Life moves us

SURGICAL TECHNIQUE




SIGNIFY®

Bioactive

GLOBUS MEDICAL

Life moves us

At Globus, we move with a sense of urgency to deliver innovations that improve the quality of life for patients with spinal disorders. We are inspired by the needs of these patients and also the needs of the surgeons and health care providers who treat them.

This passion combined with Globus' world class engineering transforms clinical insights into tangible spine care solutions. We are driven to provide the highest quality products to improve the techniques and outcomes of spine surgery so patients can resume their lives as quickly as possible. We extend our reach beyond our world class implants, instrumentation, and service by partnering with researchers and educators to advance the science and knowledge of spine care.

The energy and enthusiasm each of us bring everyday to Globus is palpable. We are constantly in the pursuit of better patient care and understand that speed is critical because life cannot wait.

GLOBUS
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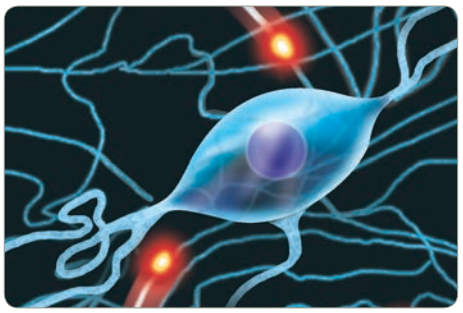
SIGNIFY® Bioactive
DISTINGUISHING CHARACTERISTICS

SIGNIFY® Bioactive's components are designed to recruit and signal osteoblasts that help promote bone formation. SIGNIFY® provides an osteoconductive matrix for new bone growth and contains activating chemistry that attracts and stimulates bone cells.

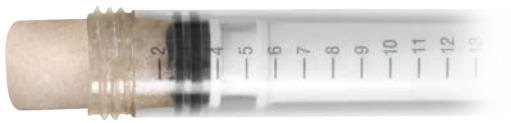
Cell Recruitment and Signaling

The regeneration of damaged tissue involves the migration and proliferation of osteoblasts to the graft site. Bioglass™ recruits these cells and stimulates the production of growth factors that amplify the activity of osteoblasts responsible for bone formation.[1, 2, 3]



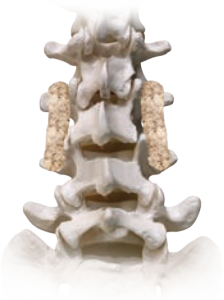
Autograft Alternative

SIGNIFY® may be used right out of the syringe without any mixing with autograft or BMA.



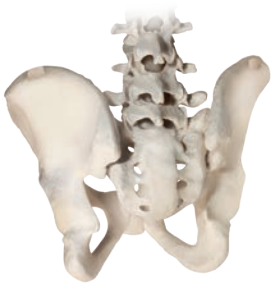
Clinical Applications

Spine
Posterolateral Fusion



SIGNIFY® Crunch

Pelvis
Filling Defects



SIGNIFY® Crunch
SIGNIFY® Putty
SIGNIFY® Gel

Extremities
Filling Defects

SIGNIFY® Crunch
SIGNIFY® Putty
SIGNIFY® Gel

Indications

SIGNIFY® Bioactive is intended for use as a bone void filler for voids or gaps that are not intrinsic to the stability of the bony structure. These osseous defects may be surgically created or created from traumatic injury to the bone. SIGNIFY® Crunch is intended to be gently packed into bony voids or gaps of the skeletal system (i.e., the extremities, pelvis, and posterolateral spine). SIGNIFY® Putty and Gel are intended to be gently packed into bony voids or gaps of the skeletal system (i.e., the extremities and pelvis). SIGNIFY® resorbs and is replaced with bone during the healing process.

IMPLANT OVERVIEW

Product Specifications

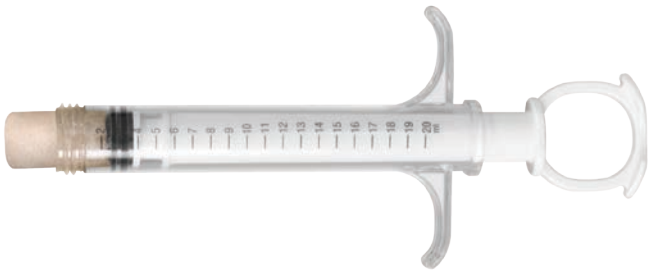
SIGNIFY® is an osteostimulative and osteoconductive bioactive bone void filler and is available in several different forms including putty, gel and crunch.

