



## TRANSPARENCY COMMITTEE OPINION 05 FEBRUARY 2020

*urokinase*  
**THERASOLV powder for solution for injection/infusion**

**First assessment**

### ► Key points

Favourable opinion for reimbursement for the lysis of blood clots in the following conditions:

- thrombosed intravascular catheters and cannulae,
- acute occlusive peripheral arterial disease with limb-threatening ischemia.

Unfavourable opinion for reimbursement for the lysis of blood clots in the following conditions:

- extensive acute proximal deep vein thrombosis,
- acute massive pulmonary embolism.

### ► What therapeutic improvement?

No clinical added value in the treatment of thrombosed intravascular catheters and cannulae or acute occlusive peripheral arterial disease with limb-threatening ischemia.

## ► Role in the care pathway?

### Thrombosed intravascular catheters and cannulae

THERASOLV (urokinase) is a first-line treatment, in the event of thrombosed intravascular catheters and cannulae, in the same way as the other thrombolytic agents currently available in this indication.

### Acute occlusive peripheral arterial disease with limb-threatening ischemia

THERASOLV (urokinase) is a first-line treatment in acute occlusive peripheral arterial disease with limb-threatening ischemia only in the absence of neurological deficit. In accordance with the SPC and current recommendations, THERASOLV (urokinase) should be administered locally via a catheter. The intravenous route must not be used.

### Extensive acute proximal deep vein thrombosis and acute massive pulmonary embolism

THERASOLV (urokinase) has no role in the care pathway.

## COMMITTEE'S CONCLUSIONS

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### Clinical Benefit

#### Thrombosed intravascular catheters and cannulae

► The presence of thrombus in the catheter lumen reduces or stops the blood flow, requiring either a conservative procedure (thrombolysis) or replacement of the catheter. The removal of a thrombosed catheter and the insertion of a new catheter present a risk of morbidity and mortality. In addition, in children, for safety and comfort reasons when inserting a new catheter, it is necessary to perform sedation, usually followed by general anaesthesia, involving its own specific risks.

► THERASOLV (urokinase) is a curative treatment for thrombosed intravascular catheters and cannulae.

► Given the available data documenting the efficacy and good safety of urokinase for the repermeabilisation of central venous catheters in children and adults, the efficacy/adverse effects ratio is high.

► There are alternatives: ACTOSOLV (urokinase).

► This is a first-line treatment, in the same way as the other thrombolytic agents currently available in this indication.

#### **Public health impact**

Considering:

- the potentially serious complications related to catheter obstruction,
- its low prevalence, which is difficult to estimate,
- the currently met medical need,
- the absence of any demonstrated impact on quality of life and the organisation of care (hospitalisation, AE, etc.),
- the lack of additional response to the identified need,

THERASOLV (urokinase) is unlikely to have an additional impact on public health.

**Considering all these elements, the Committee deems that the clinical benefit of THERASOLV is substantial in this marketing authorisation indication.**

**The Committee issues a favourable opinion for inclusion in the hospital formulary list of reimbursed proprietary medicinal products approved for use in the indication for the lysis of blood clots in thrombosed intravascular catheters and cannulae and at the marketing authorisation dosages.**

#### Extensive acute proximal deep vein thrombosis

► Extensive acute proximal deep vein thrombosis 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.

► THERASOLV (urokinase) is a curative treatment for extensive acute proximal deep vein thrombosis.

► Given the absence of any study having assessed urokinase in the treatment of iliofemoral thrombosis, the efficacy/adverse effects ratio cannot be determined in this indication.

► There is a medicinal alternative: ACTOSOLV (urokinase).

► THERASOLV (urokinase) has no role in the treatment of extensive acute proximal deep vein thrombosis.

#### **Public health impact**

Considering:

- the seriousness of extensive acute proximal deep vein thrombosis,
- its prevalence, which is difficult to estimate,
- the partially met medical need,

- the absence of any demonstrated impact on quality of life or the organisation of care (hospitalisation, AE, etc.),
  - the lack of additional response to the identified need,
- THERASOLV (urokinase) is unlikely to have an additional impact on public health.

