

ANNEX I
SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

TachoSil sealant matrix

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

TachoSil contains per cm²:

Human Fibrinogen	5.5 mg
Human Thrombin	2.0 IU

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Sealant matrix

TachoSil is an off-white sealant matrix. The active side of the matrix, which is coated with fibrinogen and thrombin, is marked by a yellow colour.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

TachoSil is indicated in adults for supportive treatment in surgery for improvement of haemostasis, to promote tissue sealing, for suture support in vascular surgery where standard techniques are insufficient, and for supportive sealing of the dura mater to prevent postoperative cerebrospinal leakage following neurological surgery (see section 5.1).

4.2 Posology and method of administration

Posology

The use of TachoSil is restricted to experienced surgeons.

The quantity of TachoSil to be applied should always be oriented towards the underlying clinical need for the patient. The quantity of TachoSil to be applied is governed by the size of the wound area.

Application of TachoSil must be individualised by the treating surgeon. In clinical trials, the individual dosages have typically ranged from 1-3 units (9.5 cm x 4.8 cm); application of up to 10 units has been reported. For smaller wounds, e.g. in minimally invasive surgery the smaller size matrices (4.8 cm x 4.8 cm or 3.0 cm x 2.5 cm) or the pre-rolled matrix (based on a matrix of 4.8 cm x 4.8 cm) is recommended.

Method and route of administration

For epilesional use only. Do not use intravascularly.

See section 6.6 for more detailed instructions.

Paediatric patients

TachoSil is not recommended for use in children below age 18 years due to insufficient data on safety and efficacy.

4.3 Contraindications

TachoSil must not be applied intravascularly.

Hypersensitivity to the active substances or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

For epilesional use only.

Do not use intravascularly. Life threatening thromboembolic complications may occur if the preparation is applied intravascularly.

Specific data have not been obtained on the use of this product in gastrointestinal anastomoses surgery.

It is not known whether recent radiation therapy affects the efficacy of Tachosil when used for dura mater sealing.

As with any protein-containing product, allergic type hypersensitivity reactions are possible. Signs of hypersensitivity reactions include hives, generalised urticaria, tightness of the chest, wheezing, hypotension and anaphylaxis. If these symptoms occur, the administration has to be discontinued immediately.

To prevent the development of tissue adhesions at undesired sites, ensure tissue areas outside the desired application area are adequately cleansed before administration of TachoSil (see section 6.6). Events of adhesions to gastrointestinal tissues leading to gastrointestinal obstruction have been reported with use in abdominal surgery carried out in proximity to the bowel.

In case of shock, the current medical standards for shock treatment should be observed.

Standard measures to prevent infections resulting from the use of medicinal products prepared from human blood or plasma include selection of donors, screening of individual donations and plasma pools for specific markers of infection and the inclusion of effective manufacturing steps for the inactivation/removal of viruses. Despite this, when medicinal products prepared from human blood or plasma are administered, the possibility of transmitting infective agents cannot be totally excluded. This also applies to unknown or emerging viruses and other pathogens.

The measures taken are considered effective for enveloped viruses such as HIV, HBV and HCV and for the non-enveloped virus HAV. The measures taken may be of limited value against non-enveloped viruses such as parvovirus B19. Parvovirus B19 infection may be serious for pregnant women (foetal infection) and for individuals with immunodeficiency or increased erythropoiesis (e.g. haemolytic anaemia).

It is strongly recommended that every time TachoSil is administered to a patient, the name and batch number of the product are recorded in order to maintain a link between the patient and the batch of the product.

4.5 Interactions with other medicinal products and other forms of interactions

No formal interaction studies have been performed.

Similar to comparable products or thrombin solutions, the sealant may be denatured after exposure to solutions containing alcohol, iodine or heavy metals (e.g. antiseptic solutions). Such substances should be removed to the greatest possible extent before applying the sealant.

4.6 Pregnancy and lactation

The safety of TachoSil for use in human pregnancy or breastfeeding has not been established in controlled clinical trials. Experimental animal studies are insufficient to assess the safety with respect to reproduction, development of the embryo or foetus, the course of gestation and peri- and postnatal development.

Therefore, TachoSil should be administered to pregnant and breastfeeding women only if clearly needed.

