HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
SUMMARY
30 JUNE 2021

The legally binding text is the original French opinion version

tranexamic acid
EXACYL 0.5 g/5 mL I.V. solution for injection

New indications

Key points

Favourable opinion for reimbursement in the prevention and treatment of haemorrhages due to general or local fibrinolysis in adults and children from one year:

- Gynaecological surgery or disorders of obstetric origin,
- Thoracic and abdominal surgery and other major surgical intervention such as cardiovascular surgery

What therapeutic improvement?

No clinical added value in the therapeutic strategy.

Role in the care pathway?

The prevention of perioperative bleeding is based on the identification and correction of pre-existing risk factors (haemostasis disorders with a bleeding risk, preoperative management of antithrombotic treatments), and the prevention of the onset or exacerbation of a coagulation disorder (correction of promoting factors such as hypothermia or severe acidosis, and in some cases, administration of prohaemostatic agents).

In the event of haemorrhage, the therapeutic approach (except in surgical or obstetric procedures) is compensation therapy (transfusion) and reduction of the amplitude of the phenomenon (administration of clotting factors, inhibition of fibrinolysis).

In addition to any surgical or obstetric procedures and strategies to compensate for or replace components that are consumed, a few medicinal products are currently authorised and recommended in the prevention and management of haemorrhage in a context of gynaecological surgery, obstetric problems or major surgery:
- uterotonic treatments (oxytocin, sulprostone, carbetocin) in the prevention and/or treatment of postpartum haemorrhage
- aprotinin, as prophylaxis, in adult patients who are at high risk of major blood loss undergoing isolated cardiopulmonary bypass graft surgery,
- tranexamic acid, recommended in the perioperative context for haemorrhagic surgery, and the use of which is suggested by certain guidelines in the treatment or prevention of postpartum haemorrhage.

The benefit of therapeutic intervention in these fields can be assessed based on the volume of bleeding, the transfusion volume, morbidity and mortality.

Role of EXACYL (tranexamic acid) 0.5 g/5 mL I.V. solution for injection in the care pathway for the prevention and treatment of haemorrhages due to general or local fibrinolysis in adults and children from one year

In gynaecological, thoracic and abdominal surgery and other major surgical intervention such as cardiovascular surgery:
Considering the clinical data available and good clinical practice guidelines, the Committee deems that EXACYL (tranexamic acid) 0.5 g/5 mL I.V. solution for injection is a first-line treatment in situations requiring inhibition of fibrinolysis:
- in the prevention of haemorrhages, its use should be reserved for major surgeries in which there is a high risk of haemorrhage given the nature of the procedure or the patient's general condition, such as heart surgery. The benefit of routine administration has not been established;
- in the event of haemorrhagic shock, management should include the administration of tranexamic acid as soon as possible within the first few hours following the onset of haemorrhagic shock.

In disorders of obstetric origin:
Considering the clinical data available and good clinical practice guidelines, the Committee deems that EXACYL (tranexamic acid) 0.5 g/5 mL I.V. solution for injection has a role in situations requiring inhibition of fibrinolysis:
- in the prevention of haemorrhages, its administration should be reserved for situations in which there is a high risk of postpartum haemorrhage (in particular caesarean section, antepartum bleeding, placental attachment abnormalities), in addition to oxytocin. The benefit of routine administration prior to any delivery has not been demonstrated.
- in the treatment of postpartum haemorrhage resistant to uterotonics. It should be administered as soon as possible, noting that cases of acute kidney injury (including cortical necrosis) have been reported with doses > 2 g.

COMMITTEE'S CONCLUSIONS

Considering all of this information and further to debate and voting, the Committee considers:

Clinical benefit

In the prevention and treatment of haemorrhages due to general or local fibrinolysis in adults and children from one year:

Gynaecological, thoracic and abdominal surgery and other major surgical intervention such as cardiovascular surgery

◗ The haemorrhagic risk, which may be major in gynaecological, thoracic, abdominal and cardiovascular surgery, can have serious consequences and be life-threatening to the patient.
◗ The proprietary medicinal product EXACYL (tranexamic acid) 0.5 g/5 mL IV solution for injection is a curative and preventive medicinal product.
◗ The efficacy/adverse effects ratio is high.
◗ There is a medicinal alternative in cardiovascular surgery, aprotinin (see section 5 of this opinion). In other situations, there are no medicinal alternatives to inhibit fibrinolysis.
◗ EXACYL (tranexamic acid) 0.5 g/5 mL IV solution for injection is a first-line treatment. In a surgical context, its use may be envisaged as prophylaxis before major surgery with a high risk of haemorrhage only, and as curative treatment in the management of haemorrhagic shocks (see section 08 of the opinion).

