Package Leaflet and Summary of Product Characteristics - please read carefully!

PUROS® ALLOGRAFT

1. Name of the medicinal product
Puros® Allograft

2. Qualitative and quantitative composition
Human cancellous tissue (with cortical component in the Puros® Allograft Blend version), preserved using the Tutoplast® process, sterilised by gamma irradiation
The pack contains either a pre-shaped block or the volume of particulate stated on the external packaging.

3. Pharmaceutical form
Tissue graft. Bone graft in the form of particles, customised blocks, blocks and dowels.
The grafts are generally a whitish colour. As a natural product, the colour of the graft is subject to variation. Any brownish discolorations are generally due to natural iron deposits and have no effect on the stability or quality of the product.

4. Clinical particulars

4.1 Therapeutic indications
To cover or fill bone defects or to create bony structures in maxillofacial surgery. Therapeutic indications for which positive experience has been reported include the following:

- Regeneration of periodontal bone defects
- Regeneration of furcation defects
- Regeneration following cyst resection and apicoectomy
- Regeneration of extraction sockets
- Regeneration of gaps between the alveolar wall and dental implants
- Regeneration of defects following block removal
- Regeneration of gaps around block grafts
- Horizontal alveolar ridge augmentation (particles)
- Sinus augmentation
- Three-dimensional (horizontal and/or vertical) alveolar ridge augmentation (block augmentation).

Further potential applications in other surgical disciplines have also been recorded.

4.2 Posology and method of administration
The dimensions of the graft are determined by the operating surgeon based on the defect to be repaired. The graft must be completely rehydrated in normal saline solution or Ringer's solution prior to use (see 6.6). Following complete rehydration, the graft can be cut to size for the individual patient so as to ensure perfectly fitting integration. The graft is intended to remain in the human body permanently.

4.3 Contraindications
None known

4.4 Special warnings and precautions for use

- Strict assessment of the indications must be performed in the following cases prior to use of the graft:
  - Implantation in a necrotic host site
  - Implantation in a hypoperfused area
  - Implantation in a host site with active or latent infection
  - In the case of disorders or conditions which could have a negative impact on the healing rate
- Based on their medical history, as well as further tests, all tissue donors are examined for possible grounds for exclusion. Before the donor tissue can be approved for processing, serological tests are carried out for possible infectious agents. This analysis includes tests for HTLV-I/-II, HIV-1/-2, hepatitis B/C and Treponema pallidum, among others. The Tutoplast® process is highly effective against all pathogenic species. However, as with all biological products, the transmission of infectious diseases can be ruled out only to the extent of current knowledge.
- The graft remains sterile provided that the packaging is undamaged.
- If the sterile packaging becomes damaged, the product must be disposed of appropriately. Do not resterilise the product! If the graft is contaminated in the course of a surgical intervention, it must be disposed of appropriately.
- When using the graft, note that the mechanical loads vary depending on the implant site and the physical stability of the product must be sufficient for the respective conditions.
- When customising the graft for the individual patient, do not allow it to be damaged by the heat generated. The structural integrity must be preserved.
- The graft must be inserted (preferably using a "press-fit" technique) and secured in such a way that it remains in side and its incorporation is facilitated.
- When inserting the blocks, it is important to avoid exerting loads exceeding the physical stability of the graft under all circumstances, so as to preserve the structural integrity of the graft.
- Puros® Allograft is intended for single use only. Unused material must be disposed of appropriately.

4.5 Interaction with other medicinal products and other forms of interaction
None known

4.6 Pregnancy and lactation
No clinical data concerning the use of the product during pregnancy and when breastfeeding are available. Based on the physical mechanism of action of the graft, undesirable effects during pregnancy or on the health of the newborn child are not to be expected and have not been determined.

4.7 Effects on ability to drive and use machines
Not relevant

4.8 Undesirable effects
The following frequency conventions are used in the rating of undesirable effects:

Very common (≥1/10)
Common (≥1/100 to <1/10)
Uncommon (≥1/1,000 to <1/100)
Rare (≥1/10,000 to <1/1,000)
Very rare (<1/10,000)
Not known (cannot be estimated from the available data)

System Organ Class	Frequency	Adverse reaction
Immune system disorders	Not known	Graft rejection
General disorders and administration site conditions	Not known	Implant site reaction Dehiscence
Injury, poisoning and procedural complications	Not known	Graft failure

As with every surgical procedure, there is the possibility of infection and wound complications with associated symptoms (swelling, redness, inflammation and pain) or other reaction due to the procedure itself.

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 Federal Institute for Vaccines and Biomedicines (Bundesinstitut für Impfstoffe und biomedizinische Arzneimittel), Paul Ehrlich Institute, Paul-Ehrlich-Str. 51-59, 63225 Langen, Germany Tel: +49 (0)6103770, Fax: +49 (0)610377 1234, www.pei.de.

4.9 Overdose
Not applicable

5. Pharmacological properties

5.1 Pharmacodynamic properties
Pharmacotherapeutic group: Allograft

Mode of action of the medicinal product
The medicinal product is primarily a physical aid, acting as a guide rail for the regeneration of osseous tissue. As it can be absorbed by osteoclasts, it is integrated into the autologous remodelling process. The regeneration of autologous structures (ossification/osteogenesis) occurs in parallel to the resorption of the allograft. Both processes are particularly dependent on the host site's ability to respond, its blood supply and the size of the graft itself. The implantation of the graft and its function as a guide rail facilitate the naturally occurring process of bone remodelling at the site of the defect. The ultimate goal is complete conversion of the graft into new autologous tissue.

