The Medicines Company

INSTRUCTIONS FOR USE (US)

RaplixaSpray™, Raplixa™ Delivery Device

For the application of Raplixa powder to stop bleeding. Raplixa is a hemostatic fibrin sealant product. It is a powder formulation in a vial and supplied separately.

1. FIELD OF APPLICATION

The RaplixaSpray device has been designed for the application of Raplixa powder. The spray device can deliver Raplixa powder to bleeding sites as an adjunct to hemostasis in adults undergoing open surgery when control of bleeding by standard surgical techniques (such as suture, ligature, and cautery) is ineffective or impractical.

1.1. Intended Use

RaplixaSpray device is intended for the topical application of the hemostatic agent Raplixa via spraying with propellant gas to control delivery of powder onto the wound surface. The accessory, the flexible nozzle, is intended to enable the RaplixaSpray device to be used in difficult to reach areas.

2. DESCRIPTION

Raplixa Delivery Kit (figure 1), consisting of:

- 1 RaplixaSpray Delivery Device applicator with attached removable fixed (rigid) nozzle tip (*Note: device comes with the fixed (rigid) nozzle attached)*
- 1 in-line gas filter (insufflation filter)
- 1 flexible nozzle

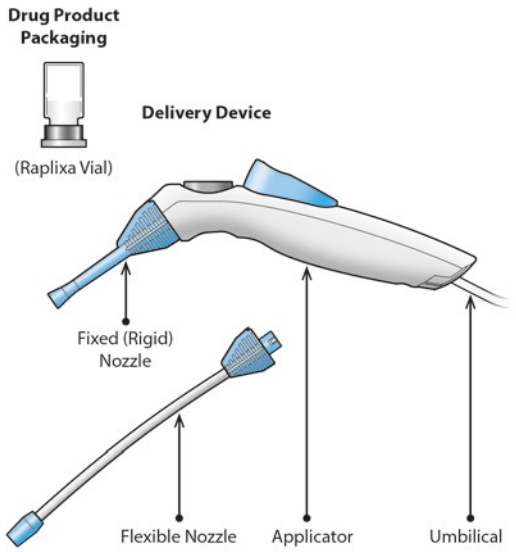

Figure 1

2.1. Principle

The RaplixaSpray device operates via pressurized gas from a central gas supply or a medical grade gas tank located in the operating room (OR). A ProFibrix gas pressure regulator must be used in order to supply gas at a reduced pressure to the RaplixaSpray device. The Raplixa vial is opened and attached to the spray device. When the operating button on the device is pushed down, the valve opens within the device allowing gas flow from the supply line (via the regulator) into the device. The gas flow has two functions: it creates vibration that mobilizes the Raplixa powder, and transports the Raplixa out of the spray device onto the bleeding site via the nozzle. The majority of the gas flow is released from the rear of the device and ≤ 4% of the incoming gas flow is used to deliver the Raplixa to the bleeding site.

The RaplixaSpray device must only be used with Raplixa powder.

The RaplixaSpray should not be used with liquid (or other) hemostatic agents

The RaplixaSpray device is packed in two pouches; the outer packaging is a Tyvek® pouch. The inner pouch is a foil pouch which maintains sterility of the RaplixaSpray device. The RaplixaSpray device is gamma irradiated.

For single use only. DO NOT RE-STERILIZE.

2.2. Frequency of Administration

Use a RaplixaSpray device only during the course of one surgery. Keep the device in the sterile field when not in use. If the device is removed from the sterile area, DO NOT use the device again.

The dose of Raplixa can vary based on the size of the area to be treated. In clinical trials, smaller bleeding sites (< 10 cm^2) used 0.5 g to 1.0 g on average. Larger bleeding sites used 1.0 to 2.0 grams (10 - 100 cm^2). It is known from in vitro testing that 1.0 g can cover 100 cm^2 using the RaplixaSpray device.

The dose of Raplixa based on the size of the bleeding surface area to be treated is shown in the table below:

Table 1: Dose of Raplixa

Maximum Surface Area Application Using RaplixaSpray	**Raplixa Package Size**
50 cm^2	0.5 g
100 cm^2	1.0 g
200 cm^2	2.0 g

Raplixa may be used at multiple bleeding sites in the same patient.

Total number of vials used with one RaplixaSpray device spray may not be more than two vials. The maximum total Raplixa dose allowed per patient is 3 grams.

2.3. Storage Instructions

Store at room temperature. Once device has been used DO NOT STORE or RE-USE.