4.7 Effects on ability to drive and use machines

Not relevant.

4.8 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 may progress 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.

Immunogenicity:

Antibodies against components of fibrin sealant/haemostatic products may occur rarely. However, in a clinical trial with TachoSil in hepatic surgery, in which patients were investigated for the development of antibodies, 26% of the 96 patients tested and treated with TachoSil developed antibodies to equine collagen. The equine collagen antibodies that developed in some patients after TachoSil use were not reactive with human collagen. One patient developed antibodies to human fibrinogen.

There were no adverse events attributable to the development of human fibrinogen or equine collagen antibodies.

There is very limited clinical data available regarding re-exposure to TachoSil. Two subjects have been re-exposed in a clinical trial and have not reported any immune-mediated adverse events; however, their antibody status to collagen or fibrinogen is unknown.

Thromboembolic complications may occur if the preparation is applied intravascularly (see section 4.4).

For viral safety see section 4.4

Summary of the safety profile

The safety data of TachoSil generally reflect the type of post-operative complications related to the surgical settings in which the trials were conducted and the underlying disease of the patients.

Data from the eight controlled clinical trials conducted by the MAH has been pooled into an integrated dataset. In the integrated analyses, 997 patients were treated with TachoSil and 984 patients were treated with comparator treatment. Due to practical reasons (comparison to standard surgical and standard haemostatic treatment), blinding was not possible in the TachoSil trials. Therefore the studies were performed as open-label studies.

Tabulated summary of adverse reactions

The following adverse reactions have been reported with TachoSil during post marketing experience. The frequency of all of the events listed below has been categorised as not known (cannot be estimated from the available data).

System organ class	Frequency not known
Immune system disorders	Anaphylactic shock, Hypersensitivity
Vascular disorders	Thrombosis
Gastrointestinal disorders	Intestinal obstruction (in abdominal surgeries)
General disorders and administration site conditions	Adhesions

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via **the national reporting system listed in Appendix V**.

4.9 Overdose

No case of overdose has been reported.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmaco-therapeutic group: Local haemostatics, ATC code: B02BC30

TachoSil contains fibrinogen and thrombin as a dried coating on the surface of a collagen matrix. In contact with physiological fluids, e.g. blood, lymph or physiological saline solution the components of the coating dissolve and partly diffuse into the wound surface. This is followed by the fibrinogen-thrombin reaction which initiates the last phase of physiological blood coagulation. Fibrinogen is converted into fibrin monomers which spontaneously polymerise to a fibrin clot, which holds the collagen matrix tightly to the wound surface. The fibrin is then cross linked by endogenous factor XIII, creating a firm, mechanically stable network with good adhesive properties and therefore provides sealing as well.

Clinical studies demonstrating haemostasis were conducted in a total of 240 patients (119 TachoSil, 121 argon beamer) undergoing partial liver resection surgery and 185 patients (92 TachoSil, 93 standard surgical treatment) undergoing surgical resection of superficial renal tumour. A further controlled study in 119 patients (62 TachoSil, 57 haemostatic fleece) demonstrated sealing, haemostasis and suture support in patients undergoing cardiovascular surgery. Tissue sealing in lung surgery was investigated in two controlled trials in patients undergoing lung surgery. The first controlled clinical trial investigating tissue sealing in lung surgery failed to document superiority over standard treatment measured by air leakage due to the inclusion of a large group of patients (53%) without air leakage. However, the second study investigating tissue sealing in 299 patients (149 TachoSil, 150 standard surgical treatment) with demonstrated intraoperative air leakage showed the superiority of TachoSil compared to standard treatment.

The efficacy of TachoSil was tested in a randomised controlled study in 726 patients (362 treated with TachoSil and 364 controls) undergoing skull base surgery as an adjunct to suture for sealing the dura mater, in which the efficacy outcome was measured post-operatively as verified cerebrospinal fluid (CSF) leaks or pseudomeningocele, or treatment failure during surgery. In this study, superiority over

current practise practice (which included suture, duraplasty and fibrin and polymer sealants or combinations of these) could not be documented. The numbers of subjects experiencing an efficacy outcome event were 25 (6.9%) and 30 (8.2%) for TachoSil and current practice treated patients, respectively, providing an Odds Ratio of 0.82 (95% CI: 0.47, 1.43). However, the 95% confidence intervals for the odds ratio results indicated that TachoSil had similar efficacy to current practice. In this study two application techniques for TachoSil were evaluated: application of TachoSil over the dura and application of TachoSil on both sides of the dura. The results did not support the second method. TachoSil was found to be well tolerated and safe for use as an adjunct to dura mater closure in neurosurgery.

