

Annex III

**Amendments to relevant sections of the summary of product characteristics
and package leaflet**

**Note: These amendments to the summary of product characteristics and
package leaflet are valid at the time of the Commission Decision.
After the Commission Decision the National Competent Authorities will
update the product information as required.**

SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

The following changes should be made to the SmPC of Quixil:

4.2 Posology and method of administration

The following text should be added to this section:

“The use of Quixil is restricted to experienced surgeons who have been trained in the use of QUIXIL.”

4.2.2 Method and Route of Administration

The text of this section should be read as follows:

“For epilesional use.

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

In open wound surgery – for spray application of Quixil, a pressure regulator device that delivers a maximum pressure of no more than 2.5 bar and uses carbon dioxide gas only should be used.

Prior to applying Quixil the surface area of the wound needs to be dried by 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 (see section 6.6).

For spray application see sections 4.4 and 6.6 for specific recommendations on the required pressure and distance from tissue.”

4.3 Contra-indications

The following contra-indication should be added at the end of the section:

[...]

- *“Spray application of Quixil should not be used in endoscopic procedures.”*

4.4 Special warnings and precautions for use

The following text:

- **“Air or gas embolism has occurred with the use of spray devices employing pressure regulator to administer Quixil. This event appears to be related to the use of the spray device at higher than recommended pressures and/or in close proximity to the tissue surface.**

When applying Quixil using a spray device, the pressure should be within the range recommended by the spray device manufacturer. In the absence of a specific recommendation the pressure should not exceed 2.0-2.5 bars. Quixil should not be sprayed at a distance closer than the recommended by the spray device manufacturer. In the absence of a specific recommendation Quixil should not be sprayed closer than 10-15 cm from the tissue surface. When spraying Quixil, changes in blood pressure, pulse, oxygen saturation and end tidal CO₂ should be monitored because of the possibility of occurrence of air or gas embolism.

When using accessory tips with this product, the instructions for use of the tips should be followed.”

Should be replaced with the following text, in bold and underlined format:

- **“Life threatening air or gas embolism has occurred with the use of spray devices employing pressure regulator to administer Quixil. This event appears to be related to the use of the spray device at higher than recommended pressures and/or in close proximity to the tissue surface.**

Quixil spray application should only be used if it is possible to accurately judge the spray distance as recommended by the manufacturer – do not spray closer than the recommended distance.

When applying Quixil using a spray device, be sure to use a pressure within the pressure range recommended by the spray device manufacturer (see table in Section 6.6 for pressures and distance).

When spraying Quixil, changes in blood pressure, pulse, oxygen saturation and end tidal CO₂ should be monitored because of the possibility of occurrence of air or gas embolism (also see section 4.2). “

4.8 Undesirable effects

The following text should be added at the end of the section, before the last sentence, as shown below:

[...]

“Life threatening air or gas embolism has occurred with the use of spray devices employing pressure regulator to administer Quixil. This event appears to be related to the use of the spray device at higher than recommended pressures and/or in close proximity to the tissue surface.”

For safety with respect to transmissible agents, see 4.4.

6.4 Special precautions for storage

The text should read as follows:

“Store at ≤ -18°C. Keep the vials in the outer carton in order to protect from light. Do not refreeze.

After thawing, unopened vials can be stored at 2 - 8°C and protected from light, for up to 30 days. When BAC and Thrombin have been drawn up into the administration device they must be used immediately.”

6.6 Special precautions for disposal and other handling

- **Handling**

[...]

Spray Application

The entire section should read as follows, in bold and underlined format where indicated:

“To avoid the risk of life threatening gas or air embolism, Quixil should only be sprayed using pressurised CO₂

When applying Quixil using a spray device, be sure to use a pressure and a distance from tissue within the ranges recommended by the manufacturer (see section 4.4)

Connect the short tube on the application device to the male luer-lock end of the long gas tube. Connect the female luer lock of the gas tube (with the bacteriostatic filter) to a pressure regulator The pressure regulator should be used in accordance with the manufacturer’s instructions.

