NORAKER®

THE BIOGLASS® COMPANY

Summary of Safety and Clinical Performance (SSCP)

Surgeons version

GlassBone® Injectable Putty

I. Device identification and general information

1. Brand name

GlassBone® Injectable Putty.

It is available in different volumes: 1cc, 2.5cc, 5cc 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) and Bio Logic Glass Injectable Putty (XBG-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

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3. Unique manufacturer registration number

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, bioactive and absorbable bone substitute, intended for the filling, reconstruction and/or fusion of bone defects or gaps in the skeletal system, in orthopedic surgery, spine, craniomaxillofacial 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, bioactive and absorbable 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 30 521 sales	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 and in orthopedic publication of:

- **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.***

GlassBone Injectable Putty was used in 42 patients (Lyon – France) who underwent mastoid or epitympanic cavity obliteration. 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. No facial paralysis has been reported post-operatively. Postoperative radiological assessments at one year revealed no silent implantation of cholesteatoma or residual disease.

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

This case report is patient undergoing transcanal endoscopic procedure for cholesteatoma with epitympanic obliteration using bioglass. About surgery, a total obliteration of the epitympanum was achieved using 45S5 Bioactive Glass (GlassBone Injectable Putty, NORAKER). The GlassBone Injectable Putty was positioned from the anterior epitympanum to the aditus ad antrum, without bulging in the external auditory canal to prevent any postoperative stenosis.

The preoperative CT scan revealed an anterior and posterior epitympanic cholesteatoma. No pre- or postoperative complication occurred. 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. 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 caliber of the external auditory canal. Imagerie is similar to 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).

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

The aim of this case report is to the results with the use of bioactive glass (GlassBone Injectable Putty) filled into 3D-printed porous titanium implant for the treatment of a bone defect following an extensive resection of the middle third of the clavicle in a patient with Langerhans cell histiocytosis.

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

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.

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

➢ Spine

A recent comparative study in spine surgery (Jean Mermoz Private Hospital, Santy Orthopaedic Center, Lyon, France) shows that the fusion results are comparable between GlassBone Injectable Putty and the autologous bone (iliac crest). The objective was to determine the intra-patient fusion rates of bioactive glass-filled chambers relative to autologous iliac crest bone on computed tomography (CT) at a minimum follow-up of one year after ALIF. Forty patients (58 levels) who underwent fusion at a single level (L5-S1 only) or two-level fusion (L4-L5 and L5-S1) ALIF (Anterior Lumbar Interbody Fusion) were evaluated.

There were two postoperative complications (hematoma, radiculopathy), none of which required reintervention. The results indicate that the bioactive glass allows an equivalent or even better fusion compared to the bone of the autologous iliac crest. The results of this study suggest that for patients undergoing ALIF, bioactive glass can be used as a substitute for the autologous bone of the iliac crest; thus, avoiding an increase in operating time and blood loss, as well as morbidity at the donor site. At the 14±4-month decline, the merger rate was 97% and the complication rate was 5%. At the decline of 17 ± 6 months, the 5 clinical scores improved compared to preoperative values.

- **PMCF Follow-up**

Following the implementation of a post-market clinical follow-up study, 8 studies have been completed:

➢ Spine

In a retrospective study (HCL and Centre des Massues – Lyon), 377 patients, representing 445 cases, were included to confirm 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). The majority of patients had degenerative disc disease and in 97% of cases, GB-IP was used for intervertebral cage filling. 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.

➢ Spine

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). Pr Courvoisier: Not published.

A retrospective study (grade C) was to conduct 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). GlassBone-IP device was used in posterior thoracolumbar spinal fusion for paediatric patients with idiopathic scoliosis. GlassBone-IP is used for fusion of the instrumented vertebrae allowing consolidation of the instrumentation after surgery. The safety and bone fusion are evaluated.

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%). No adverse effects were observed during the follow-ups. 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.

The reduction in Cobb angle for the included patients is significant ($p<0.05$). The loss of correction is 1.8± 5.2°, 1.4 ± 5.7° and 4.8 ± 7.5° for the 3-6, 12- and 24-months postoperative follow-ups compared to the immediate postoperative radiograph measurements. A decrease in pain was observed during the postoperative follow-ups. Indeed, at the preoperative visit, 100% of patients had pain (mild, moderate or severe). At the postoperative follow-up 63% of patients at 3-6 months and 12 months felt no pain and 78% of patients at 24 months. These data show that the surgery had a positive impact on the majority of patients.

- Cranio maxillo facial

A prospective study (HCL Sud) was conducted with the aim of confirming the safety and performance of GlassBone Injectable Putty (GB-IP) under its normal conditions of use in mineralized periodontal reinforcement 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. 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, and no product-related adverse events occurred.

- Cranio maxillo facial

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

This is a retrospective study that was conducted in February 2022 including 52 patients who undergone craniotomy to treat 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. The safety and performance of bioactive glass have been evaluated.

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

- Cranio maxillo facial

Performance and safety of Aktibone in orthognatic surgery for maxillary repositioning. Retrospective study on 82 adult patients.

This is a retrospective study was conducted on January 2022 including 82 patients who has orthognatic surgery for maxillary repositioning. Aktibone Injectable Putty has been used to fill bone defect due to maxilla and periodontium pathologies: face fracture in 15% and congenital pathologies for 85%. Data from clinical follow ups including bone union, side effects, pain were analysed. The safety and performance of bioactive glass have been evaluated.

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%). The injected volume ranged from 1 cc to 10 cc. Only 1 (2.5%) inflammation of the surgical site and 1 (2.5%) partial healing was observed, unrelated to Aktibone IP. 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. 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.

- Ortho

Treatment of traumatic or surgical bone defects in the tibia, ankle, or foot with GlassBone Injectable Putty (GlassBone IP). Evaluation of complications and bone healing. Meusnier T. and Mukish P., 2022. Not published.

