplostim, eltrombopag) 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.

Outside these occasional uses, given the primarily suspensive effect and uncertainties with respect to the long-term safety data for these products, TPO-R agonists may be considered in the treatment of ITP lasting more than 6 months from diagnosis in patients who are refractory to first-line treatments (corticosteroids, immunoglobulins) and who have not responded to one of the second-line treatments (immunosuppressant, rituximab or splenectomy).
Splenectomy is a last resort treatment in children.

COMMITTEE'S CONCLUSIONS

Clinical Benefit

◗ Immune thrombocytopenia (ITP) is characterised by thrombocytopenia, generally combined with a bleeding syndrome, usually limited to purpura, ecchymosis, petechiae and/or mucosal bleeding. In children, it is a benign, post-infectious disease in the majority of cases. Chronicization (present for more than 12 months) is less common in children than in adults and spontaneous remissions remain possible, even after several years. In very rare cases of very severe thrombocytopenia, 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.
◗ Given its suspensive mechanism of action (TPO-R agonist), REVOLADE (eltrombopag) can be considered to be a symptomatic treatment.
◗ The efficacy/adverse effects ratio of this medicinal product is high in the short term.
◗ There are therapeutic alternatives.
◗ Treatment with REVOLADE (eltrombopag) may be envisaged in ITP lasting 6 months or longer from diagnosis refractory to first-line treatments (corticosteroids, immunoglobulins) and following the failure of one of the second-line treatments (rituximab, immunosuppressant). However, the occasional use of REVOLADE 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 (see section 07).

Public health impact

Considering:
- the seriousness of primary immune thrombocytopenia lasting 6 months or longer from diagnosis refractory to first-line treatments and not responding to one of the second-line treatments,
- the prevalence of this disease in adults,
- the unmet medical need in situations of multirefractory chronic ITP,
- the partial response to the identified medical need: short-term efficacy, uncertainties with respect to the long-term safety,
- the absence of robust data on quality of life,
- the absence of any demonstrated impact on the organisation of care,

REVOLADE is likely to have an impact on public health in adults.
REVOLADE is unlikely to have an impact on public health in children one year of age and older.

Given all these elements, the Committee deems that the clinical benefit of REVOLADE remains substantial 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 marketing authorisation indication(s) and dosages.

Clinical Added Value

Considering:

- **the lack of long-term efficacy and safety data for the product, which has a primarily suspensive effect,**
- **the absence of comparative data versus the other treatments used in second-line therapy,**
- **the absence of any demonstration of efficacy in patients refractory to first-line medicinal treatments and not responding to second-line treatments,**

the Transparency Committee considers that REVOLADE (eltrombopag), in the same way as NPLATE (romiplostim), provides a minor clinical added value (CAV IV) in the treatment of primary ITP lasting 12 months or longer from diagnosis in patients one year of age and older who are refractory to first-line treatments (corticosteroids, immunoglobulins) and who have not responded to one of the second-line treatments (immunosuppressant, rituximab or splenectomy).

REVOLADE (eltrombopag) provides a minor clinical added value (CAV IV) in the treatment of primary ITP lasting 6 to 12 months from diagnosis in patients one year of age and older who are refractory to first-line treatments (corticosteroids, immunoglobulins) and who have not responded to one of the second-line treatments (immunosuppressant, rituximab or splenectomy).

However, the clinical relevance of making a distinction between ITP lasting 12 months or longer from diagnosis and ITP lasting 6 to 12 months from diagnosis is low.