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

| <i>Surgery</i> | <i>Spray set to be used</i> | <i>Applicator tips to be used</i> | <i>Pressure regulator to be used</i> | <i>Recommended distance from target tissue</i> | <i>Recommended spray pressure</i> |
|---------------------|---------------------------------|-----------------------------------|--------------------------------------|--|-----------------------------------|
| <i>Open surgery</i> | <i>Quixil Applicator Device</i> | <i>6 cm Yellow Flexible Tip</i> | <i>Omrrix Pressure Regulator</i> | <i>10-15 cm</i> | <i>2.0 – 2.5 bar</i> |

The product should then be sprayed onto the surface of the tissue in short bursts (0.1-0.2 ml) to form a thin, even layer. Quixil forms a clear film over the area of application.

When spraying Quixil, changes in blood pressure, pulse, oxygen saturation and end tidal CO₂ should be monitored because of the possibility of occurrence of air or gas embolism (See sections 4.2 and 4.4).

The solution should be clear or slightly opalescent. Do not use solutions that are cloudy or have deposits."

PACKAGE LEAFLET

The following changes should be made to the package leaflet of Quixil:

2. BEFORE YOU ARE TREATED WITH QUIXIL

You must not be treated with Quixil:

The following text should be added at the end of the section:

[...]

- „*Quixil should not be used in endoscopic surgery or for keyhole surgery.*“

When special care should be taken with Quixil:

The following text:

- **“Air or gas embolism has occurred with the use of spray devices employing pressure regulator to administer Quixil. This event appears to be related to the use of the spray device at higher than recommended pressures and/or in close proximity to the tissue surface. When applying Quixil using a spray device, be sure to use the pressure within the pressure range recommended by the spray device manufacturer. In the absence of a specific recommendation avoid using pressure above 2.0-2.5 bars. Do not spray at a distance closer than the recommended by the spray device manufacturer. In the absence of a specific recommendation avoid spraying closer than 10-15 cm from the tissue surface. When spraying Quixil, changes in blood pressure, pulse, oxygen saturation and end tidal CO₂ should be monitored because of the possibility of occurrence of air or gas embolism.**

When using accessory tips with this product, be sure to follow carefully the instructions for use.”

Should be replaced with the following text, in bold and underlined format where indicated

- **“Life threatening air or gas embolism (air getting into the blood circulation which can be serious or life-threatening) has occurred with the use of spray devices employing pressure regulator to administer Quixil. This event appears to be related to the use of the spray device at higher than recommended pressures and/or in close proximity to the tissue surface.**

Spray devices and the accessory tip provide instructions for use with recommendations for pressure ranges and to the spraying distance from the tissue surface. To avoid the

risk of potentially life threatening air embolism your surgeon is recommended to spray Quixil using pressurised CO2 only.

When spraying Quixil, changes in blood pressure, pulse, oxygen saturation and end tidal CO₂ will be monitored because of the possibility of occurrence of air or gas embolism.

When using an accessory tip with this product, be sure to follow carefully the instructions for use."

3. HOW QUIXIL IS USED

The following text:

"Quixil should only be used by experienced surgeons.

When applying Quixil using a spray device, be sure to use only the pressure within the range recommended by the spray device manufacturer. In the absence of a specific recommendation avoid using pressure above 2.0-2.5 bars. Do not spray at a distance closer than the recommended by the spray device manufacturer. In the absence of a specific recommendation avoid spraying closer than 10-15 cm from the tissue surface. When spraying Quixil, changes in blood pressure, pulse, oxygen saturation and end tidal CO₂ should be monitored because of the possibility of occurrence of air or gas embolism."

Should be replaced with the following text, in bold and underlined format where indicated

"The use of Quixil is restricted to experienced surgeons who have been trained in the use of QUIXIL.

Prior to applying Quixil the surface area of the wound needs to be dried by standard techniques (e.g. intermittent application of compresses, swabs, use of suction devices).

When applying Quixil using a spray device, be sure to use a pressure and a distance from tissue within the range recommended by the manufacturer as follows:

| <i>Surgery</i> | <i>Spray set to be used</i> | <i>Applicator tips to be used</i> | <i>Pressure regulatory to be used</i> | <i>Recommended distance from target tissue</i> | <i>Recommended spray pressure</i> |
|-----------------------|------------------------------------|--|--|---|--|
| <i>Open surgery</i> | <i>Quixil Applicator Device</i> | <i>6 cm Yellow Flexible Tip</i> | <i>Omrrix Pressure Regulator</i> | <i>10-15 cm</i> | <i>2.0 – 2.5 bar</i> |

When spraying Quixil, changes in blood pressure, pulse, oxygen saturation and end tidal CO₂ should be monitored because of the possibility of occurrence of air or gas embolism."