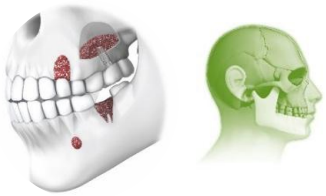
NORAKER®

THE BIOGLASS® COMPANY

Summary of Safety and Clinical Performance (SSCP)

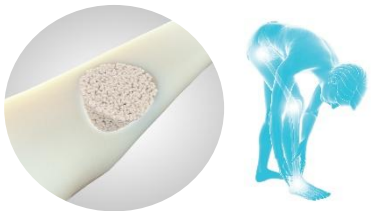
Surgeons version

Injectable Putty Range



BiologicGlass
Bioactive Bone Substitute

GlassBone®
Bioactive Bone Substitute



AktiBone®
Bioactive Bone Substitute

This summary of safety and clinical performance is intended to provide public access to the main aspects of the safety and clinical performance of the device.

The summary of safety and clinical performance is not intended to replace the Instructions for Use as the main document to ensure the safe use of the device, nor is it intended to provide diagnostic or therapeutic suggestions to intended users or patients.

Version E.1 (EN) of this summary of safety and clinical performance has been validated by a notified body.

The following information is intended for users/healthcare professionals.

I. Device identification and general information

1. Brand name

GlassBone™ Injectable Putty.

It is available in different volumes: 1cc, 1.5cc, 2.5cc, 5cc, 6cc and 10cc.

There are several other trade names (brands) under which the GlassBone Injectable Putty (GB-IP) device is marketed: these devices are identical, only the name changes.

These brands are: AktiBone™ Injectable Putty (XAK-IP), BiologicGlass™ Injectable Putty (XBG-IP), MectaGlass™ Injectable Putty (XMG-IP), BioActys™ Injectable Putty (XBA-IP), CicaGlass™ Injectable Putty (CIG-IP) and CareGlass™ Injectable Putty (CAG-IP).

The volumes available are the same as GlassBone™ Injectable Putty.

When "GlassBone Injectable Putty" is cited in the document, this includes the brands mentioned above.

2. Name and address of the manufacturer

Name: NORAKER®

Address: 60 avenue Rockefeller – 69008 LYON - France

Phone: +33 4 78 93 30 92

SAS CAPITAL 300 000 €

N° RCS Lyon 483 190 518

SIRET: 483 190 518 000 41

Intra-community T.V.A: FR74 483 190 518

Contact address for vigilance: vigilance@noraker.com

3. Manufacturer's single registration number (SRN)

FR-MF-000000325

4. Unique Device Identifier (UDI-DI)

Basic UDI-DI for GlassBone™ Injectable Putty range of products is: 0376019113DT735 MA (control key: MA).

5. Nomenclature

GMDN: 16966 - Prosthesis, internal, bone, synthetic

EMDN: P900402 – IMPLANTABLE PROSTHETICS AND OSTEOSYNTHESIS DEVICES; ABSORBABLE FILLING AND RECONSTRUCTION DEVICES

Regulation 2017/2185 codes are: MDN 1102, MDT 2003, MDT 2006, MDT 2008, MDT 2011, MDS 1005 irradiation and MDS 1008

6. Device class

This product is a medical device in accordance with Article 2 of Regulation 2017/745, class III according to the applicable classification rule 8 of Annex VIII to Regulation 2017/745.

7. Year of affixing of the first CE marking

The first affixing of the CE marking and placing on the market dates from 2017.

8. Agent, name and unique registration number

Not applicable

9. Notified Body, name and unique identifier number

Name: GMED

Unique Identifier Number: 0459

II. Destination of the device

1. Intended use of the device

GlassBone™ Injectable Putty is a synthetic, resorbable, biocompatible and bioactive substitute device (bioactive glass 45S5), intended for the filling, reconstruction and / or fusion of bone defects or gaps of the skeletal system, in orthopedic surgery, spine, cranio-maxillofacial surgery and ENT.

2. Indications and target population

Loss or lack of bone substance for bone defects of traumatic, pathological or surgical origin when autologous solutions are not applicable or sufficient in orthopedics, neurosurgery, cranio maxillo facial and otorhinolaryngology surgery in children and adult population:

- Fusion or reconstruction of deformities and degenerative diseases in spine
- Fusion or reconstruction of deformities and degenerative bone pathologies in orthopedic
- Filling and reconstruction of bone defects due to resection of tumors, cyst or infection and in case of prosthetic revision
- Filling after surgical bone defect (donor sites after removal of autograft, trepanation, …)
- Filling after removal of cholesteatoma
- Filling and reconstruction due to maxilla and periodontium pathologies (in adult only).

3. Contraindications and limits

GlassBone Injectable Putty should not be used:

- In case of chronic or acute infection not treated with appropriate therapy
- In patients who have suffered serious trauma with external wounds open near the defect, which could become infected.
- In patients with known allergy to bioactive glass or its constituents (Ca^{2+}, PO_4^{3-}, Na^+ and $Si(OH)_4$).
- In patients with pre-existing conditions or disease that may interfere with the good healing of tissues (patients treated with bisphosphonates, for example).
- In patients who have undergone or will undergo chemotherapy or radiation therapy at or near the site of implantation.
- In irradiated bone (according to radiological criteria indicating osteonecrosis)
- To replace structures subject to high mechanical stresses
- During severe renal and hepatic infections.
- In conjunction with a treatment known to affect the skeleton.
- In case of unsutured meningeal breach in cranio-spinal surgery.
- In neonatology service

To date, we do not have any studies conducted in pregnant women or data related to use during breastfeeding. As a safety measure, the implantation of GlassBone Injectable Putty is not recommended during the periods of pregnancy and lactation.

III. Device description

1. Description

GlassBone™ Injectable Putty is a synthetic, resorbable, biocompatible and bioactive substitute device for filling bone defects and gaps in the skeletal system in adults and children.

- Composition: 45S5 bioactive glass granules, polyethylene glycol and glycerol.

45S5 bioactive glass granules are only composed of elements naturally present in bone tissue (Calcium, Phosphate, Sodium, Silicon). The release of these ions during the resorption of bioactive glass will allow the formation on the surface of a layer of carbonate hydroxyapatite whose composition and structure are similar to the mineral phase of the bone. This layer provides GlassBone Injectable Putty an osteoconduction property and creates a strong chemical bond between granules and living tissues. *In vitro* cell culture assays have also shown that the released ions have a stimulating effect on the proliferation, differentiation and activity of the cells responsible for the formation of bone tissue. This medical device does not contain any medicinal substance or tissues of human origin.