Public health impact

Considering:

- the seriousness of the disease and its prevalence
- the partially met medical need in cardiovascular surgery and the unmet need in other surgeries.
- the lack of response to the identified need considering:
    - the absence of additional impact on patients' morbidity and mortality apart from transfusion sparing only in the context of major surgery with a high haemorrhagic risk
    - the lack of any demonstrated impact on quality of life and organisation of care

EXACYL (tranexamic acid) 0.5 g/5 mL IV is unlikely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of EXACYL (tranexamic acid) 0.5 g/5 mL IV solution for injection is substantial in the MA indication extensions.

Disorders of obstetric origin

◗ The haemorrhagic risk can have serious consequences and be life-threatening for the patient. Obstetric haemorrhage is the leading cause of severe maternal morbidity and ICU admission.
◗ The proprietary medicinal product EXACYL (tranexamic acid) 0.5 g/5 mL IV solution for injection is a curative and preventive medicinal product.
◗ The efficacy/adverse effects ratio is high.
◗ There are no medicinal alternatives to inhibit fibrinolysis.
◗ EXACYL (tranexamic acid) 0.5 g/5 mL IV solution for injection has a role in situations requiring inhibition of fibrinolysis. In an obstetric context, its use may be envisaged as prophylaxis only in women at high risk of postpartum haemorrhage (PPH) in addition to oxytocin, and in the treatment of PPH resistant to uterotonics. (see section 08 of the opinion).

Public health impact

Considering:

- the seriousness of disorders of obstetric origin, which can be life-threatening, and their prevalence
- the unmet medical need
- the lack of response to the identified need considering:
    - the absence of any demonstrated additional impact on morbidity and mortality, apart from a reduction in the incidence of postpartum haemorrhage, of low clinical relevance, in the event of prophylactic administration in a caesarean section context;
    - the absence of any demonstrated impact on quality of life or the organisation of care

EXACYL (tranexamic acid) 0.5 g/5 mL IV is unlikely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of EXACYL (tranexamic acid) 0.5 g/5 mL IV solution for injection is substantial in the prevention and treatment of haemorrhages due to general or local fibrinolysis in adults and children from one year in disorders of obstetric origin.

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

Clinical Added Value

In the prevention and treatment of haemorrhages due to general or local fibrinolysis in adults and children from one year:

Gynaecological, thoracic and abdominal surgery and other major surgical intervention such as cardiovascular surgery

Considering:

- The recommended use of tranexamic acid, well established in clinical practice, both as prophylaxis in situations at high risk of haemorrhage, and to treat haemorrhages occurring in a surgical context,
- Data supporting this use, obtained, in particular, from a meta-analysis having assessed tranexamic acid in the prevention and treatment of perioperative haemorrhages, all types of surgeries and dosages combined, which suggests transfusion sparing compared to placebo,
- The results of a randomised study assessing the efficacy of tranexamic acid administered before coronary surgery with a risk of complications, also suggesting significant transfusion sparing (exploratory endpoint) in comparison to placebo, but without any demonstration of a reduction in deaths or thrombo-embolic complications (composite primary endpoint),
- Safety data from these studies not demonstrating any increase in thrombotic events versus placebo, but showing an increase in convulsions in cardiovascular surgery where dosages higher than those recommended in the MA are used,
- Limited and heterogeneous clinical data in the other types of surgery covered by the MA in terms of findings and level of evidence,
- The medical need in this MA indication, considering the impact on morbidity and mortality of haemorrhages due to fibrinolysis occurring in a surgical context,

the Committee considers that EXACYL (tranexamic acid) 0.5g/5 mL IV solution for injection provides no clinical added value (CAV V) in the therapeutic strategy in the prevention and treatment of haemorrhages due to general or local fibrinolysis in adults and children from one year in gynaecological, thoracic and abdominal surgery and other major surgical intervention such as cardiovascular surgery.

Disorders of obstetric origin

Considering:

- The recommended use of tranexamic acid, well established in clinical practice, both as prophylaxis in situations at high risk of haemorrhage, and to treat haemorrhages in an obstetric context,
- Available clinical studies with a high level of evidence assessing this use, limited to the prevention and treatment of postpartum haemorrhage,
- The results of these studies versus placebo, demonstrating an efficacy of tranexamic acid only in the prevention of postpartum haemorrhage following caesarean deliveries, on an endpoint of low clinical relevance, and without any demonstrated impact on mortality and transfusion requirements,
- Safety data from these studies, demonstrating adverse effects such as nausea and vomiting, with no increase in the risk of thrombotic events or kidney failure due to cortical necrosis,
- The medical need in this MA indication, considering the impact of haemorrhages due to fibrinolysis on maternal morbidity and mortality,

the Transparency Committee considers that EXACYL (tranexamic acid) 0.5g/5 mL IV solution for injection provides no clinical added value (CAV V) in the therapeutic strategy in the prevention and treatment of haemorrhages due to general or local fibrinolysis in adults and children from one year in disorders of obstetric origin.