A retrospective study was conducted since January 2022 to March 2022 including 103 patients who has undergone foot and ankle surgeries. 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. Data from clinical follow ups including side effect, pain, mobility were analysed. The safety and performance of bioactive glass have been evaluated.

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. 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. Safety and quality of life complain with acceptability criteria. In the foot cohort, 26% of pseudarthrosis was highlighted.

- Ortho: filling after tumour resection

Performance and safety of Aktibone Injectable Putty for bone tumour treatment. Retrospective study on 33 adult and children's patients.

A study was conducted on January 2022 including 33 patients who has 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%). 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.

33 patients were included in this study; average age is 41 years old [range: 11-75] with a distribution of 19 women (58%) and 14 men (42%) and 8 smokers (24%). The volume of Aktibone injected ranged from 3 cc to 20 cc (easy handling and proper injectability in all cases). 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. 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.

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.

- Ortho: osteomyelitis

Performance and safety of Aktibone (45S5, synthetic bone substitute) used in orthopaedic surgery, in osteomyelitis indication. Retrospective study on 48 adult patients.

A retrospective study was conducted on January 2022 including 48 patients treated for osteomyelitis. for maxillary repositioning. Aktibone Injectable Putty has been used to fill bone defects due to debridement of osteomyelitis localized in femur (70.8%), tibia (14.6%), humerus (14.6%). 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.

48 patients were included in this study; 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%). The main isolated pathogen is *Staphylococcus aureus* (62.5%). According to Cierny–Mader classification, anatomic osteomyelitis are type 3 (localized osteomyelitis- 60.4%) and 4 (diffuse osteomyelitis- 39.6%). The injected volume ranged from 5 cc to 10 cc. Only 4 patients have infection (2 resolved and 2 ongoing) were observed, unrelated to Aktibone IP. 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.

The use of Aktibone IP 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.

PMCF studies ongoing:

Two prospective studies are underway, and an interim report has been prepared for each:

- Spine

1. Surgical treatment of degenerative pathologies of the lumbar spine by intersomatic cage filled with GlassBone Injectable Putty in L4-L5 and / or L5-S1 (Centre des Massues, Lyon - France). The main objective is the evaluation of the merger at 1 year. Currently, 31/50 patients are included and among the patients who reached the visit at 1 year, 23/24 (96%) patients have fusion with the presence of a bone bridge. Clinical scores (EVA, ODI, EIFEL) show an improvement in quality of life. One patient suffered from an infection at the surgical site (3%) and no adverse events related to the substitute were identified.

2. Surgical treatment of degenerative pathologies of the lumbar spine by intersomatic cage filled with GlassBone Injectable Putty in L5-S1 (HCL-France). There are also 31/50 patients included and among the patients who reached the visit at 1 year, 12/13 (92%) patients have fusion. Clinical scores (EVA and ODI) show an improvement in quality of life. Two complications occurred: hemorrhagic complication and malposition of the pedicle screws. No substitute-related complications were identified.

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 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
Straub_2021	Injectable Putty	Adult	Filling and reconstruction due to maxilla and periodontium pathologies	100% reconstruction	10
HCL spine (in progress)	Injectable Putty	Adult	Fusion or reconstruction of deformities and degenerative diseases in spine	96% fusion	24
Massues spine (in progress)	Injectable Putty	Adult	Fusion or reconstruction of deformities and degenerative diseases in spine	92% fusion	12
Szadkowski_2021	Injectable Putty	Adult	Fusion or reconstruction of deformities and degenerative diseases in spine	96% fusion	14
SCOTYPE	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
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
Tumour	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				
Spine	Pathologies of the spine	Ongoing	-	Confirm indications and safety per operatively.
Ortho	Trauma	Ongoing	-	Confirm indications and safety per operatively.
Ortho (Brazil)	Tumors Infections Maxilla	Ongoing	-	Confirm indications and safety per operatively.
Prospective studies in progress				
Spine	Degenerative pathology of the lumbar spine	31/50	B	- Performance evaluation via analysis of fusion in L4-L5 and/or L5-S1. - Evaluation of tolerance through analysis of complication rate

	Degenerative pathology of the lumbar spine	31/50	B	- Performance evaluation via analysis of fusion in L4-L5 and/or L5-S1. - Evaluation of tolerance through analysis of complication rate
Ortho	Tibial bone defect	17/50	B	- Evaluation of filling and bone remodelling - Evaluation of tolerance via complication rate analysis via radiographic and CT analysis
Upcoming clinical investigations				
ORL	Cholesteatoma	Forthcoming 0/50	B	- Evaluation of tolerance through complication rate analysis - and performance through filling analysis
Ortho deformation	Lower limb deformation	Forthcoming 0/46	B	- Evaluation of performance with bone consolidation - Evaluation of tolerance
Cervical spine	Deformities and degenerative diseases in spine	Forthcoming 0/50	B	- Performance evaluation via analysis of fusion in ACDF - Evaluation of tolerance through analysis of complication rate
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
Surgical bone defect ortho	Surgical bone defect (after ligament removal (Kenneth Jones technique))	Forthcoming 88 patients	C	- Performance evaluation via bone consolidation in surgical bon defect and bone filling Retrospective comparison with others bone substitute.
Ortho - infection	Diabetic foot surgery	Forthcoming TBD	TBD	- Evaluation of filling and bone reconstruction - Evaluation of infection recurrence - Evaluation of tolerance via complication rate analysis and imagery

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:

Sterilization Standards		
NF EN ISO 11137-1 (+A2 2019)	2016	Sterilization of health care products - Radiation - Part 1: Requirements for development, validation, and routine control of a sterilization process for medical devices
NF 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