The radio-opacity of GlassBone™ Injectable Putty makes it possible to discern bone substitute granules following their implantation. As the granule's resorption, the radio-opacity of the bone defect approaches that of the surrounding bone.

GlassBone™ Injectable Putty biomaterial is a non-hardening paste, ready to use.

It is a single-use device.

Bone defects are consolidated in about 12 months while GlassBone™ Injectable Putty gradually resolves. This resorption time varies depending on the patient's metabolism, bone site and implanted volume.

The current expiration date is 2 years after gamma sterilization.

The device is MR safe.

2. Reference to previous model(s) and description of changes

There is no previous model for this device.

3. Description of accessories intended for use with the device

No accessories are used with our device.

4. Description of other devices intended for use in combination with the device

No other devices are used.

IV. Risks and warnings

1. Residual risks and adverse effects

The residual risks of the device itself, i.e., the risks remaining after the implementation of the risk management measures, concern the allergic risks.

To date, no adverse effects directly related to the device are reported or detected.

The occurrences of risks and damages are 0% directly related to the device.

Possible complications following the procedure are general complications due to surgery or anaesthesia: post-surgery symptoms (pain, redness, inflammation, oedema, hematoma, seroma, swelling, ...), post-operative infection, delayed consolidation, loss of fracture reduction, fusion failure, fracture, loss of bone graft, protuberance of the graft.

These complications are the same as those that can occur with autologous bone grafting (see part 6. Other therapeutic solutions).

Device-related complications	Frequency of occurrence	Source
Allergy to the constituents of the dispositive	Not detected to date out of 102 826 sales (data until 30/06/2025)	PMS and available clinical data

The profit/risk ratio is positive since the benefit is greater than the risk with an acceptable residual risk.

2. Warnings and Precautions

GlassBone™ Injectable Putty should be used by qualified surgeons (orthopaedists, neurosurgeons, craniomaxillofacial surgeons, stomatologists and ENT surgeons) who are trained in bone grafting and fixation techniques and who have read these instructions for use.

In relation to the surgical procedure

- The general principles of asepsis and patient medication should be respected when using GlassBone Injectable Putty. GlassBone™ Injectable Putty does not substitute antibiotic therapy treatment during infection.
- The combination of any drug substance with GlassBone™ Injectable Putty during implantation is the responsibility of the surgeon.
- Handle GlassBone™ Injectable Putty with a surgical instrument to avoid piercing surgical gloves.
- It is advisable to trim up the recipient site before implantation.
- Avoid placing paste outside the bone defect. Remove it if necessary.
- If positioned outside the implantation site, moving or migrating, bioactive glass can cause wear of the joints and interfere with movement.

- Do not exert excessive pressure on the defect. Excessive pressure could cause an embolism of fat or paste in the bloodstream or cause the paste to be extruded beyond the implantation site, damaging the surrounding tissues.
- GlassBone Injectable Putty does not have sufficient mechanical strength to withstand a load before the bone tissue is formed. When used in load-bearing areas such as mandible fractures, standard internal or external stabilization techniques should be used to achieve rigid stabilization in all planes.
- It is necessary to follow the usual post-operative procedures of treatment and rehabilitation associated with bone grafts.

In relation to the medical device

- GlassBone™ Injectable Putty is a device that resorbs over time to make way for a regenerated bone. The binder is reabsorbed in a few days. Regarding the granules, no clinical studies currently available demonstrate complete resorption.
- GlassBone™ Injectable Putty is a non-hardening, ready-to-use paste.
- GlassBone™ Injectable Putty is a sterile single-use device and must not be re-sterilized or reused under any circumstances. Reuse can cause contamination and impaired performance of the bone substitute.

3. Other aspect of security, if applicable

The medical device has not been the subject of FSCA (Field Safety Corrective Action) or FSN (Field Safety Notice).

V. Summary of Clinical evaluation and Post-Market Clinical Follow-up (PMCF)

1. Summary of clinical data on equivalent devices, if applicable

Not Applicable

2. Summary of clinical data relating to investigations of the device prior to CE marking, if applicable

Not Applicable

3. Summary of clinical data from other sources, if applicable

- **In literature**

Currently, the Device Glassbone™ Injectable Putty is found in two ENT publications, two in spinal surgery, and two in orthopedic publication of:

a) ENT

AL Tamami, N et al (2021). Tolerance and safety of 45S5 bioactive glass used in obliteration procedures during middle ear surgery: Preliminary results. *Am J Otolaryngol.*

- Surgery

Patients had undergone obliteration of mastoid or/and epitympanic cavity with 45S5 bioactive glass

- Methods

This retrospective study analyzed 42 patients (Lyon-France) treated by 45S5 bioactive glass between November 2017 to January 2019.

- Results

- Performance – Microscopic examinations showed dry and well-healed tympanic membranes as well as external auditory canals for 95.2% of patients after 1 year. Inner ear lesions after obliteration were not observed when comparing pre- and postoperative bone-conduction audiometry. Postoperative radiological assessments at one year revealed no silent implantation of cholesteatoma or residual disease.
- Safety – No facial paralysis has been reported post-operatively

- Conclusion

Mastoid and epitympanic obliterations with 45S5 bioactive glass seem to be a tolerable and safe option in cholesteatoma surgery with favorable outcomes similar to other member of bioactive glass especially the S53P4.

Ayache, S. Transcanal Endoscopic Ear Surgery for Epitympanic Cholesteatoma with Obliteration Using Bioglass. Laryngoscope, 2021. 00:1-3

- Surgery

Patients underwent a transcanal endoscopic procedure for cholesteatoma epitympanic obliteration using 45S5 Bioactive Glass (GlassBone™ Injectable Putty, NORAKER). The obliteration extended from the anterior epitympanum to the aditus ad antrum, without bulging in the external auditory canal to prevent any postoperative stenosis.

- Methods

This is a single-patient case report. Follow-up included clinical evaluation and diffusion-weighted MRI performed 12 months after surgery to assess for recurrence or residual disease. The preoperative CT scan revealed an anterior and posterior epitympanic cholesteatoma

- Results

- Performance – The healing of the external auditory canal was complete without leakage of the GlassBone™ Injectable Putty. After 12 postoperative months, the patient had a self-cleaning intact ear canal, without stenosis (Fig. 3, bellow). The first diffusion-weighted imaging magnetic resonance imaging performed at 12 post-operative months was negative. The texture of the 45S5 Bioactive Glass was well-suited for the epitympanic obliteration using a one-handed endoscopic technique. Its consistency in the form of a paste facilitates its handling.
- Safety – No pre- or postoperative complication occurred.

