HAUTE AUTORITÉ DE SANTÉ

NEUROSURGERY
New indication
October 2014

BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

EVICEL, sealant based on human fibrinogen and thrombin

The Transparency Committee does not recommend reimbursement as suture support for suture line sealing in dura mater closure as the clinical benefit is insufficient

Main points

- EVICEL is the only fibrin sealant with Marketing Authorisation in neurosurgery, as suture support for suture line sealing in dura mater closure.
- EVICEL improves the intraoperative watertight closure when the gap between the margins of the suture line is less than 2 mm after the primary closure, but its contribution to the reduction in associated postoperative complications (CSF leakages and infections) has not been demonstrated.
- No comparison with a supportive treatment (such as a medical device) in situations with the highest risk of postoperative complications is available.
- Consequently, EVICEL has not been shown to be beneficial in therapeutic management in the current state of the data.

Pre-existing indications

- EVICEL is used as supportive treatment in surgery where standard surgical techniques are insufficient, for the improvement of haemostasis, as well as for suture support for haemostasis in vascular surgery.
- This summary does not cover these indications.

Therapeutic strategy

- The objective of reinforcement of sutures in the dura mater during neurosurgical procedures is to achieve the most watertight closure in order to minimize leaks of cerebrospinal fluid (CSF), which could cause complications.
- If sutures prove to be inadequate, supplementary suturing techniques (including medical devices or dural substitutes) may be necessary, particularly in situations with the highest risk of postoperative complications. Even though off-label use of fibrin sealants has been reported, adequate data to support and validate their use in neurosurgery are not available.

Role of the medicinal product in the therapeutic strategy

Within the scope of its indication in neurosurgery, which is restricted to the reinforcement of the dural suture line, the available data do not demonstrate that EVICEL is beneficial:

- the efficacy of EVICEL in the event of persistence of a CSF leak has only been demonstrated, in relation to intraoperative leaks, by comparison with additional sutures, when the objective is to ensure a watertight closure (not haemostasis) and in surgery with a low risk of postoperative complications;
- the clinical benefit of EVICEL in relation to the reduction of neurosurgical complications, particularly infections, postoperative CSF leaks and reinterventions, has not been demonstrated. On the contrary, postoperative CSF leaks were more frequent at D5 and D30 in the EVICEL group than in the additional sutures group;

and bear in mind the fact that EVICEL cannot be used in the following situations, which are the subjects of contraindications or warnings: when the dura mater cannot be sutured, when there are still gaps of greater than 2 mm after suturing the margins of the incision in the dura mater, as a glue for the fixation of dural patches, with implants of synthetic material or dural patches, or if complete haemostasis has not been obtained before the application of EVICEL.

- In addition, there is a risk of misuse instead of meticulous sutures or in surgical situations that have not been subjected to rigorous scientific assessment.

Clinical data

- The efficacy of EVICEL as an adjunct to sutures in the event of the persistence of leakage of CSF through the dural suture line has been investigated in an open study carried out in 139 patients undergoing elective neurosurgical procedures in situations where there was a low risk of postoperative complications (gap between the margins of the durotomy of less than 2 mm after primary closure, no use of a patch or implant). Its efficacy as adjunct to sutures has been demonstrated in terms of intraoperative watertight closure of the dura mater (primary endpoint) by comparison withadditional sutures: 92.1% in the EVICEL group (82/89) versus 38% in the suture group (19/50), $p < 0.001$.
  Overall, the frequency of adverse events was comparable in the two groups: 64% in the EVICEL group (including serious events in 11.2%) and 62% in the additional sutures group (including serious events in 8%). However, postoperative CSF leaks (a more relevant endpoint than intraoperative leaks) were more frequent in the EVICEL group than in the additional sutures group on D5: 1.1% (1/89) versus 0%, and on D30: 4.5% (4/89) versus 2% (1/50).

- The informative value of the conclusions of this study is limited for the following reasons:
  - the surgical situations assessed were simple, the patient selection criteria envisaged the exclusion of the more delicate situations. The results obtained in this study cannot, therefore, be extrapolated to situations with a higher risk of complications.
  - the frequency of postoperative complications, in particular of CSF leaks during the 30 days after surgery, was higher in the EVICEL group than in the additional sutures group. However, the more relevant endpoints for the assessment of the clinical benefit of EVICEL are the associated postoperative complications (in particular CSF leaks and infections).
  - the follow-up is limited in this study. No data after the 30-day period are available.

Benefit of the medicinal product

- The actual benefit* of EVICEL in the reinforcement of the suture to ensure the watertightness of the suture line after closure of the dura mater is insufficient.
- The Transparency Committee does not recommend inclusion on the list of reimbursable products for hospital use for this extension of the indication.

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This document was created on the basis of the Transparency Committee Opinion of 01 October 2014 (CT-13403) and is available at **www.has-sante.fr**

[i] * The actual benefit (AB) of a proprietary medicinal product describes its benefit primarily in terms of its clinical efficacy and the seriousness of the condition being treated. The HAS Transparency Committee assesses the AB, which can be substantial, moderate, low or insufficient for reimbursement for hospital use.

** The clinical added value (CAV) describes the improvement in treatment provided by a medicinal product compared with existing treatments. The HAS Transparency Committee assesses the degree of CAV on a scale from I (major) to IV (minor). A level V CAV means “no clinical added value”.