EVICEL® Core Educational Material

February 2019

Background

Air/gas embolism, while very rare, has occurred with sprayed application of EVICEL®. **Some of the reported cases have been fatal.**

Closer than recommended spray distances and/or higher than recommended pressures have been a common root cause.

When used in accordance with recommended spray distance and pressure for EVICEL®, air/gas embolisms have not been reported.

Pressure regulators that allow for a pressure greater than the approved 1.4-1.7 bars must not be used with EVICEL®.

Actions

From 2013 onwards, Ethicon Biosurgery completed field actions which include the following:

1. A Direct to Health Care Professional letter (DHCP) was sent out with new measures to minimize the risk of air/gas embolism during spray application.
2. Biosurgery representatives performed hospital in-service to ensure up-to-date SmPC were available that reinforced the correct application of EVICEL®.
3. CO2 compatible pressure regulators were developed to replace air regulators (CO2 is far better tolerated than air if introduced into the vasculature).
4. Labels for the pressure regulator were developed to inform of correct pressures and distances in open and laparoscopic procedures
5. A warning card was provided to inform of the correct pressures and distances for the spray application for open and laparoscopic procedures.
6. A tag was placed on the device air hose, which provides instructions for use.
7. The pressure regulators were capped to prevent excessive pressure application

Materials

Healthcare professionals are provided with the following materials available to educate on the correct, safe usage of EVICEL ®

MATERIAL	
Up-to-date SmPC	X
Information for Medical or HC professional only	X
Preparation poster	X

BE AWARE:
Contraindication

Spray application of EVICEL® should not be used in endoscopic procedures.

BE AWARE:

Special Warning and Precautions for Use

Life threatening air or gas embolism has occurred with the use of spray devices employing pressure regulators to administer EVICEL®.

EVICEL® spray application should only be used if it is possible to accurately judge the spray distance, especially during laparoscopy. Spray distance from tissue and pressure should be within the ranges recommended by the manufacturer.

BE AWARE:

Posology and Method of Administration

The use of EVICEL® is restricted to experienced surgeons who have been trained in the use of EVICEL®.

To avoid the risk of potentially life threatening air embolism EVICEL® should be sprayed using pressurised CO2 gas only.

Prior to applying EVICEL® the surface area of the wound should be dried using standard techniques (e.g. intermittent application of compresses, swabs, use of suction devices).

The product should only be reconstituted and administered according to the instructions and with the devices recommended for this product.

Recommended Spray Application of EVICEL®

EVICEL® should be sprayed using pressurized CO2 gas only.

Spray application of EVICEL® should not be used in endoscopic procedures.

Prior to applying EVICEL® the surface area of the wound should to be dried using standard techniques (e.g. intermittent application of compresses, swabs, use of suction devices).

Blood pressure, pulse rate, oxygen saturation and end tidal CO2 should be monitored closely when spraying EVICEL®, due to the possibility of the occurrence of gas embolism.

Recommended Spray Application of EVICEL®

When applying EVICEL® using a spray device, be sure to use a pressure and a distance from the tissue within the ranges recommended by the manufacturer:

Surgery	Spray set to be used	Applicator tips to be used	Pressure regulator to be used	Distance from target tissue	Spray pressure
Open Surgery	**Evicel®** Applicator Device	6 cm flexible tip	**Omrix Pressure Regulator**	10-15 cm (4-6 in)	20-25 psi (1.4-1.7 bar)
		35 cm rigid tip			
		45cm flexible tip			
Laparoscopic procedures		35 cm rigid tip		4-10 cm (1.6- 4in)	15-20 psi (1.0-1.4 bar)
		45cm flexible tip			20psi (1.4 bar)

Summary of product characteristics section 6.6

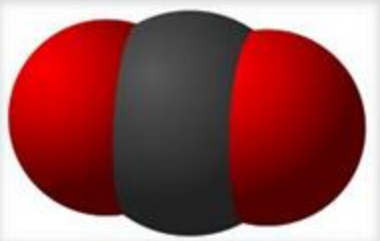
Recommended Spray Application of EVICEL®

When applying by spray application, EVICEL® must be:

- Sprayed **10 - 15 cm** from the tissue surface in an open procedure
- Sprayed greater than **4 -10 cm** from the tissue surface in a laparoscopic procedure
- Sprayed using **only CO_2**
- Sprayed using a pressure that does not exceed **1.0 - 1.4 bar (35cm rigid tip laparoscopic), 1.4 bar (45cm flexible tip laparoscopic) or 1.4- 1.7 bar (tips used in open surgery)**

Verify spray pressure

CO_2



Pressure Regulator Connector Options for CO_2

1. **Available/new solutions to spray with CO_2 :**
   Please ask the Biosurgery representative.

Abbreviated Prescribing Information

EVICEL® Solutions for Sealant
Abbreviated Prescribing Information:

Please read Summary of Product Characteristics (SmPC) for full product information before prescribing.

COMPOSITION: Component 1: Human clottable protein (mainly fibrinogen and fibronectin): 50-90 mg/ml. Component 2: Human thrombin: 800-1200 IU/ml.

INDICATIONS: Indicated in adults as supportive treatment in surgery where standard surgical techniques are insufficient, for improvement of haemostasis. Suture support for haemostasis in vascular surgery and for suture line sealing in dura mater closure.