- Conclusion

The healing Closed technique cholesteatoma surgery is thought to improve the postoperative quality of life of patients. Indeed, this case report a good quality of healing and the calibre of the external auditory canal. Imagery is like that existing for cholesteatomas. 45S5 Bioactive Glass are used in mastoid obliteration procedures without risk of loss of volume presents with the use bone chips or bone paté (autologous material).

Fieux, et al., 2023. Allograft bone vs. bioactive glass in rehabilitation of canal wall-down surgery.

- Surgery

All patients undergoing canal wall down reconstruction tympanomastoidectomy (CWRT) after canal wall down mastoidectomy for cholesteatoma. Reconstruction was performed using either allograft bone (CBM group) or 45S5 bioactive glass Injectable Putty (GlassBone™ IP – BG group).

- Method

This was a single centre controlled observational trial. Thirty-two patients were included and divided into two groups based on the obliteration material: 15 received bone allografts and 17 received 45S5 bioactive glass. Preoperative symptoms and postoperative outcomes were evaluated, with follow-up at 18 months. The primary outcome was recurrence of otorrhea. Most frequent preoperative symptom was otorrhea (100.0%, 32/32), and only 12.5% (4/32) had dizziness.

- Results

- Performance – At 18 months postoperatively, 53.3% of patients (8/15) in the CBM group presented with recurrent otorrhea versus 5.9% (1/18) of patients in the BG group (p=0.005).
- Safety – No data indicated an increased risk of residual or recurrent cholesteatoma with the use of 45S5 bioactive glass

- Conclusion

The use of GlassBone™ IP in canal wall down mastoidectomies improve the quality of life of patients without increasing the risk of recurrent or residual cholesteatoma.

b) Orthopaedic

Moriel-Garceso et al. 2021. Three-dimensional printed titanium pseudo-prosthesis for the treatment of a tumoral bone defect. *JSES Reviews, Reports, and Techniques*.

- Surgery

The patient underwent resection of the middle third of the clavicle due to Langerhans cell histiocytosis, followed by reconstruction using a 3D-printed porous titanium implant filled with bioactive glass (GlassBone™ IP)

- Methods

This is a single-patient case report with clinical and radiographic follow-up extending to 2 years post-surgery. Functional outcomes were assessed using the Constant score and the Disabilities of the Arm, Shoulder and Hand (DASH) score.

- Results

- Performance – At 3 months post-surgery, the patient presented with a complete range of motion and no pain on palpation or mobilization. The patient was authorized to initiate progressive loading of the operated extremity and to resume his regular physical activities. On his last follow-up appointment, 2-years after surgery, the patient lead a normal life without any type of functional limitation, he had a Constant score of 100, and a Disabilities of the arm, shoulder, and hand score (DAHS) of 2.5. His follow-up x-ray was also satisfactory.
- Safety – No postoperative complications were reported in this study

- Conclusion

The use of a 3-D printed pseudo-prosthesis achieved filling with bioactive glass an excellent clinical and functional outcome in the treatment of a large bone defect, following a resection of a LCH of the clavicle. 3-D printed pseudo-prostheses could be useful instruments for the treatment of bone defects following large bone resections in musculoskeletal tumours.

Fares, et al., 2023. The impact of bone graft type used to fill bone defects in patients undergoing ACL reconstruction with bone–patellar tendon–bone (BPTB) autograft on kneeling, anterior knee pain and knee functional outcomes. Eur J Orthop Surg Traumatol.

- Surgery

Patients underwent anterior crucial ligament (ACL) reconstruction. Bone defects were filled with one of three different bone substitutes:
- Bioactive glass 45S5 ceramic Glassbonne IP (GB-IP)
- Collagen and hydroxyapatite bone void filler in sponge form Collapat® II (CP)
- Treated human bone graft Osteopure®(OP) bone substitutes.

- Methods

This was a prospective monocentric cohort study conducted between January 2018 and March 2020. A total of 102 patients were included, all with at least two years of follow-up. Patients were dividied into three groups according to the type of bone substitute used: GB-IP (36 patients), CP and OP. Outcomes assessed included kneeling pain, anterior knee pain, and general functional results at 12 and 24 months.

- Results

- Performance – In terms of Kneeling pain, the percentage of GB and CP patients' who kneel with ease were much higher than that of OP patients (77.78%, 76.5% vs 65.6%, respectively) at 12 months. There was no difference in anterior knee pain between the groups.
- Safety – No postoperative complications were observed with GB

- Conclusion

The use of GlassBone™ IP and Collapat II® bone substitutes reduced the incidence of kneeling pain compared to Osteopure®. There was no influence of the bone substitute type on the functional outcome of the knee or on the anterior knee pain at two years of follow.

Romano, A.M., et al., (review) An Evolution of Shoulder Periprosthetic Infections Management: MicroDTTect, Bioactive Glass and Tantalum Cones Employment J. Clin. Med. 2020, 9, 3683.

- Surgery

Periprosthetic joint infection of the shoulder (PJIS) is a rare but serious complication that is challenging to treat. Success depends on early identification of microorganisms, appropriate surgical procedures, and efficient antibiotic administration. PJIS is the major cause for revision within the first two post-operative years after an Arthroplasty. Treatment options for PJIS include intravenous antibiotics, tissue debridement with retention of the prosthesis, resection arthroplasty, one-stage and two-stage exchange procedures, arthrodesis, and amputation. GlassBone Putty was routinely employed in revision surgeries requiring bone loss filling in these surgeries. Obtaining stable osseointegration of prostheses implants is an even greater issue in infected revised arthroplasties; the deposition of bioactive coatings on the implant surface to be in contact with the bone may be a valuable strategy in favouring “physiological” osseointegration, whilst preventing reinfection.

- Methods

This is a review and technical note with the use of bioactive glass in PJIS revision with examples of cases. The bioactive glass 45S5 were used to increase prosthesis-bone interface stability and fill bone defects in PJIS revision surgeries. A porous tantalum cone could be employed for extensive defects of humeral metaphyseal bone. Bioactive glass was added both between the stem and cones, and as a proximal humerus augmentation.