SIGNIFY® Putty

- Composition: Bioglass™, glycerol, polyethylene glycol (PEG)
- Packaged sterile in a syringe
- Available in three sizes:
  - 2, 5, and 10cc
- Uniform Bioglass™ particle size

SIGNIFY® Gel

- Composition: Bioglass™, glycerol, PEG
- Packaged sterile in a syringe
- Available in three sizes:
  - 2, 5, and 10cc
- Uniform Bioglass™ particle size



SIGNIFY® Crunch

- Composition: Bioglass™, glycerol, PEG
- Packaged sterile in a syringe
- Available in three sizes:
  - 2, 5, and 10cc
- Mixture of Bioglass™ particle sizes

CONTENTS

The Surgical Technique shown is for illustrative purposes only. The technique(s) actually employed in each case always depends on the medical judgment of the surgeon exercised before and during surgery as to the best mode of treatment for each patient. Additionally, as instruments may occasionally be updated, the instruments depicted in this Surgical Technique may not be exactly the same as the instruments currently available. Please consult with your sales representative or contact Globus directly for more information.

SIGNIFY® Bioactive
SURGICAL TECHNIQUE

Step 1 Preoperative Planning

The approximate defect size or volume should be determined prior to surgery through the use of MRI, CT or X-ray. Select the SIGNIFY® implant that will best completely fill the void.

Step 2 Site Preparation

Proper positioning of the patient is determined by the surgical approach. Clean the defect of debris. The surfaces of the defect may be smoothed using an instrument such as a burr. Prepare the walls of the defect that will contact the SIGNIFY® product so that bleeding bone is exposed. Determine the amount of SIGNIFY® to be used based on the size or volume of the defect to be filled.

Step 3 Implant Preparation

SIGNIFY® is provided sterile. Open the sterile packaging.

SIGNIFY® implants may be used alone and do not require any additional preparation.

Step 4 Implant Insertion

Gently pack the defect or the posterolateral spine with SIGNIFY®, avoiding overfilling the bony defect or compressing the treatment site.

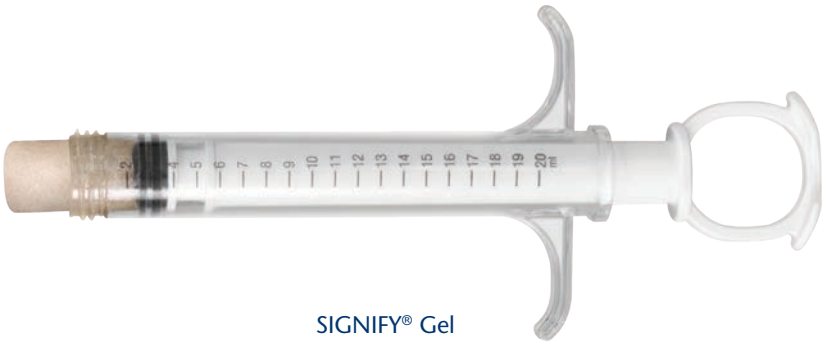
Step 5 Closure

Remove any excess SIGNIFY® material. Close the site using standard closure techniques and discard any unused SIGNIFY® product.

Note: SIGNIFY® implants are not intended to provide structural support. Rigid fixation methods are recommended as needed to ensure stabilization of the defect.

SIGNIFY® Putty

SIGNIFY® Crunch



SIGNIFY® Gel

SIGNIFY® IMPLANT SET

SIGNIFY® Implant Set 9112.9001

Implants		Qty
8112.0002S	SIGNIFY® Bioactive Putty, 2cc	2
8112.0005S	SIGNIFY® Bioactive Putty, 5cc	1
8112.0010S	SIGNIFY® Bioactive Putty, 10cc	2
8112.0102S	SIGNIFY® Bioactive Gel, 2cc	2
8112.0105S	SIGNIFY® Bioactive Gel, 5cc	1
8112.0110S	SIGNIFY® Bioactive Gel, 10cc	1
8112.0202S	SIGNIFY® Bioactive Crunch, 2cc	2
8112.0205S	SIGNIFY® Bioactive Crunch, 5cc	1
8112.0210S	SIGNIFY® Bioactive Crunch, 10cc	2
9112.0001	SIGNIFY® Soft Case	

IMPORTANT INFORMATION ON SIGNIFY® BIOACTIVE

DESCRIPTION

SIGNIFY® Bioactive is a resorbable bone void filler for the repair of bony defects. It is an osteoconductive and osteostimulative material that guides bone regeneration. When SIGNIFY® is placed in direct contact with host bone, new bone grows in apposition to the implant. As the implant resorbs, bone and other connective tissues grow into the space previously occupied by SIGNIFY®.