3. OPERATING INSTRUCTIONS

3.1. Set-up Gas Pressure Regulator

Prior to the procedure, prepare the ProFibrix gas regulator by connecting the regulator hose to the OR gas supply or medical grade gas tank (see also IFU ProFibrix regulator). The pictures below provide instructions to connect the device to the pressure regulator (see also Quick Reference Guide).

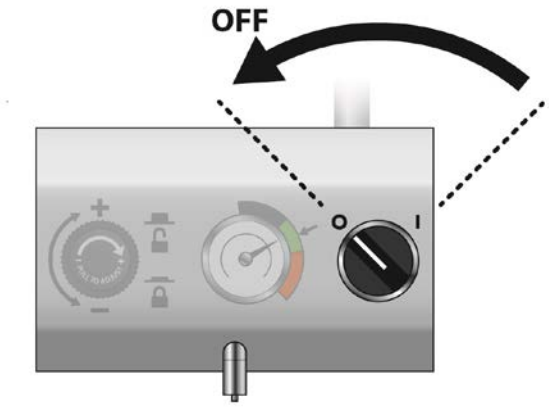

Figure 2a

Check regulator is set
OFF'O'

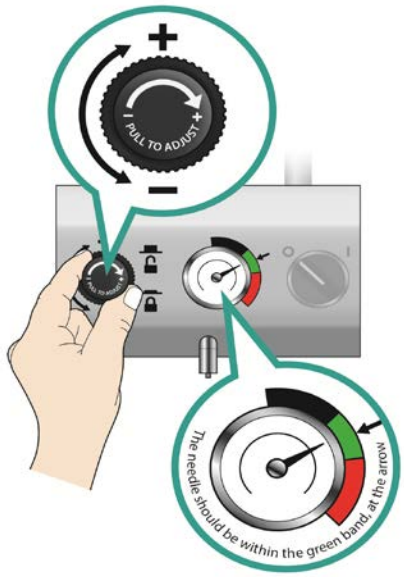

Figure 2b

Pull out the control knob and adjust the pressure to 22 psi (1.5bar)
Push control knob back in

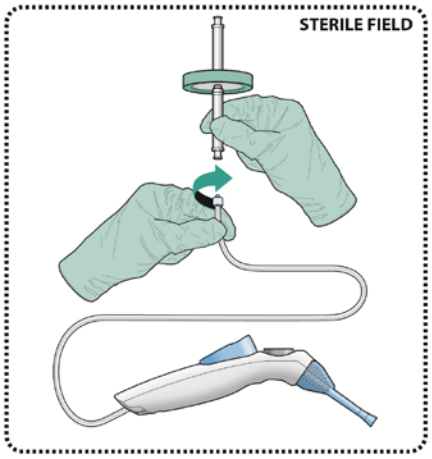

Figure 2c

Connect one end of the filter to the device line in the sterile field

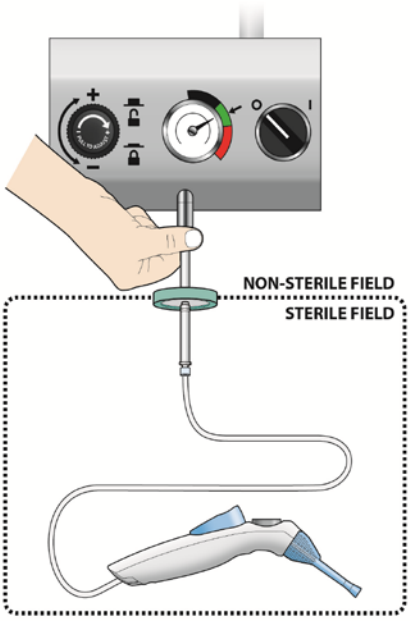

Figure 2d

Connect the other end of the filter to the regulator

3.2. Test the Device

Check the device function prior to attaching a Raplixa vial. Turn on the gas flow by switching the right knob on the regulator to “I” (on). Press the operating button on the RaplixaSpray device. A continuous uniform vibration should be apparent as a buzzing sound. The delivery rate can be controlled with this button. Turn off the gas flow by switching the right knob on the regulator to “O” (off) until the device is ready to be used and set the device within the sterile field until needed.

3.3. Select Nozzle

If the bleeding site is difficult to reach, the fixed (rigid) nozzle that comes attached with the device can be replaced by the flexible nozzle.

The nozzle can be changed at any time during a procedure. First, set the regulator off or “O”.

Twist to remove the fixed (rigid) nozzle. Attach flexible nozzle by twisting until it clicks into place.

Bend the flexible nozzle to desired position. Do not bend the flexible nozzle more than 90 degrees.