- Results

- Performance – Bioactive glass demonstrated good regenerative and osseointegration properties and fill bone defects in PJIS revision surgeries, contributing to the prevention of re-infection
- Safety – No postoperative complications were observed with GB

- Conclusion

Although no clear guidelines have been defined in PJIS, the results of the instruments discussed regarding pathogen detection, prosthetic revision, and bone loss management are encouraging. In the literature to date, no reports have been found that discuss the application of bioactive glass in shoulder revisions and infections. Obtaining stable osseointegration of prosthetic implants is one of the greatest issues in orthopedic surgery, and even more crucial in revisions. Bioactive glasses demonstrated good regenerative and osseointegration properties, and an excellent candidate as a bone graft, scaffold and antibiotics deliverer.

c) Spine

Szadkowski M et al,.2022. Bioactive glass grants equivalent or better fusion compared to autologous iliac crest bone for ALIF. *Spine*

- Surgery

Patients underwent anterior lumbar interbody fusion (ALIF) at either single-level (L5-S1 only) or two-level (L4-L5 and L5-S1). Intervertebral cages had one chamber filled with bioactive glass (GlassBone™ IP and the other with autologous iliac crest bone. Posterior fixation was performed in 24 patients.

- Methods

A series of 40 patients (58 levels) that underwent ALIF were assessed with a mean follow-up of 14±4 months. CT scans were graded using the Bridwell classification. Comparison was made between chambers filled with bioactive glass and those filled with autologous bone.

- Results

- Performance – Chambers filled with bioactive glass had Bridwell grade I at 30 levels (52%), grade II at 26 levels (45%), and grade III at 2 levels (3%), compared to chambers filled with autologous bone which had Bridwell grade I at 23 levels (40%), grade II at 33 levels (57%), and grade III at 2 levels (3%) (p=0.416). The two patients with Bridwell grade III at both chambers of the L4-L5 cages required reoperation using posterior instrumentation.
- Safety – There were two postoperative complications (one hematoma, one radiculopathy), neither of which required reoperation.

- Conclusion

The findings of this study suggest that for patients undergoing ALIF, bioactive glass can be used as a substitute to autologous iliac crest bone; thus, avoiding increased operative time and blood loss, as well as donor site morbidity.

Courvoisier et al. 2023. Safety and Efficacy of Stand-Alone Bioactive Glass Injectable Putty or Granules in Posterior Vertebral Fusion for Adolescent Idiopathic and Non-Idiopathic Scoliosis. *Children*

- Surgery

GlassBone™ IP was used in posterior thoracolumbar spinal fusion for paediatric patients with idiopathic scoliosis. The device was applied to promote fusion of the instrumented vertebrae, ensuring consolidation of the instrumentation after surgery.

- Methods

This was a retrospective study was conducted at CHU Grenoble to confirm the performance and tolerability of the GlassBone™ IP device in idiopathic scoliosis in children and adolescents (deformation and degeneration of the spine). 32 paediatric patients, all operated by Prof. Courvoisier, were included in the study. The average age was 15.2 ± 1.84 years [11-19] with a distribution of 26 women (81%) and 6 men (19%).

- Results

- Performance – All patients had good health status at 3-6 months, 12 months and 24 months postoperatively. At 3-6 months postoperative follow-up, 67% (n=30) had a non-fused construct, 30% (n=9) were in the process of acquiring fusion and 3% (n=1) were acquired. At 12 months postoperatively, 100% (n=24) had a fused construct.
- Safety – No adverse effects were observed during the follow-ups.

- Conclusion

GlassBone™ IP demonstrated good performance and safety when used in posterior spinal fusion for idiopathic scoliosis in pediatric patients. The study supports its use to achieve vertebral fusion and consolidation without adverse events.

- **Data held by the manufacturer (white paper)**

a) Spine

Illharreborde B. 2022. Efficacy and safety of Glassbone injectable putty in the treatment of adolescent idiopathic scoliosis. Preliminary results of the first year of experience in 126 patients

- Surgery

GlassBone™ Injectable Putty (GlassBone™ IP) was used in posterior thoracolumbar spinal fusion procedures for children and adolescents with idiopathic scoliosis.

- Methods

This retrospective study was conducted between December 2023 and December 2021 and included 126 paediatric patients (age at surgery averaged 14.8 years (± 1.5)) idiopathic scoliosis in children and adolescents (deformation and degeneration of the spine). GlassBone™ IP device was used in posterior thoracolumbar spinal fusion for paediatric patients with idiopathic scoliosis. The objective was to confirm the performance and tolerability of the GlassBone™ IP device.

- Results

- Performance – With a 12 months follow-up, no pseudarthrosis and no significant loss of correction was reported during follow-up. In addition, no proximal junctional failure occured, and no osteolysis was observed around the proximal and distal implants.
- Safety – No infection, no inflammatory reaction and no other adverse effect was reported during the study period.

- Conclusion

GlassBone™ injectable putty can be considered as a safe alternative to other bone substitutes in AIS surgery.

b) ENT (Thesis)

Nakhleh, L. Mastoid obliteration with bone substitute in the management of cholesteatoma in children. Thesis (2021), Hospital Robert Debré, Paris.

- Surgery

GlassBone™ Injectable Putty (GlassBone™ IP) was used in mastoid and epitympanic obliteration in the treatment of cholesteatoma in children.

- Methods

This multicentric retrospective study including 55 pediatric patients which underwent mastoid and epitympanic obliteration between January 2012 and 2020. The mean age of patients were 12 years [3-17]. Patients were divided into surgical technique groups: open technique rehabilitation (n=17), a canal-wall-down “on demand” mastoidectomy (n=17) or a canal-wall-up mastoidectomy technique (n=21). Data from clinical follow ups and audiological assessment were analyzed.

- Results

- Benefits – Bioactive glass is associated with the lowest failure rate (10% (2/20) with S53P4 and 5.3% (1-19) with 45S5) vs 25% with others bones substitutes). Air bone gap was less than 20 dB in 66% of patients and all case open technique obliteration have an audiometric benefit. All patients had at least 12 months postoperative otoscopic follow-up and only 3 (5.45%) presented a recurrent cholesteatoma. The probability at 18 months of being free from recurrent cholesteatoma was 94.25% and the probability at 12 months of being free from residual cholesteatoma was 72%.
- Safety – No allergy/ infection occurred.

- Conclusion

The use of GlassBone Injectable Putty in these types of mastoidectomies improve the hearing of patients. Technics with the use of bone substitute reduce the recurrence and residual rate of cholesteatoma. The tolerance and benefits were confirmed.