SIGNIFY® implants consist of Bioglass™ (per ASTM F1538), polyethylene glycol (PEG), and glycerol, and is available in putty, gel, and crunch forms to accommodate surgical and anatomical needs.

INDICATIONS

SIGNIFY® Bioactive is intended for use as a bone void filler for voids or gaps that are not intrinsic to the stability of the bony structure. These osseous defects may be surgically created or created from traumatic injury to the bone. SIGNIFY® Crunch is intended to be gently packed into bony voids or gaps of the skeletal system (i.e., the extremities, pelvis, and posterolateral spine). SIGNIFY® Putty and Gel are intended to be gently packed into bony voids or gaps of the skeletal system (i.e., the extremities and pelvis). SIGNIFY® resorbs and is replaced with bone during the healing process.

WARNINGS

SIGNIFY® implants are not designed with sufficient mechanical strength to support reduction of a defect site prior to soft and hard tissue ingrowth. Rigid fixation methods are recommended as needed to ensure stabilization of the defect. Complete postoperative wound closure is essential.

SIGNIFY® Putty and Crunch are intended for manual application and are not intended for injection through a constrained opening or under high pressure. SIGNIFY® Gel may be injected into the desired location. High pressure injection of SIGNIFY® should not be conducted as pressurization in closed cavities can lead to device extrusion beyond the intended application site, which could damage surrounding tissue, or to embolization of fat or the device into the bloodstream.

Packaging should be intact up on receipt. Damaged packages and/or contaminated products should not be used and should be returned to Globus Medical.

PRECAUTIONS

SIGNIFY® Bioactive is intended for use by surgeons familiar with bone grafting techniques. If fixation is used, the labeling for the use of the fixation system chosen should be followed and the fixation must gain purchase in the host bone. Standard postoperative practices for the treatment and rehabilitation associated with bone grafting must be strictly followed.

Mental or physical impairment which compromises a patient's ability to comply with necessary limitations or precautions may place that patient at a particular risk during postoperative rehabilitation.

A successful result is not always achieved in every surgical case. This is particularly true in spinal surgery where many extenuating circumstances may compromise the results.

As with any surgical procedure, care should be demonstrated in treating patients with preexisting conditions that may impact the success of the surgical procedure. This includes patients with bleeding disorders of any etiology, long-term steroid therapy, immunosuppressive therapy, or high dose radiation therapy.

Use this device as supplied and in accordance with the handling and use information provided below.

CONTRAINDICATIONS

SIGNIFY® must not be used in patients with a history of anaphylaxis or a history of multiple allergies.

Conditions representing relative contraindications include:

1. Severe neurological or vascular disease
2. Hypercalcemia
3. Pregnancy
4. Cases of fracture fixation or where load support is required, unless standard internal or external stabilization techniques are followed to obtain rigid stabilization in all planes
5. Systemic and/or metabolic disorders that affect the bone or wound healing
6. Conditions in which general bone grafting is not advisable
7. Local infection
8. Any patient unwilling to follow postoperative instructions
9. Vertebroplasty or kyphoplasty procedures
10. To gain screw purchase or to stabilize screw placement
11. Any case not described in the indications

POTENTIAL ADVERSE EVENTS

Possible complications are the same as to be expected of autogenous bone grafting procedures and include but are not limited to:

1. Deformity of the bone at the surgical site
2. Fracture or extrusion of the SIGNIFY® implant(s), with or without generation of particulate debris
3. Wound complications including hematoma, site damage, infection (superficial, deep or deep with osteomyelitis), bone fracture, and other complications common to any surgical procedure
4. Incomplete, or lack of, osseous ingrowth into bone void, as possible with any bone void filler
5. Delayed union or failure of fusion
6. Transient hypercalcemia
7. Loss of bone graft, graft protrusion and/or dislodgement, which could damage surrounding tissue
8. General complications that may arise from anesthesia and/or surgery

Occurrence of one or more of these conditions may require an additional surgical procedure and may also require removal of the bone void filler.

