OPINION ON MEDICINAL PRODUCTS

noradrenaline tartrate

CRONOMIR 10 MICROGRAMS/ML,

solution for injection/infusion

First assessment

Adopted by the Transparency Committee on 21 September 2022

SUMMARY

The legally binding text is the original French opinion version

Key points

Approval of reimbursement for CRONOMIR 10 micrograms/ml (noradrenaline tartrate), solution for injection/infusion for the restoration and maintenance of peri-operative blood pressure following hypotension induced by spinal anaesthesia or general anaesthesia in adults.

Therapeutic improvement?

No improvement over other available vasopressors.

Role in therapeutic strategy?

The management of hypotension during anaesthesia is based on the modification of anaesthetic depth according to routine monitoring data, the correction of low cardiac output by volume expansion, and/or the correction of low vascular resistance by administration of a vasopressor. These actions can be undertaken simultaneously. The different vasopressors differ in their mechanisms of action on vascular and cardiac functions according to their affinity for alpha- and beta-adrenergic receptors.

According to the recommendations of the French Anaesthesia and Intensive Care Society (SFAR), the two vasopressors used as a first-line treatment are ephedrine and noradrenaline, due to their combined α and β actions which allow for the correction of arterial hypotension with the

maintenance of cardiac output despite the increase in arterial resistance. Given its short half-life, continuous intravenous administration is preferred (except for ephedrine).

Role of CRONOMIR 10 micrograms/ml (noradrenaline tartrate), solution for injection/infusion in the therapeutic strategy:

The medical use of noradrenaline as a vasopressor is a well-established option in the operating theatre for peri-operative blood pressure control.

Therefore, like the other available vasopressors, CRONOMIR 10 micrograms/ml (noradrenaline tartrate), solution for injection/for infusion is a first-line treatment for the restoration and adapted maintenance of blood pressure following spinal anaesthesia or general anaesthesia, particularly in the latter case for patients with comorbidities undergoing major surgery.

The available clinical data do not provide a basis to reach a conclusion on the contribution of noradrenaline compared to the other available vasopressors in terms of efficacy and tolerance, nor compared to other noradrenaline-based specialities in terms of the delivery of care. As a reminder, according to the SmPC, the concentration of this presentation is not suitable for critical care situations such as the treatment of septic or cardiogenic shock and cardiac arrest, in particular.

Clinical Benefit

- Low blood pressure is common during the perioperative period and is the cause of many complications. It is associated with the occurrence of death, renal, myocardial, and cerebral lesions.
- The proprietary medicinal product CRONOMIR 10 micrograms/ml (noradrenaline tartrate), solution for injection/for infusion, falls within the scope of symptomatic and preventive treatment.
- The efficacy/adverse effects ratio of this proprietary medicinal product is high.
- There are alternative medications. This specialty is a first-line treatment.

Public health benefit

Considering:

– the severity of complications following perioperative hypotension and its prevalence;

– the medical need to have effective and well-tolerated drugs in patients requiring the correction of arterial hypotension with the maintenance of cardiac output and an increase in arterial load, as well as to regulate use outside Marketing Authorization for noradrenaline;

– the medical need partially covered by the alternatives;

– the use of diluted noradrenaline (off-label) in the perioperative control of blood pressure but the lack of response to the identified need due to an undemonstrated additional impact on morbidity/mortality by the proprietary medicinal product CRONOMIR 10 micrograms/ml (noradrenaline tartrate), solution for injection/infusion;

– the absence of data on a possible impact on the healthcare organization,

CRONOMIR 10 micrograms/ml (noradrenaline tartrate), solution for injection/infusion is not likely to have an impact on public health. Considering all these elements, the Committee deems that the actual benefit of CRONOMIR 10 micrograms/ml (noradrenaline tartrate), solution for injection/for infusion is significant in the Marketing Authorization indication.

The Committee approves inclusion in the list of proprietary medicinal products approved for community use in the Marketing Authorization indication and at the Marketing Authorization dosages.

Clinical Added Value

Considering:

- the limited data from the literature demonstrating the efficacy of diluted noradrenaline in restoring and maintaining perioperative arterial pressure after hypotension induced by spinal or general anaesthesia in adults,
- the established medical use of diluted noradrenaline in perioperative arterial pressure control,
- the greater manageability of the ready-to-use, diluted presentation,

But in the light of:

- the modest effect size of diluted noradrenaline demonstrated in relation to other vasopressors in robust clinical studies,
- the lack of specific efficacy and safety data for the proprietary medicinal product CRONOMIR 10 micrograms/ml (noradrenaline tartrate), solution for injection/infusion versus the other vasopressors,
- the lack of formal evidence that the risk of error is reduced when administering the pre-diluted presentation,

the Committee deems that CRONOMIR 10 micrograms/ml (noradrenaline tartrate) solution for injection/infusion provides no clinical added value (CAV V) compared to the other vasopressors available in France.