- **PMCF Follow-up**

Following the implementation of a post-market clinical follow-up study, 10 studies have been completed:

a) Spine

i. Indications – Spinal pathologies

- Surgery

GlassBone™ Injectable Putty (GB-IP) was primarily used for intervertebral cage filling in spinal surgeries, mostly in patients with degenerative disc disease and in 97% of cases, GB-IP was used for intervertebral cage filling.

- Methods

This retrospective study (HCL and Centre des Massues – Lyon) included 377 patients, representing 445 cases. The objective was to assess the safety and tolerability of GlassBone™ Injectable Putty (GB-IP) under its normal conditions of use in spinal pathologies with a minimum setback of 12 months (France).

- Results

- Performance – No performance metrics (fusion rate or clinical outcomes) were explicitly reported
- Safety – The main complications noted postoperatively concerned 3.5% of infection (ISO) and during follow-up 6% of mechanical complications. These complications were not related to the substitute.

- Conclusion

This large retrospective study confirms the good safety and tolerability profile of GlassBone™ Injectable Putty in spinal applications, with a low rate of complications unrelated to the device.

ii. Indications – Spinal deformities: Children and adolescent idiopathic scoliosis

Surgical treatment of idiopathic scoliosis in children and adolescents by posterior vertebral instrumentation, arthrodesis and fusion of the instrumented segments with the GlassBone™-Injectable Putty (GlassBone™-IP). The study is finished and Pr Courvoisier have published in 2023 (see previous part).

iii. Indications – Spinal pathologies

- Surgery

Patients underwent surgical treatment for degenerative lumbar pathologies using a combined arthrodesis approach. The procedure involved the placement of an interbody fusion cage, which was filled with GlassBone™ Injectable Putty (GlassBone™-IP) to promote vertebral fusion and stabilize the lumbar segment.

- Methods

A prospective study (grade B) was conducted in Pierre Wertheimer neurological hospital (Lyon). This study assesses GlassBone™ Injectable Putty (IP) synthetic bone substitute in real life and aims to provide sufficient evidence of the device's clinical performance and safety. A total of 50 patients operated for degenerative lumbar pathology requiring arthrodesis by Prof. Cédric Barrey between 2019 and 2022 were included in the study. Mean age was 49.5 ± 13.65 years, with a majority of women (60%) and a mean BMI of 25.02 ± 4.32 kg/m². The main surgical indications were spondylolisthesis (54%), stenosis (26%) and disc herniation (20%), with a predominance of interventions at the L5-S1 level (76%).

- Results

- Performance – At 12 months, fusion on scanner(N=43) was achieved in 97.7% of patients with only one pseudoarthrosis. Low back pain (VAS/10) decreased significantly, from 6.9 ± 1.88 preoperatively to 3.49 ± 2.58 at 12 months ($p < 0.001$).
- Safety – The post-operative complication rate was low (4%) and unrelated to the medical device, including pedicle screw malposition and hemorrhage.

- Conclusion

Safety was confirmed because no serious adverse events occurred and adverse events which was detected were not related to the device. Performance was confirmed with a good fusion rate.

iv. Indications – Spinal pathologies

- Surgery

Patients underwent surgical treatment for degenerative lumbar pathologies using a combined arthrodesis approach. The procedure involved the placement of an interbody fusion cage, which was filled with GlassBone™ Injectable Putty (GlassBone™-IP) to promote vertebral fusion and stabilize the lumbar segment.

- Methods

A observational, prospective study (grade B) was conduct in Massue's center (Lyon). This study assesses GlassBone™ Injectable Putty (IP) synthetic bone substitute in real life and aims to provide sufficient evidence of the device's clinical performance and safety. There are 37 patients who was included in the study. The study stopped before reaching the expected number of patients. Mean age was 53.3 years [min 33 – max 78], with a

majority of women (73%) and a mean BMI of 26 kg/m2 [min 14 – max 33.6]. The main surgical indications were degenerative disc disease (84%). At 12 months, fusion on scanner was achieved in 94% of patients.

- Results

- Performance – At 12 months, fusion on scanner was achieved in 94% of patients. Low back pain (VAS/10) decreased significantly, from 7.10 [min 3 – max 10] preoperatively to 4.1 at 12 months ($p < 0.001$).
- Safety – The post-operative complication rate was low, no substitute-related complications occurred. One patient suffered an infection (ISO) after surgery and was resumed unrelated to the bone substitute.

- Conclusion

The results obtained in this study confirm that the benefits provided by the GlassBone™ Injectable Putty device remain greater than the potential risks. No new damage has been identified and the calculation of risk levels is not impacted. Safety was confirmed because no serious adverse events occurred and adverse events which was detected were not related to the device. Performance was confirmed with a good fusion rate.

Although the initial target was to enroll 50 patients anticipating possible losses to follow-up, the study was able to include 37 participants, corresponding to 88% of the minimum required sample size of 42 subjects. While this recruitment shortfall may limit the statistical power for confirming the primary endpoint, the data collected remain robust enough to support meaningful descriptive and exploratory analyses. These analyses contribute valuable information regarding the effectiveness of the bone substitute in adult patients undergoing lumbosacral arthrodesis via a combined surgical approach (posterior followed by anterior). In accordance with ethical principles and good clinical practice, analysing the available data is considered appropriate in order to maximize the scientific value of the study and honor the contribution of enrolled participants. The reduced sample size and its implications will be explicitly acknowledged in the interpretation of results, which will be presented with the necessary methodological caution.

v. Indications – Spinal pathologies

- Surgery

Patients underwent surgical treatment for degenerative lumbar pathologies using a combined arthrodesis approach. The procedure involved the placement of an interbody fusion cage, which was filled with GlassBone™ Injectable Putty (GlassBone™-IP) to promote vertebral fusion and stabilize the lumbar segment.

- Methods

A retrospective study (grade C) was to conduct in Clinique de la Sauvegarde (69). This study assesses GlassBone Injectable Putty (GB-IP) synthetic bone substitute in real life and aims to provide sufficient evidence of the device's clinical performance and safety. 56 cases who had undergone spine surgery with GlassBone Injectable Putty bioactive glass between January 2021 and August 2023 treatment of degenerative thoracic and/or lumbar pathologies. The population represented 33 women (59%) and 23 men (41%). The pathologies concerned are 73% discopathies, 21% spondylolisthesis, 4% stenosis and 2% pseudoarthrosis.

- Results

- Performance – Pain was improved at 12 months in 92% of cases and bone fusion at 12 months in 91.1% of cases.
- Safety – A total of 12.5% of complications were found in 7 cases for 5 patients.

