HAUTE AUTORITÉ DE SANTÉ

SURGERY
New medicinal product
July 2015

BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

EVARREST, sealant matrix based on human fibrinogen and thrombin

No clinical benefit demonstrated in current surgical treatment in improving haemostasis when standard surgical techniques are insufficient.

Main points

- EVARREST has Marketing Authorisation as supportive haemostatic treatment when standard surgical techniques to improve haemostasis are insufficient.
- It comprises a dry layer of human fibrinogen and thrombin and a flexible and resorbable matrix, the absorption of which is considered complete after about 8 weeks.
- EVARREST, as an adjunct to standard methods, improves the percentage success of perioperative haemostasis in the course of elective surgery. However, its contribution in reducing morbidity and mortality (in particular transfusions, repeat surgical procedures, operating time, duration of hospitalisation, deaths) has not been demonstrated.
- In the absence of studies comparing EVARREST with another fibrin sealant or thrombin-based product, its therapeutic benefit cannot be assessed in relation to the alternatives used in practice.

Therapeutic use

- The quality of haemostasis depends primarily on that of the surgical technique. Surgical haemostatic agents cannot replace meticulous surgical haemostasis based on standard methods such as compression, sutures and ligatures and various electrocoagulation techniques.
- The use of surgical haemostatic agents is not recommended if there is no identified bleeding or as an alternative to standard surgical haemostasis methods when there is identified bleeding. Their use should not be systematic. Judicious use, limited to certain rescue situations and to specific cases, is recommended. We still await specific data on the use of EVARREST as a tissue adhesive, in neurosurgery, in the treatment of bleeding when applied using a flexible endoscope, in vascular surgery or in the treatment of gastrointestinal anastomoses in children (indications not validated by the Marketing Authorisation).
- **Role of the medicinal product in the therapeutic strategy**
  In common with other surgical haemostatic agents including fibrin sealants, EVARREST is an adjuvant treatment of last resort in rescue situations as an adjunct to standard methods, to improve haemostasis when standard surgical techniques are insufficient.

Clinical data

- In the course of abdominal, pelvic, retroperitoneal or (non-cardiac) chest surgery, the perioperative efficacy of EVARREST has been demonstrated in terms of the success of perioperative haemostasis (i.e. 4 min after randomisation and in the absence of bleeding requiring further treatment for an additional 6 minutes or in the absence of any new bleeding at the treated site up to the time of closure):
  - in comparison with SURGICEL (oxidised regenerated cellulose) for mild to moderate tissue bleeding;
  - in comparison with treatment left to the choice of the surgeon (excluding products based on fibrin or thrombin) for severe soft-tissue bleeding.

  In the course of elective liver surgery, the perioperative efficacy of EVARREST has been demonstrated in bleeding that did not respond to manual compression for 30 seconds, in terms of the success of perioperative haemostasis compared with the choice of the surgeon. The adverse effects reported most frequently in the clinical studies were haemorrhages and an increase in the fibrinogen level; the most serious adverse effects were inhalation, pulmonary embolism and haemorrhage. The data from the clinical studies come from the use of a

single EVARREST patch. Subsequent exposure to a fibrin sealant (in terms of immunogenicity) was not evaluated.

The relevance of the results presented and their transposability to current surgical practice are debatable, particularly in view of:

- the choice of treatment in the control group,
- the fairly uncomplicated surgical situations mostly studied,
- the fact that no conventional method of haemostasis was practised before randomisation in about 50% of cases,
- the fact that the studies were open and carried out with small patient numbers,
- a primary endpoint that is interim rather than clinical in nature,
- the fact that the benefit of EVARREST has not been demonstrated on clinically relevant parameters,
- the short follow-up period (≤ 2 months).

Special prescribing conditions

- Reserved for hospital use.
- Medicinal product derived from human blood

Benefit of the medicinal product

- The actual benefit* of EVARREST as supportive treatment to improve haemostasis when standard surgical techniques are insufficient is substantial.
- In the absence of a comparative study versus a product based on fibrin or thrombin, EVARREST does not provide clinical added value** (CAV V) in current surgical treatment in improving haemostasis when standard surgical techniques are insufficient.
- Recommends inclusion on the list of reimbursable products for hospital use as an adjuvant treatment to improve haemostasis when standard surgical techniques are insufficient.

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This document was created on the basis of the Transparency Committee Opinion of 01 July 2015 (CT-14248) and is available at **www.has-sante.fr**

* 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.