5.2. Pharmacokinetic properties

TachoSil is intended for epilesional use only. Intravascular administration is contraindicated. As a consequence, intravascular pharmacokinetic studies were not performed in man.

Fibrin sealants/haemostatics are metabolized in the same way as endogenous fibrin by fibrinolysis and phagocytosis.

In animal studies, TachoSil biodegrades after administration to a wound surface with few remnants left after 13 weeks. Complete degradation of TachoSil was seen in some animals 12 months after its administration to a liver wound, whereas small remnants were still observed in others. The degradation was associated with infiltration of granulocytes and formation of resorptive granulation tissue encapsulating the degraded remnants of TachoSil. No evidence of local intolerance has been observed in animal studies.

From the experience in humans there have been isolated cases where remnants were observed as coincidental findings with no signs of functional impairment

5.3 Preclinical safety data

Single dose toxicity studies in different species of animals have shown no signs of acute toxic effects.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Equine collagen
Human albumin
Riboflavine (E101)
Sodium chloride
Sodium citrate (E331)
L-arginine-hydrochloride.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

Once the foil sachet is opened, TachoSil must be used immediately.

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

Each sealant matrix is packed in a PET-GAG blister sealed with a coated PE foil. The blister is packed in an aluminium-bonded foil sachet with a desiccant bag included and packed in a folding carton.

Pack sizes:

Package with 1 matrix of 9.5 cm x 4.8 cm

Package with 2 matrices of 4.8 cm x 4.8 cm

Package with 1 matrix of 3.0 cm x 2.5 cm

Package with 5 matrices of 3.0 cm x 2.5 cm

Package with 1 pre-rolled matrix of 4.8 cm x 4.8 cm

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

TachoSil comes ready to use in sterile packages and must be handled accordingly. Use only undamaged packages. Once the package is opened, post-sterilisation is not possible. The outer aluminium foil sachet may be opened in a non-sterile operating area. The inner sterile blister must be opened in a sterile operating room area. TachoSil should be used immediately after opening the inner sterile cover.

TachoSil is used under sterile conditions. Prior to application the wound area should be cleansed, e.g. from blood, disinfectants and other fluids. After removal of the conventional, flat TachoSil from the sterile package it should be pre-moistened in saline solution and then applied immediately. The yellow, active side of the matrix is applied to the bleeding/leaking surface and held against it with a gentle pressure for 3-5 minutes. This procedure enables an easy adhesion of TachoSil to the wound surface.

After removal of the pre-rolled TachoSil from the sterile package it should be applied immediately through the trocar **without** pre-moistening. While unrolling the matrix the yellow, active side of the matrix is applied to the bleeding/leaking surface using e.g. a pair of cleansed forceps and held against it with a moist pad under gentle pressure for 3-5 minutes. This procedure enables an easy adhesion of TachoSil to the wound surface.

Pressure is applied with moistened gloves or a moist pad. Due to the strong affinity of collagen to blood, TachoSil may also stick to surgical instruments, gloves or adjacent tissues covered with blood. This can be avoided by cleansing surgical instruments, and gloves and adjacent tissues before application. It is important to note that failure to adequately clean adjacent tissues may cause adhesions (see section 4.4). After pressing TachoSil to the wound, the glove or the pad must be removed carefully. To avoid TachoSil from being pulled loose it may be held in place at one end, e.g. with a pair of forceps.

Alternatively, e.g. in case of stronger bleeding, TachoSil may be applied without pre-moistening, while also pressing gently to the wound for 3-5 minutes.

The active side of TachoSil should be applied so that it extends 1-2 cm beyond the margins of the wound. If more than one matrix is used they should overlap. TachoSil can be cut to the correct size and shaped if too large.

In neurosurgery, TachoSil should be applied on top of the primary dura closure.