- Conclusion

Safety was confirmed because no serious adverse events occurred and adverse events which was detected were not related to the device. Performance was confirmed with a good fusion rate and an improvement of pain.

b) Cranio maxillo facial

i. Indications – Periodontal reinforcement

- Surgery

GlassBone™ Injectable Putty (GB-IP) was used under its normal conditions of use in mineralized periodontal reinforcement

- Methods

This prospective study (HCL Sud) was conducted with the aim of confirming the safety and performance of with a conventional follow-up of 10 months (France). Thirty-one patients were enrolled in this study; the average age is 32.5 years with a distribution of 24 women and 7 men.

- Results

- Performance – The preoperative mean is significantly different with an increase in the thickness of the alveolar bone of 0.95 mm compared to the postoperative ($p < 0.0001$). A total of 93 measurements to assess marginal tissue recessions were made and the average of the differences is 1.95 ± 0.35 mm ($p < 0.0001$). For all patients (100%), the periodontium became resistant and thick
- Safety – No product-related adverse events occurred.

- Conclusion

GlassBone™ Injectable Putty demonstrated both good performance and a favorable safety profile in periodontal reinforcement procedures, contributing to increased bone thickness and improved gingival tissue condition without adverse effects.

ii. Indications – Surgically created bone defects for cranial therapies – Evaluation of complications and bone filling

- Surgery

Patients underwent caniotomy for the treatment of various cranial pathologies. GlassBone™ Injectable Putty was not used to treat the pathologies but to help to fill the bone defects that were created to reach the operative site.

Evaluation of complications and bone filling during the treatment of surgically created bone defects for cranial therapies. (HCL Lyon) Not Published.

- Methods

This is a retrospective study that was conducted in February 2022 including 52 patients. The safety and performance of bioactive glass have been evaluated. Follow-up evaluations were conducted at 3 and 12 months postoperatively.

- Results

- Performance – No loss of filling was to be noted except for one patient where a cranial deformation was noted at 12 months postoperatively. No revision surgery due to filling was necessary.
- Safety – No complications occurred after surgery, GlassBone™ IP was well fill in the defect with sufficient quantity. Complications occurred during the follow up: scalp paraesthesia (2%), infection (2%), deficit/nervous disorder (8%) at 3 months and 8% of deficit/nervous disorder at 12 months. No allergy was noted.

- Conclusion

GlassBone™ IP is safe and effective when filling burr holes since its use in 2018.

iii. Indications – Orthognathic surgery, maxillary repositioning – Performance and safety of Aktibone

- Surgery

Patients underwent orthognathic surgery for maxillary repositioning. Aktibone Injectable Putty was used to fill bone defects related to maxillary and periodontal pathologies, including facial fractures (15%) and congenital conditions (85%). The injected volume ranged from 1 cc to 10 cc.

- Methods

This retrospective study was conducted on January 2022 . Eighty-two patients were included in this study; average age is 32 years old with a distribution of 48 women (58%) and 34 men (42%) and 26 smokers (32%). Data from clinical follow ups including bone union, side effects, pain were analysed. The safety and performance of bioactive glass have been evaluated.

- Results

- Performance – At 6 months after surgery, pain improved in 80% of cases. 91% have an acquired bone fusion, 7% have partial fusion and 2% have a non-union. 91% have a good soft tissue support with an excellent aesthetic outcome. Aktibone completely filled the osteotomy sites in 71 (87%) patients and 100% have a resistant periodontium (reflecting a bond between the underlying bone and the gum). The final healing of all the patients treated with Aktibone injectable putty for osteotomy site grafting was very promising. The shape of the mandibular body was retained very well.
- Safety – Only 1 (2.5%) inflammation of the surgical site and 1 (2.5%) partial healing was observed, unrelated to Aktibone IP

- Conclusion

Aktibone injectable putty providing reliable long-term bone regeneration at the osteotomy site with special emphasis to the inferior mandibular border followed by an excellent aesthetic outcome

c) Orthopaedic

i. Indications – Bone defects

- Surgery

Treatment of traumatic or surgical bone defects in the tibia, ankle, or foot with GlassBone™ Injectable Putty (GlassBone™ IP). GlassBone™ Injectable Putty has been used to fill a surgically created bone defect (tibial), a non-union bone defect or inter space in arthrodesis fusion. Evaluation of complications and bone healing. Meusnier T. and Mukish P., 2022. Not published.

- Methods

This retrospective study was conducted since January 2022 to March 2022 and included 103 patients. Data from clinical follow ups including side effect, pain, mobility were analysed. The safety and performance of bioactive glass have been evaluated.

- Results

- Performance – Regarding the pain, 51.6% have less intense pain in comparison with the preoperative visit, in the foot cohort. Moreover, more than 50% of patients have better mobility. In the foot cohort, 26% of pseudarthrosis was highlighted.
- Safety – On the 103 treated patients, only 2 patients declared a surgical site infection in the foot cohort and none in the tibial cohort. Regarding more general complications, 23.6% (deformation, arthropathy, amputation, revision surgery) was highlighted for patients in the foot cohort and 2.9% for the tibial cohort. Moreover, more than 50% of patients have better mobility. Safety and quality of life complain with acceptability criteria.

- Conclusion

GlassBone™ Injectable Putty appears to be a generally safe and well-tolerated option for managing bone defects in the tibia, ankle, and foot. While outcomes in the tibial cohort were favorable, the higher rate of complications and pseudarthrosis in the foot cohort suggests that clinical context and patient-specific factors should be carefully considered.

ii. Indications – Filling after tumour resection – Performance and safety of Aktibone

- Surgery

Patients undergone tumour surgery. Aktibone Injectable Putty has been used to fill bone defects due to resection of benign (63%), monostatic (3%), polystatic (12%) and malignant (21%) tumours localized in tibia (12%), hand (15%), femur (33%), foot (18%), pelvis (18%) and humerus (3%)

- Methods

This retrospective study was conducted on January 2022 and included 33 patients, average age is 41 years old [range: 11-75] with a distribution of 19 women (58%) and 14 men (42%) and 8 smokers (24%). Data from clinical follow ups including bone reconstruction, side effects (complications and recurrence), activity and weight bearing were analysed. The safety and performance of bioactive glass have been evaluated. The volume of Aktibone injected ranged from 3 cc to 20 cc (easy handling and proper injectability in all cases).