POSOLOGY & ADMINISTRATION: For epilesional use. Use restricted to experienced trained surgeons. Use by dripping or spraying. To avoid the risk of potentially life-threatening air or gas embolism spray using pressurised CO_2 only. See the table below for spray pressure and distance from tissue recommendations. Dose applied governed by several variables and must be individualised. In controlled clinical trials in vascular surgery, individual dosage was up to 4 ml whereas in retroperitoneal or intra-abdominal surgery individual dosage used was up to 10 ml. For suture line sealing in dura mater closure, doses of up to 8 ml were used. For some procedures (eg liver traumata) larger volumes may be required. Initial volume applied should be sufficient to cover intended application area. Application can be repeated, if necessary.

CONTRAINDICATIONS: Must not be applied intravascularly. Hypersensitivity to active substances or any excipient. Spray application should not be used in endoscopic procedures. For laparoscopy, spray only if the spray distance can be judged accurately. Not for use for sealing the suture line in dura mater if there are gaps of greater than 2 mm after suturing. Not for use as a glue for fixation of dural patches. Not for use as a sealant when the dura mater cannot be sutured.

SPECIAL WARNINGS & PRECAUTIONS: Life-threatening thromboembolic complications if applied intravascularly. Life-threatening air or gas embolism has occurred with spray devices employing a pressure regulator. This may be related to use of spray devices at higher than recommended pressures and/or in close proximity to tissue. Apply Evicel only with CE-marked Evicel application devices and accessory tips and OMRIX pressure regulator. Spray only if able to accurately judge spray distance.

Surgery	Tip	Distance	Pressure
Open	6cm flexible	10 – 15 cm (4 - 6 in)	1.4 – 1.7 bar (20 - 25 psi)
Open	35 cm rigid	10 – 15 cm (4 - 6 in)	1.4 – 1.7 bar (20 - 25 psi)
Open	45 cm flexible	10 – 15 cm (4 - 6 in)	1.4 – 1.7 bar (20 - 25 psi)
Laparoscopic	35 cm rigid	4 – 10 cm (1.6 - 4 in)	1.0 – 1.4 bar (15 - 20 psi)
Laparoscopic	45 cm flexible	4 – 10 cm (1.6 - 4 in)	1.4 bar (20 psi)

When spraying EVICEL, changes in blood pressure, pulse, oxygen saturation, and end tidal CO_2 should be monitored because of the possibility of occurrence of a gas embolism. Apply as thin layer; excessive clot thickness may impede efficacy and wound healing. Inadequate data to support use in tissue gluing, application through a flexible endoscope for treatment of bleeding or in gastrointestinal anastomoses.

Concomitant use for dural suture line sealing with implants from synthetic materials or dural patches not evaluated in clinical studies. Use in patients undergoing radiotherapy within 7 days after surgery not evaluated. Not known if radiation therapy could affect the efficacy of fibrin sealant when used for suture line sealing in dura mater closure. Complete haemostasis required before sealing the dural suture line. Use as a sealant in transphenoidal and otoneurosurgical procedures not studied.

Before administration, adjacent areas should be protected. Allergic type hypersensitivity reactions possible. If these occur, discontinue immediately. In case of shock, standard medical treatment for shock should be implemented. The possibility of transmitting infectious agents including unknown or emerging viruses and other pathogens cannot be excluded. It is strongly recommended that name and batch number of the product are recorded to maintain a link between patient and product batch.

There is not enough information available to know whether any particular risks are associated with the use of EVICEL during pregnancy or whilst breast-feeding. T he product should be administered to pregnant and breast-feeding women only if clearly needed.

UNDESIRABLE EFFECTS:

Hypersensitivity or allergic reactions (which may include angioedema, burning and stinging at the application site, bronchospasm, chills, flushing, generalised urticaria, headache, hives, hypotension, lethargy, nausea, restlessness, tachycardia, tightness of the chest, tingling, vomiting, wheezing) may occur in rare cases in patients treated with fibrin sealants/haemostatics. In isolated cases, these reactions have progressed to severe anaphylaxis. Such reactions may especially be seen if the preparation is applied repeatedly, or administered to patients known to be hypersensitive to constituents of the product. . Antibodies against product components may occur. Inadvertent intravascular injection could lead to thromboembolic event, disseminated intravascular coagulation and a risk of anaphylactic reaction.
In abdominal clinical trials, abdominal abscess was reported commonly. In vascular clinical trials the following events were reported uncommonly: graft infection, staphylococcal infection, haematoma, decreased haemoglobin, peripheral oedema, incision site haemorrhage, vascular graft occlusion, wound, post procedural haematoma, post-operative wound complication. In a neurological study the following events were reported commonly: meningitis, intracranial hypotension, CSF rhinorrhoea, headache, hydrocephalus, subdural hygroma, haematoma.

LEGAL CAREGORY: POM
COST: 2ml – EVB02DE €250 and 5ml – EVB05DE €487.36
MA HOLDER: Omrix Biopharmaceuticals NV, Leonardo Da Vinci Laan 15, B-1831 Diegem, Belgium.
MA NUMBER(S): EU/1/08/473/001, EU/1/08/473/002, EU/1/08/473/003.
DATE OF PREPARATION: August 2019

PHARMACOVIGILANCE: Adverse events should be reported. Reporting forms and information can be found at the HPRA online reporting system https://www.hpra.ie/homepage/about-us/report-an-issue **Adverse events should also be reported to Omrix Biopharmaceuticals Ltd by one of the following methods: Fax number: +972-3-5350265 Email address: RA-OMRILPV@its.jnj.com Tel: +972 3 5316 531**

Additional Resources

•Please contact your ETHICON sales representative for the latest SmPC and educational information for EVICEL in the EU.

•Please contact your ETHICON sales representative with any questions or for additional educational requests.

•Please read Summary of Product Characteristics (SmPC) for full product information before using Evicel.