**Considering all these elements, the Committee deems that the clinical benefit of THERASOLV is insufficient in the marketing authorisation indication to justify its funding by the French national health insurance system.**

**The Committee issues an unfavourable opinion for inclusion in the hospital formulary list of reimbursed proprietary medicinal products approved for use in the indication for the lysis of blood clots in extensive acute proximal deep vein thrombosis and at the marketing authorisation dosages.**

### **Acute massive pulmonary embolism**

- Acute massive pulmonary embolism is a serious, life-threatening disease.
- THERASOLV (urokinase) is a curative treatment for acute massive pulmonary embolism.
- Given the absence of any study having assessed urokinase in the treatment of acute massive pulmonary embolism, the efficacy/adverse effects ratio cannot be determined in this indication.
- There are alternatives: ACTOSOLV (urokinase) and ACTILYSE (alteplase).
- THERASOLV (urokinase) has no role in the treatment of acute massive pulmonary embolism.

### **Public health impact**

Considering:

- the seriousness of acute massive pulmonary embolism,
  - its prevalence, which is difficult to estimate,
  - the currently met medical need,
  - the absence of any demonstrated impact on quality of life or the organisation of care (hospitalisation, AE, etc.),
  - the lack of additional response to the identified need,
- THERASOLV (urokinase) is unlikely to have an additional impact on public health.

**Considering all these elements, the Committee deems that the clinical benefit of THERASOLV is insufficient in the marketing authorisation indication to justify its funding by the French national health insurance system.**

**The Committee issues an unfavourable opinion for inclusion in the hospital formulary list of reimbursed proprietary medicinal products approved for use in the indication for the lysis of blood clots in acute massive pulmonary embolism and at the marketing authorisation dosages.**

### **Acute occlusive peripheral arterial disease with limb-threatening ischemia**

- Acute occlusive peripheral arterial disease with limb-threatening ischemia 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.
- THERASOLV (urokinase) is a curative treatment for acute occlusive peripheral arterial disease with limb-threatening ischemia.
- Given the clinical data available in acute ischaemia of the limbs, obtained from studies with a low level of evidence, which do not demonstrate any difference between urokinase and surgery in terms of efficacy but suggest an additional bleeding risk with urokinase, the efficacy/adverse effects ratio of urokinase is low in this indication.
- There is a medicinal alternative: ACTOSOLV (urokinase).
- THERASOLV (urokinase) is a first-line treatment in acute arterial ischemia only in the absence of neurological deficit.

### **Public health impact**

Considering:

- the seriousness of acute occlusive peripheral arterial disease with limb-threatening ischemia,
- its low prevalence,
- the partially met medical need,
- the absence of any demonstrated impact on quality of life and the organisation of care,
- the lack of additional response to the identified partially met need,

THERASOLV (urokinase) is unlikely to have an additional impact on public health.

**Considering all these elements, the Committee deems that the clinical benefit of THERASOLV is low in this marketing authorisation indication.**

**The Committee issues a favourable opinion for inclusion in the hospital formulary list of reimbursed proprietary medicinal products approved for use in the indication for the lysis of blood clots in acute occlusive peripheral disease with limb-threatening ischemia and at the marketing authorisation dosages.**

## **Clinical Added Value**

### **Thrombosed intravascular catheters and cannulae**

In the absence of a study demonstrating a clinical benefit of thrombolysis using urokinase compared to the available alternatives, and in view of the met medical need in this indication, the Committee considers that THERASOLV (urokinase) provides no clinical added value (CAV V) in the care pathway for thrombosed intravascular catheters and cannulae.

### **Acute occlusive peripheral arterial disease with limb-threatening ischemia**

In the absence of a study demonstrating a clinical benefit of thrombolysis using urokinase compared to the available alternatives, and considering the bleeding risk associated with the use of thrombolytic agents, the Committee considers that THERASOLV (urokinase) provides no clinical added value (CAV V) in the care pathway for acute occlusive peripheral arterial disease with limb-threatening ischemia.

### **Extensive acute proximal deep vein thrombosis**

Not applicable.

### **Acute massive pulmonary embolism**

Not applicable.