- Results

- Performance – At 6 months after surgery, 88 % of patients have an improvement of pain. 88% have an acquired bone union, 9% have partial fusion and 3% have a non-union. There was no leakage of Aktibone injectable putty outside the bone. The VAS score decreases from 5 points to 2 points at 6 months. MSTS (functional improvement) score was inscrease -31 at 6 months.
- Safety – Only 2 (6.1%) inflammation of the surgical site were observed, unrelated to Aktibone IP. Neither allergic symptoms, abnormal wound healing nor infections were observed.

- Conclusion

Aktibone Injectable Putty can be successfully used as a bone substitute in patients with various bone tumors. Aktibone IP can provide an effective and long-term solution for reconstructive procedures following curettage of bone tumors, is easy to use, safe and well tolerated by patients. New bone formation was clearly demonstrated in all cases. Aktibone Injectable Putty can provide a safe and effective alternative to autograft and allografts.

iii. Indications – Osteomyelitis – Performance and safety of Aktibone

- Surgery

Patients underwent surgical debridement for osteomyelitis, with bone defects filled using Aktibone Injectable Putty (45S5 bioactive glass). he infected sites were mainly located in the femur (70.8%), tibia (14.6%), and humerus (14.6%).

- Methods

This retrospective study was conducted on January 2022 and included 48 patients; average age is 57.9 years old [range: 27-76] with a distribution of 19 women (39.6%) and 34 men (60.4%) and 16 smokers (33.3%). Data from clinical follow ups including bone recmodeling, maintenance of bone volume and side effects (complications and recurrence) were analysed. The safety and performance of bioactive glass have been evaluated.

The main isolated pathogen is *Staphylococcus aureus* (62.5%). According to Cierny–Mader classification, anatomic osteomyelitis is type 3 (localized osteomyelitis- 60.4%) and 4 (diffuse osteomyelitis- 39.6%). The injected volume ranged from 5 cc to 10 cc.

- Results

- Performance – At 12 months after surgery, 100% have a maintenance of bone volume and 91.6% of patients have an acquired bone remodelling on bone defect.
- Safety – Only 4 patients have infection (2 resolved and 2 ongoing) were observed, unrelated to Aktibone IP.

- Conclusion

The use of Aktibone in a one-stage procedure, with no second operation required and no harvesting of autologous graft from the iliac crest, makes Aktibone IP as a cost-effective, as well as a rapid method in the treatement of osteomyelitis. It can provide a safe and effective alternative to autograft and allografts. Aktibone IP can provide an effective and long-term solution for reconstructive procedures following curettage of infected bone and it safe and well tolerated by patients and with successfully remodelled bone defect.

4. Overall Summary of Clinical Performance and Safety

The clinical claimed clinical performance is the filling, reconstruction and / or fusion of bone defects allowing the regeneration of the bone. The claimed performance[1] is consistent with the results we currently have:

Reference	Device's form	Population	Indication	Performance (%)	Follow-up (months)
Al Tamami et al._2020	Injectable Putty	Adult and child	Filling after removal of cholesteatoma	100% filling	12
RPM Putty (Straub_2020)	Injectable Putty	Adult	Filling and reconstruction due to maxilla and periodontium pathologies	100% reconstruction	10
HCL spine	Injectable Putty	Adult	Fusion or reconstruction of deformities and degenerative diseases in spine	97.7% fusion	24
Massues spine	Injectable Putty	Adult	Fusion or reconstruction of deformities and degenerative diseases in spine	94% fusion	12
ACITYAD	Injectable Putty	Adult	Fusion or reconstruction of deformities and degenerative diseases in spine	91.1% fusion	12
Szadkowski_2022	Injectable Putty	Adult	Fusion or reconstruction of deformities and degenerative diseases in spine	96% fusion	14
Fares 2023	Injectable Putty	Adult	Filling after surgical defect	100% filling	12
SCOTYPE (Courvoisier et al. 2023)	Injectable Putty	Children	Fusion or reconstruction of deformities and degenerative diseases in spine	100% fusion	12
MIOTYAD	Injectable Putty	Adult	Fusion or reconstruction of deformities and degenerative bone pathologies in orthopedic	100% filling 26% pseudarthroses	12

[1] Only the data with the performance claimed by the manufacturer were used.

Reference	Device's form	Population	Indication	Performance (%)	Follow-up (months)
CRANTYAD	Injectable Putty	Adult	Filling after surgical bone defect (donor sites after removal of autograft, trepanation, …)	100% filling	12
Osteomyelitis	Injectable Putty	Adult	Filling and reconstruction of bone defects due to resection of tumors, cyst or infection and in case of prosthetic revision	100% filling 91,6% reconstruction	12
Tumor	Injectable Putty	Adult and child	Filling and reconstruction of bone defects due to resection of tumors, cyst or infection and in case of prosthetic revision	88% reconstruction	6
MAXTYAD	Injectable Putty	Adult	Filling and reconstruction due to maxilla and periodontium pathologies	91% reconstruction	6

Current clinical results indicate that the benefits far outweigh the risks since the only risk associated with the identified device would be allergy

	Benefits	Risk
Manufacturer's claim	- No bone sampling from patient - Improved quality of life	Allergic
Available performance data	- Improvement in quality of life: improvement in EVA and ODI scores - No bone harvest	No complications related to GlassBone™ Injectable Putty substitute

5. Ongoing or planned post marketing clinical follow-up

The table below lists all ongoing and planned studies or registers concerning this medical device.

Destination	Indication	Statue	Grade	Objective
Register				
Ortho	Trauma	Ongoing	-	Confirm indications and safety per operatively.
Studies in progress				
Cervical spine (HCL Lyon)	Deformities and degenerative diseases in spine	Ongoing 4/50	B	- Performance evaluation via analysis of fusion in ACDF - Evaluation of tolerance through analysis complication rate
Cervical spine (Foch hospital and Rotschild hospital (Paris))	Deformities and degenerative diseases in spine	Ongoing 1/50	B	- Performance evaluation via analysis of fusion in ACDF - Evaluation of tolerance through analysis of complication rate
Ortho	Tibial bone defect	Ongoing 32/50	B	- Evaluation of filling and bone remodelling - Evaluation of tolerance via complication rate analysis via radiographic and CT analysis
ORL	Cholesteatoma	Ongoing 14/50	B	- Evaluation of tolerance through complication rate analysis - And performance through filling analysis
Ortho	Diabetic foot infection – osteomyelitis	Ongoing 13	C	Retrospective study. - Performance evaluation via healing rate and non recidive Tolerance via complications rate
Upcoming clinical investigations				
Surgical defect CMF	Surgical defect cranio (burr holes)	Forthcoming 0/45	B	- Performance evaluation via bone consolidation in surgical bon defect and bone filling - Evaluation of tolerance through analysis of complication rate
Ortho – Cyst	Unicameral bone cyst	Forthcoming TBD	TBD	- Evaluation of filling, bone reconstruction and bone healing - Evaluation of tolerance via complication rate analysis and imagery

For each study, a follow-up of complications is planned throughout the duration of the study. Events should be reported to NORAKER at any time. In addition, post-market surveillance data and other clinical data that will be collected will be incorporated as part of the annual updates of the clinical assessment.