Pre-rolled TachoSil can be used for both open surgery and in minimally invasive surgery, and it can pass through a 10 mm or larger port or trocar.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Takeda Austria GmbH
St. Peter Strasse 25
A-4020 Linz
Austria

8 MARKETING AUTHORISATION NUMBER

EU/1/04/277/001-005

9 DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

Date of first authorisation: 8 June 2004

Date of latest renewal: 8 June 2009

10 DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency (EMA) <http://www.ema.europa.eu/>

ANNEX II

- A. MANUFACTURER OF THE BIOLOGICAL ACTIVE SUBSTANCES AND MANUFACTURER RESPONSIBLE FOR BATCH RELEASE**
- B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE**
- C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION**
- D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT**

A. MANUFACTURER OF THE BIOLOGICAL ACTIVE SUBSTANCES AND MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer of the biological active substances

CSL Behring GmbH
Emil-von-Behring-Strasse 76
35041 Marburg
Germany

Name and address of the manufacturer responsible for batch release

Takeda Austria GmbH
St. Peter Strasse 25
A-4020 Linz
Austria

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to restricted medical prescription (See Annex I: Summary of Product Characteristics, section 4.2)

- **Official batch release**

In accordance with Article 114 of Directive 2001/83/EC as amended, the official batch release will be undertaken by a state laboratory or a laboratory designated for that purpose.

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic Safety Update Reports**

The marketing authorisation holder shall submit periodic safety update reports for this product in accordance with the requirements set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and published on the European medicines web-portal.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk Management Plan(RMP)**

The MAH shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the Marketing Authorisation and any agreed subsequent updates of the RMP.

In addition, an updated RMP should be submitted

- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

If the dates for submission of a PSUR and the update of a RMP coincide, they can be submitted at the same time.

ANNEX III
LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON

1. NAME OF THE MEDICINAL PRODUCT

TachoSil, sealant matrix
Human fibrinogen/Human thrombin

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each matrix contains per cm²
Human fibrinogen 5.5 mg
Human thrombin 2.0 IU

3. LIST OF EXCIPIENTS

Equine collagen, human albumin, riboflavine (E101), sodium chloride, sodium citrate (E331),
L-arginine-hydrochloride

4. PHARMACEUTICAL FORM AND CONTENTS

Sealant matrix
1 matrix of 9.5 cm x 4.8 cm
2 matrices of 4.8 cm x 4.8 cm
1 matrix of 3.0 cm x 2.5 cm
5 matrices of 3.0 cm x 2.5 cm
1 pre-rolled matrix of 4.8 cm x 4.8 cm

5. METHOD AND ROUTE(S) OF ADMINISTRATION

For epilesional use.
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Once the foil sachet is opened, use immediately. Do not resterilise.

8. EXPIRY DATE

EXP {MM/YYYY}

9. SPECIAL STORAGE CONDITIONS

Do not store above 25°C

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

Any unused product or waste material should be disposed of in accordance with local requirements.

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Takeda Austria GmbH
St.Peter Strasse 25
A- 4020 Linz, Austria

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/04/277/001 1 matrix of 9.5 cm x 4.8 cm
EU/1/04/277/002 2 matrices of 4.8 cm x 4.8 cm
EU/1/04/277/003 1 matrix of 3.0 cm x 2.5 cm
EU/1/04/277/004 5 matrices of 3.0 cm x 2.5 cm
EU/1/04/277/005 1 pre-rolled matrix of 4.8 cm x 4.8 cm

13. BATCH NUMBER

Batch

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE**16. INFORMATION IN BRAILLE**

Justification for not including Braille accepted

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS
ALUMINIUM-BONDED FOIL SACHET

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

TachoSil, sealant matrix
Human fibrinogen/Human thrombin
For epilesional use

2. METHOD OF ADMINISTRATION

Read the package leaflet before use

3. EXPIRY DATE

EXP {MM/YYYY}

4. BATCH NUMBER

Batch

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

1 matrix of 9.5 cm x 4.8 cm
1 matrix of 4.8 cm x 4.8 cm
1 matrix of 3.0 cm x 2.5 cm
1 pre-rolled matrix of 4.8 cm x 4.8 cm

6. OTHER

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

POLYETHYLENE TEREPHTHALATE BLISTER

1. NAME OF THE MEDICINAL PRODUCT

TachoSil

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Takeda

3. EXPIRY DATE

EXP {MM/YYYY}

4. BATCH NUMBER

Batch

5. OTHER

B. PACKAGE LEAFLET

Package leaflet: Information for the user

TachoSil sealant matrix Human fibrinogen/Human thrombin

Read all of this leaflet carefully.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor.
- If you get any side effects talk to your doctor. This includes any possible side effects not listed in this leaflet.