5.2 Pharmacokinetic properties
Puros® Allograft is primarily a physical aid, acting as a guide rail for the regeneration of osseous tissue. The process of cell colonisation, remodelling and resorption generally begins after 1-2 days. The conversion process depends on the size of the graft and the host site's ability to respond. As such, it can take a considerable period of time to complete (several months or even years).

5.3 Preclinical safety data
Studies on animals and in vitro studies have shown that the graft is biocompatible, is incorporated quickly and maintains the space until replaced by autologous tissue. As such, the preclinical data do not indicate any risks to humans and confirm that the product can be used safely.

6. Pharmaceutical particulars

6.1 List of excipients
None

6.2 Incompatibilities
None known

6.3 Shelf life
Puros® Allograft can be stored for 5 years in the undamaged original packaging. The graft must not be used after the expiry date shown on the packaging.

6.4 Special precautions for storage
The graft should be stored in a clean, dry place protected from exposure to direct sunlight and at no higher than 30°C. The product must not be frozen.

6.5 Nature and contents of container
The graft is kept sterile in a double-layered primary packaging.
Blocks are additionally packaged in a tubular bag, granulate in a vail.
The packaging contains either a pre-shaped block or the volume of particulate stated on the external packaging.

	Form, size	Packaging unit
Block	8 mm x 8 mm x 8 mm, 10 mm x 10 mm x 20 mm, 10 mm x 20 mm x 20 mm, 15 mm x 10 mm x 20 mm, 15 mm x 15 mm x 15 mm	1 item
Patient customised block standard	min. 5 mm x 5 mm x 1 mm max. 27 mm x 15 mm x 15 mm	1 item
Patient customised block large	min. 27,1 mm x 15 mm x 15 mm max. 60 mm x 30 mm x 30 mm	1 item
Dowel	Ø 5 mm, Length 14 mm - 15 mm, Ø 5 mm, Length 20 mm - 20 mm	1 item
Particles	Ø 0,25 mm - 1 mm	0,5 cm³, 1 cm³, 2 cm³
Particles	Ø 1 mm - 2 mm	0,5 cm³, 1 cm³, 2 cm³, 3 cm³
Particles	Ø 2 mm - 4 mm	3 cm³
Cortico-cancellous Particles	Ø 0,25 mm - 1 mm	0,5 cm³, 1 cm³, 2 cm³
Cortico-cancellous Particles	1 mm - 2 mm	0,5 cm³, 1 cm³, 2 cm³

Note: Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling
Information on disposal of remnants
If the packaging is opened and the graft not used, the cancellous bone must not be resterilised. Remnants must be disposed of in accordance with the pertinent national regulations. The contents of the packaging are exclusively intended for use in one patient.

Special information on handling

- Please observe the general principles of aseptic handling when using Puros® Allograft.

The graft should must be completely rehydrated in normal saline solution or Ringer's solution prior to its use.

- If the graft is to be shaped customised before use, this should only be performed done after it is completely rehydrationed.
- Any dust which forms must be thoroughly rinsed away with normal saline solution or Ringer's solution.
- Autologous blood, blood components or bone marrow aspirate may only be added after rehydration and immediately prior to the product's implantation.

a) Standard rehydration for all forms

- Immerse the graft completely in a normal saline solution (or Ringer's solution) in a sterile container – the deeper the water, the better.
- Weigh blocks down with a sterile instrument to prevent them from floating to the surface.
- The rehydration time should be at least 30 minutes.
- During the rehydration process, agitate the cancellous bone and/or shake the container repeatedly.
- Rehydration is complete when no more air bubbles escape the cancellous bone when it is agitated and the bone remains on the bottom of the container without being weighed down instead of floating to the surface.
- Store the graft in the rehydration solution until ready for implantation.

b) Vacuum rehydration for all forms (vacuum rehydration permits quicker, more efficient rehydration and is thus particularly recommended for blocks)

- The graft is placed in an appropriately sized, sterile, disposable syringe.
- Draw up normal saline solution (or Ringer's solution) with the filled syringe until the graft is completely covered.
- Turn the syringe vertical and eject all the air.
- Seal off the opening of the syringe so that it is airtight (using a gloved finger, for example).
- Pull the plunger down with force. Holding the plunger retracted, shake the syringe back and forth repeatedly. Air bubbles can be seen escaping the cancellous bone. Repeat the procedure a number of times.
- When correctly rehydrated, the bone will settle at the bottom of the syringe. When this occurs, repeat the procedure at least once more.
- Store the graft in the rehydration solution until ready for implantation.

7. Marketing authorisation holder
Tutogen Medical GmbH, Industriestraße 6, 91077 Neunkirchen am Brand, Germany
Tel.: +49 (0)9134 9988-0, Fax: +49 (0)9134 9988-99, tutogen@rtix.com

8. Marketing authorisation number
PEI.H.04761.01.1

9. Date of first authorisation:
Authorisation date: 05.03.2009
Authorisation renewal: 16.10.2015

10. Date of revision of the text
07/2019 „12"

11. General classification for supply
Medicinal product subject to medical prescription

Notes:
The product package contains adhesive labels for the documentation in the patient record.
Tutoplast® is a registered trademark of Tutogen Medical GmbH.
PUROS® is a registered trademark of Zimmer Biomet or its affiliates.

Pharmaceutical Entrepreneur:

Tutogen Medical GmbH
Industriestraße 6
91077 Neunkirchen am Brand, Germany
Tel.: 09134-9988-0 Fax: 09134-9988-99
tutogen@rtix.com

Co-distributor:

ZIMMER BIOMET

Zimmer Dental GmbH
Wilhelm-Wagenfeld-Str. 28
80807 München, Germany
Tel.: 089 - 3246221 - 10 Fax: 089 - 3246221 - 99
Customer service: 0800 - 1016 420
zb.bestellung@zimmerbiomet.com