VI. Other therapeutic solutions

Grafts are used when conservative treatments (first line approaches when pathologies are not severe) have failed and when surgery is required. In this case, they are mainly used in combination with others implants such as rods, screws, plates and prothesis. They can also be used alone or not at all. Their mains functions (prevent progression of disease, mechanical support etc.) are different as bone grafts functions. Thus, these alternative treatments cannot be compared with bone grafts. They are considered as complementary implants
Likewise, drug treatments, chemotherapy, radiotherapy, physiotherapy… are complementary and can't be considered as a total alternative solution.
Therapeutic alternatives to GlassBone Injectable Putty are autologous bone, allograft, xenograft, and other families of synthetic substitutes.

The gold standard remains the autologous bone but involves a sampling site on the patient and therefore a second surgical site that can cause additional complications: pain, infection, fracture, loss of sensation or hematomas. These complications, the lengthening of the operating time, the limited quantity and the variable quality of the available material are the main limitations of autologous transplantation, leading professionals to resort to bone substitutes. The most common options for replacing autograft are: allogeneics, xenografts and synthetic bone substitutes.

Allografts are tissues of human origin and are distributed by tissue banks and are subject to authorization. Xenografts are made from non-viable tissues of animal origin, stripped of their bone marrow, or derivatives made non-viable. They are of various origins: coral, cuttlefish, mammals. Most bone substitutes of animal origin come from cattle. The risk of pathogen transmission is not excluded.

As regards synthetic substitutes, they do not contain any derivative or tissue of biological origin and are not derived from such derivatives. Their composition varies (calcium phosphate, calcium sulfate, bioactive glass...) and can be absorbable or non-absorbable

GlassBone Injectable Putty, like other synthetic bone substitutes, makes it possible to overcome the constraints of the sampling site (morbidity of the donor site) and to achieve the expected performance of the gold standard.

This summary table shows the advantages (+) and disadvantages (-) of other available solutions.

	Manipulation	Bioactivity	Transmission of possible pathogens	Availability	Osteoconduction	Osteoinducteur	Bioresorbable
Autograft	-	-	+	-	+	+	-
Allograft	+	-	-	-	+	-	-
Xenograft	+	-	-	+	+	-	-
Synthetic substitute	+	+	+	+	+	-	+ / -
BMP	+	-	-	+	+	+	+
Bioactive glass	+	+	+	+	+	-	+

VII. Suggested profile and training for users

Users are experienced surgeons (orthopaedists, neurosurgeons, cranio-maxillofacial surgeons, stomatologists and ENT surgeons) with bone graft techniques. There is no specific training on the use of the device.

VIII. Reference to harmonized standards and common specifications applied

At the moment of writing this document, no common specification is published on our product, and only a few standards are harmonized according to Regulation 2017/745.

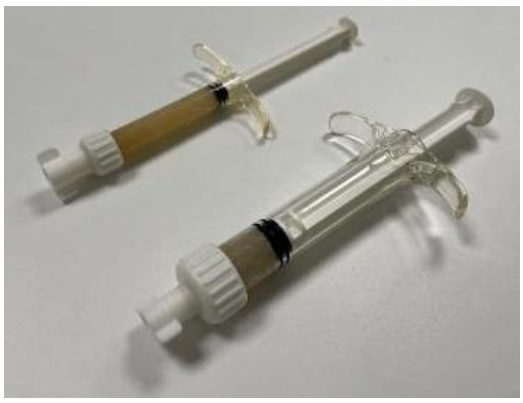
The list of harmonized standards applied is as follows for this device:

Number	Year	Title of standard
EN ISO 11137-1 + A2 (2018)	2015	Sterilization of health care products - Radiation - Part 1 : requirements for development, validation and routine control of a sterilization process for medical devices
EN ISO 11137-2 + A1 (2023)	2015	Sterilization of health care products - Radiation - Part 2: Establishing the sterilization dose
EN ISO 13485 + A11 (2021)	2016	Medical devices, Quality management systems, Requirements for regulatory purposes
EN ISO 14971 + A11 (2021)	2019	Medical devices - Applications of risk management to medical devices
EN ISO 11737-1 + A1 (2021)	2018	Sterilization of medical devices - Microbiological methods Part 1: Determination of the population of microorganisms on products
EN ISO 11737-2	2020	Sterilization of medical devices - Microbiological methods - Part 2 : tests of sterility performed in the definition, validation and maintenance of a sterilization process
EN ISO 10993-9	2020	Biological evaluation of medical devices - Part 9: Framework for identification and quantification of potential degradation products
EN ISO 10993-10	2023	Biological evaluation of medical devices - Part 10: Tests for skin sensitization
EN ISO 10993-12	2021	Biological evaluation of medical devices - Part 12: Sample preparation and reference materials
EN ISO 10993-17	2023	Biological evaluation of medical devices - Part 17: Establishment of allowable limits for leachable substances
EN ISO 10993-18	2020	Biological evaluation of medical devices - Part 18: Chemical characterization of medical device materials within a risk management process
EN ISO 10993-23	2021	Biological evaluation of medical devices - Part 23: Tests for irritation

EN ISO 11607-1	2020	Packaging for terminally sterilized medical devices — Part 1: Requirements for materials, sterile barrier systems and packaging systems
EN ISO 11607-2	2020	Packaging for terminally sterilized medical devices — Part 2: Validation requirements for forming, sealing and assembly processes
EN ISO 15223-1	2021	Medical devices - Symbols to be used with medical device labels, labelling, and information to be supplied - Part 1: General requirements
NF EN 556-1	2024	Sterilization of medical devices - Requirements for medical devices to be labeled “STERILE” - Part 1: Requirements for terminally sterilized medical devices

IX. Device pictures

Picture of the cardboard box containing the pouches and the syringe (unlabelled side)



Picture of a small and medium syringes containing the putty

Picture of a syringe as represented in the brochure

Picture of the pouches (only external pouch is the sterile barrier)

Picture of the cardboard box containing the pouches and the syringe (labelled side)