What is in this leaflet:

1. What TachoSil is and what it is used for
2. What you need to know before TachoSil is used.
3. How to use TachoSil
4. Possible side effects
5. How to store TachoSil
6. Contents of the pack and other information

1. What TachoSil is and what it is used for

How does TachoSil work?

The yellow side of TachoSil contains the active components: fibrinogen and thrombin. The **yellow** side of TachoSil is therefore the **active side**. When the active side comes into contact with fluids (such as blood, lymph or saline solution) the fibrinogen and the thrombin are activated and form a fibrin network. This means that the TachoSil sticks to the tissue surface, the blood coagulates (local haemostasis) and the tissue is sealed. In the body TachoSil will dissolve and disappear completely.

What is TachoSil used for?

TachoSil is used during surgery to stop local bleeding (haemostasis) and to seal tissue surfaces on internal organs.

2. What you need to know before TachoSil is used

Do not use TachoSil

- if you are allergic (hypersensitive) to human fibrinogen, human thrombin or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions

TachoSil is for local use only and should not be applied inside a blood vessel. Blood clots may occur if TachoSil is unintentionally applied inside a blood vessel.

It is possible that you could suffer an allergic reaction after TachoSil has been applied. You may suffer hives, or a rash similar to nettle rash, chest discomfort or tightness, wheezing or low blood pressure. You should contact your doctor immediately if you discover any of these symptoms.

After abdominal surgery and if TachoSil sticks to nearby tissues, it is possible that scar tissues can develop in the operated area. Scar tissues can cause surfaces in your bowel to stick together, which can lead to blockage of the bowel.

When medicines are made from human blood or plasma, certain measures are put in place to prevent infections being passed on to the patients. These include careful selection of blood and plasma donors to make sure those at risk of carrying infections are excluded, and the testing of each donation and

pools of plasma for signs of virus/infections. Manufacturers of these products also include steps in the processing of the blood or plasma that can inactivate or remove viruses. Despite these measures, when medicines prepared from human blood or plasma are administered, the possibility of passing on infection cannot be totally excluded. This also applies to any unknown or emerging viruses or other types of infections.

The measures taken are considered effective for enveloped viruses such as human immunodeficiency virus (HIV), hepatitis B virus and hepatitis C virus, and for the non-enveloped hepatitis A virus. The measures taken may be of limited value against non-enveloped viruses such as parvovirus B19. Parvovirus B19 infection may be serious for pregnant woman (fetal infection) and for individuals whose immune system is depressed or who have some types of anaemia, (e.g. sickle cell disease or haemolytic anaemia).

It is strongly recommended that when you receive TachoSil the name and batch number of the product are recorded at the hospital in order to maintain a record of the batches used.

Other medicines and TachoSil

Tell your doctor if you are taking, have recently taken or might take any other medicines.

3. How to use TachoSil

The doctor treating you will apply TachoSil during surgery. The quantity of TachoSil used depends on the size of the wound. The doctor will place TachoSil on the internal organ to stop the bleeding or to seal the tissue. During the following time TachoSil will dissolve and disappear.

4. Possible side effects

Like all medicines, this medicine can cause side effects although not everybody gets them.

TachoSil is made of protein-containing components. The active components are made from human blood. All medicines based on human blood may uncommonly cause allergic reactions. In isolated cases these allergic reactions may progress to anaphylactic shock.

These allergic reactions may occur especially if TachoSil is used repeatedly or if you are allergic to any of the ingredients in TachoSil.

A clinical study has shown that some patients produced antibodies against the components of TachoSil, however, no side effects were reported resulting from the development of these antibodies.

Scar tissues may develop in some patients after surgery and use of TachoSil. Bowel obstruction and pain following abdominal surgeries can also occur. The frequency of these types of events is not known (cannot be estimated from available data). Your surgeon will make sure to clean the operating area when applying TachoSil to reduce this risk.

