HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
OPINION
11 DECEMBER 2019

iloprost
ILOMEDINE 0.1 mg/1 ml concentrate for solution for infusion

New indications

Key points

Favourable opinion for reimbursement in the treatment of severe Raynaud's phenomena in patients with progressive trophic disorders.

Unfavourable opinion for reimbursement in the treatment of severe chronic ischaemia of lower limbs in patients in whom revascularisation has failed or is not indicated.

What therapeutic improvement?

No clinical added value in the treatment of severe Raynaud's phenomena in patients with progressive trophic disorders.

Role in the care pathway?

Treatment of severe chronic ischaemia of lower limbs:

ILOMEDINE has no role in the care pathway in severe chronic ischaemia of lower limbs when revascularisation has failed or is not indicated.

Treatment of severe Raynaud's phenomena:

ILOMEDINE is a last-line treatment, in addition to lifestyle and dietary measures, which must be reserved for Raynaud’s phenomenon patients with severe trophic lesions following the failure of oral therapies.

01 COMMITTEE'S CONCLUSIONS

01.1 Clinical Benefit

1.1.1 Treatment of severe chronic ischaemia of lower limbs

◗ Chronic ischaemia of the lower limbs is a serious condition, which can lead to a marked deterioration in quality of life, be limb-threatening and be life-threatening to the patient as a result of cardiovascular complications.

◗ ILOMEDINE (parenteral iloprost) is a symptomatic treatment for severe chronic ischaemia of lower limbs.

◗ Considering:
- the efficacy of parenteral iloprost demonstrated on a purely symptomatic outcome measure (pain relief) versus placebo for a duration inferior to that recommended, and the absence of data with a good level of evidence on clinically relevant outcome measures (morbidity and mortality, including amputation-free survival),
- in view of the safety profile and therapeutic constraints of this medicinal product, generally requiring treatment for 28 days,

the efficacy/adverse effects ratio of iloprost cannot be established in this indication.

◗ There is no therapeutic alternative to parenteral iloprost when revascularisation has failed or is not indicated.

◗ ILOMEDINE has no role in the treatment of severe chronic ischaemia of lower limbs.

◗ Public health impact

Considering:
- the seriousness of chronic ischaemia of lower limbs,
- its low prevalence,
- the unmet medical need but the absence of a response to the identified need, in the absence of data enabling assessment of the impact of parenteral iloprost on morbidity or mortality (clinically relevant criteria),
- the lack of any demonstrated impact on quality of life or the organisation of care,

ILOMEDINE is unlikely to have an impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of ILOMEDINE is insufficient to justify its funding by the French national health insurance system in the indication "Treatment of severe chronic ischaemia of lower limbs in patients at risk of amputation, in whom surgical revascularisation or angioplasty has failed or is not indicated, following an interdisciplinary meeting of physicians, surgeons and radiologists".
The Committee issues an unfavourable opinion for inclusion in the hospital formulary list of reimbursed proprietary medicinal products approved for use in this indication and at the MA dosages.

1.1.2 Treatment of severe Raynaud's phenomena

◗ Severe Raynaud's phenomena with progressive trophic disorders, which mainly develop consecutive to a systemic disease, are rare and serious.

◗ ILOMEDINE (parenteral iloprost) is a symptomatic treatment for severe Raynaud's phenomena.

◗ Considering:
- exploratory data concerning the efficacy of parenteral iloprost on relevant outcome measures (severity and frequency of Raynaud's attacks, healing of lesions),
- the absence of clinical data enabling assessment of its impact in terms of morbidity (in particular, amputations), and the safety profile and modalities of use of this medicinal product requiring prolonged hospitalisation,

the efficacy/adverse effects ratio of ILOMEDINE is low in this indication.

◗ There are no therapeutic alternatives to parenteral iloprost.

◗ It is a last-line treatment, in addition to lifestyle and dietary measures, which must be reserved for Raynaud's phenomenon patients with severe trophic lesions following the failure of oral therapies.

◗ Public health impact

Considering:
- the rarity and seriousness of severe forms of Raynaud's phenomenon with progressive trophic disorders,
- the partially met medical need but the absence of an additional response to the identified need, in the absence of data enabling assessment of the impact of parenteral iloprost on morbidity,
- the lack of any demonstrated impact on quality of life or the organisation of care,

ILOMEDINE is unlikely to have an impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of ILOMEDINE is low in the indication "Treatment of severe Raynaud's phenomena in patients with progressive trophic disorders".

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

01.2 Clinical Added Value

1.2.1 Treatment of severe chronic ischaemia of lower limbs

Not applicable.

1.2.2 Treatment of severe Raynaud's phenomena

Considering:
- **the low quality of clinical evidence for the efficacy of ILOMEDINE versus placebo on the frequency and severity of attacks and on ulcer healing in patients with Raynaud's phenomenon secondary to systemic scleroderma (old study with multiple outcome measures without correction of alpha risk inflation and in which only half the patients included corresponded to the MA),**
- **the absence of clinical data enabling assessment of the impact of parenteral iloprost on morbidity (in particular, amputations),**

the Committee considers that ILOMEDINE provides no clinical added value (CAV V) in the care pathway for severe Raynaud's phenomena with progressive trophic disorders.