3.4. Attach Vial and Switch Regulator On

Remove the Raplixa vial from the aluminum pouch.

Raplixa is hygroscopic (readily takes up and retains moisture), so only remove the crimp and rubber stopper from the vial prior to application.

Remove the rubber stopper from the Raplixa vial, hold the vial upright.

Invert the device. Holding the device upside down, snap the powder vial into the rubber cup.

The device is then turned upright in order to deliver Raplixa and is handed to the surgeon.

After handing over and just before application of Raplixa by the surgeon, activate the gas flow by turning the right knob on the regulator from “O” (off) to “I” (on).
Be careful not to push the RaplixaSpray device operating button when handing the device to the surgeon.

3.5. Powder Delivery

Check that the pressure is 1.5 bar (22 psi) and the needle of the pressure indicator gauge on the ProFibrix regulator is within the green band as indicated on the regulator with an arrow (see figure 2b).

Hold the device upright. Ensure the vial is kept within 45^0 of vertical at all times.

Hold the nozzle at a minimum distance of 5 cm (2 inches) from the bleeding site. Start application by gently pressing the operating button and cover the bleeding site with a thin layer. Powder should cover the bleeding surface as a uniform thin coating. Apply Raplixa rapidly, preferably within 10-60 seconds.

Note: *Be careful not to touch the tip of the device on anything wet to avoid clogging the nozzle. In the unlikely event that blockage occurs, discard the device and prepare a new one.*

Immediately after Raplixa application is completed, place a gelatin sponge, trimmed to the approximate size, on top of the Raplixa. The gelatin sponge may be used dry or moistened with sterile saline. A moistened sponge molds more easily to irregularly-shaped and contoured bleeding areas. Hold the gelatin sponge in place with manual pressure using sterile gauze.

3.6. Using a 2nd Vial of Raplixa

Switch the regulator to the off or “O” position. Hold device upside down, carefully remove the empty vial, snap the second powder vial into the rubber cup, and follow Section 3.4. Operate the device as described in Section 3.5.

4 CONTRAINDICATIONS

Do not administer Raplixa intravascularly.
Do not use for the treatment of severe or brisk arterial bleeding.

5. WARNINGS

Only use the RaplixaSpray device with the Raplixa powder.
Only use the RaplixaSpray device with a ProFibrix gas regulator.
Only use ProFibrix accessories. The use of accessories of other manufacturers is not permitted.

A RaplixaSpray device can be used with at most two vials. To administer a third vial, a new device must be opened. The maximum total dose per patient is 3 grams.

The RaplixaSpray device and accessory must be used within 1 hour of opening the device package.
Raplixa powder must be used within 1 hour of opening the vial.

Air or gas embolism can occur using air- or gas-pressurized sprayers to administer

fibrin sealants. Operate the device according to the manufacturer's instructions.
Be sure to take appropriate measures to exclude these risks, by control of maximum pressure of 1.5 bar (22 psi) and at a minimum distance of 5 cm (2 inches). Do not touch the tip against the bleeding site. Do not bend the flexible nozzle more than 90 degrees.
Ensure the vial is kept within 45^0 of vertical at all times.
Do not cut the nozzle to length.
Be careful not to push the RaplixaSpray device operating button when handing the device to the surgeon.

Do not re-use the device. The Raplixa powder contains human blood-derived materials and might remain in the device after use. To prevent contamination the device or its accessory must not be reused.

Caution: There is the potential for powder loss from the nozzle tip during or after usage. Minor leakage/drop of powder from the nozzle tip can occure when transferring the device back to the table After the blue button is released and application of Raplixa podwer is stopped some minor powder is still present in the nozzle . A single occurrence of powder leakage during transfer of device after use during Phase 3 clinical trial was noticed. The hazard is trivial and the user may not even be aware of it.

6 ACCESSORIES

ProFibrix Gas Regulator (PF-FC-001 (medical air), PF-FC-009 (CO2))

Manufacturer:

ProFibrix BV (The Medicines Company)

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2333 CR, Leiden

The Netherlands

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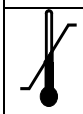
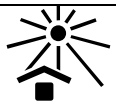
Explanation of symbols used in the labelling

CE	Conform European standards
	Single use only
	Use by
	Read the instructions for use
LOT	Batch number
REF	Article number
STERILE R	Sterilisation by gamma irradiation
	Temperature limit
Rx	Prescription Use only
	Manufacturer
Specific Symbols used for the filter	
STERILE EO	Sterilised using ethylene oxide
	Keep dry
	Keep away from sunlight