Reporting of side effects

If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet.

You can also report side effects directly via [the national reporting system listed in Appendix V](#). By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store TachoSil

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the label. The expiry date refers to the last day of that month.

Do not store above 25°C.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help to protect the environment.

6. Contents of the pack and other information

What TachoSil contains

- The active substances are human fibrinogen (5.5 mg per cm²) and human thrombin (2.0 IU per cm²).
- The other ingredients are equine collagen, human albumin, riboflavin (E101), sodium chloride, sodium citrate (E331) and L-arginine-hydrochloride.

What TachoSil looks like and contents of the pack

TachoSil is a sealant matrix made of collagen, which is coated on the yellow side with human fibrinogen and human thrombin.

The product is available in different sizes and comes in packages with up to 5 units:

Package with 1 matrix of 9.5 cm x 4.8 cm

Package with 2 matrices of 4.8 cm x 4.8 cm

Package with 1 matrix of 3.0 cm x 2.5 cm

Package with 5 matrices of 3.0 cm x 2.5 cm

Package with 1 pre-rolled matrix of 4.8 cm x 4.8 cm

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Takeda Austria GmbH
St. Peter Strasse 25
A-4020 Linz, Austria

For any information about this medicinal product, please contact the local representative of the Marketing Authorisation Holder:

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This leaflet was last revised in {month/YYYY}

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site:
<http://www.ema.europa.eu>.

This leaflet is available in all EU/EEA languages on the European Medicines Agency website.

The following information is intended for medical or healthcare professionals only:

INSTRUCTIONS FOR USE

Read this before you open the package:

TachoSil comes in sterile packages and therefore it is important:

- *only* to use undamaged packages which have not been opened (post-sterilisation is not possible).
- to have a *non-sterile person* open the outer aluminium cover
- to have a *sterile person* open the inner sterile package
- to use TachoSil *soon after* opening the outer aluminium cover.
- to use TachoSil *immediately* after opening the inner sterile package.

Instructions

Use TachoSil under sterile conditions only.

Find out which size of TachoSil is needed. The size of the sealant matrix depends on the size of the wound. But please note that the matrix should cover 1-2 cm beyond the margins of the wound. If more than one matrix is needed, they should overlap. For smaller wounds, e.g. in minimally invasive surgery, the smaller sizes (4.8 x 4.8 cm or 3.0 x 2.5 cm) or the pre-rolled TachoSil (4.8 cm x 4.8 cm) is recommended. TachoSil can be cut to the appropriate size and shaped to fit the wound.

1. Wipe the wound surface gently before placing TachoSil on the wound. Strong (pulsating) bleeding should be stopped surgically.
2. Open the inner sterile package and remove the matrix. Pre-moisten the flat TachoSil matrix in saline solution and place it on the wound immediately (if the wound is completely wetted by blood and other fluids, there is no need to moisten the matrix before application). The pre-rolled TachoSil should **not** be pre-moistened before passing through the trocar or port.
3. Cleanse surgical instruments, gloves and adjacent tissues, if necessary. TachoSil may stick to surgical instruments, or gloves or adjacent tissues covered with blood. It is important to note that failure to adequately clean adjacent tissues may cause adhesions.
4. If a trocar is used for getting access to the wound, the inside of the trocar should be dry. It is recommended to remove the top part of the trocar prior to passing the pre-rolled TachoSil through the trocar.
5. Place the **yellow, active side** of TachoSil against the wound. Hold down TachoSil with a gentle pressure for 3-5 minutes. Use a moistened glove or a moist pad to keep TachoSil in place. For minimally invasive surgery, the pre-rolled matrix can be un-rolled with instruments at the site of application. The un-rolled TachoSil should then be moistened at the site of application with a moist pad and held in place under gentle pressure for 3-5 minutes.
6. Remove the light pressure carefully after 3-5 minutes. To make sure that TachoSil does not cling to the moistened glove or swab, and loosens itself from the wound, TachoSil can be held down at one end e.g. by using a pair of forceps. There is no residual product which needs to be removed; the entire matrix is dissolved (resorbed).

It is strongly recommended that every time TachoSil is administered to a patient, the name and batch number of the product are recorded in order to maintain a link between the patient and the batch of the product.