OSTEOSTIMULATION

SIGNIFY® is an osteostimulative and osteoconductive device. Osteostimulation is defined as an accelerated bone formation process, characterized by the active stimulation of osteoblast proliferation and differentiation in an osseous defect. This stimulatory action has been demonstrated during in vivo tests of Bioglass™ particulate to be more rapid than simple osteoconduction.[1,2] These tests have been supported by in vitro cell culture tests, which demonstrate the mechanisms of cell stimulation as being the result of cellular interaction with the ionic dissolution products released from Bioglass™ particulate during its absorption.[3-6] Clinical data on this acceleration of bone formation in the human has not been established.

SIGNIFY® has only been demonstrated to form bone in osseous defects. SIGNIFY® therefore is not osteoinductive. Such osteoinductive devices can be characterized by their ability to form new bone tissue in non-osseous (soft-tissue) sites.

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2. Fujishiro Y, Hench LL, Oonishi H: *Quantitative Rates of In vivo Bone Generation for Bioglass and Hydroxyapatite Particles as Bone Graft Substitute.* J Mater Sci Mat Med 8:649-652, 1997.

3. Vrouwenvelder WCA, Groot CG, de Groot K: *Histological and Biochemical Evaluation of Osteoblasts Cultured on Bioactive Glass, Hydroxyapatite, Titanium Alloy and Stainless Steel.* J. Biomed Res 27:465-475, 1993.

4. Xynos ID, Hukkanen MVJ, Batten JJ, Buttery LD, Hench LL, Polak, JM: *Bioglass 45S5 Stimulates Osteoblast Turnover and Enhances Bone Formation In vitro: Implications and Applications for Bone Tissue Engineering.* Calcif Tissue Int 67:321–329, 2000.

5. Xynos ID, Edgar AJ, Buttery LDK, Hench LL, Polak JM: *Ionic Products of Bioactive Glass Dissolution Increase Proliferation of Human Osteoblasts and Induce Insulin-Like Growth Factor II mRNA Expression and Protein Synthesis.* Biochem Biophys Res Comm 276:461-465, 2000.

6. Bosetti M, Cannas M: *The Effect of Bioactive Glasses on Bone Marrow Stromal Cells Differentiation.* Biomaterials 26(18):3873-3879, 2005.

CONTACT INFORMATION

Globus Medical may be contacted at 1-866-GLOBUS1 (456-2871). A surgical technique manual may be obtained by contacting Globus Medical.

HANDLING AND USE

SIGNIFY® should be implanted into bony defects or for posterolateral spine fusion according to the following technique. Prepare the wall of the defect that will contact the SIGNIFY® product, as needed. Gently pack the site but avoid overfilling the bone void or compressing the treatment site. Remove excess material from the treatment site. Close the site using standard closure techniques and discard any unused SIGNIFY® product.

STORAGE

Do not freeze or expose to extreme heat. Store at ambient temperature.

STERILIZATION

SIGNIFY® Bioactive is provided sterile in an unopened and undamaged package. This product must be used on or before the expiration date that is provided on the package label. This device is for single patient use and should never be reused.

CAUTION: Federal (U.S.A) Law Restricts this Device to Sale by or on the order of a Physician.

SYMBOL TRANSLATION			
QTY	QUANTITY	STERILE R	STERILIZED BY IRRADIATION

DI169A
REV C

REFERENCES

[1] Xynos ID, Edgar AJ, Buttery LDK, Hench LL, Polak JM. *Ionic products of bioactive glass dissolution increase proliferation of human osteoblasts and induce insulin-like growth factor II mRNA expression and protein synthesis.* Biochem. Biophys. Res. Commun. 2000; 276: 461–465.

[2] Xynos ID, Hukkanen MV, Batten JJ, Buttery LD, Hench LL, Polak JM. *Bioglass 45S5 Stimulates Osteoblast Turnover and Enhances Bone Formation In Vitro: Implications and Applications for Bone Tissue Engineering.* Calcif. Tissue Int. 2000; 67: 321–329.

[3] Ducheyne P, Qiu Q: *Bioactive ceramics: the effect of surface reactivity on bone formation and bone cell function.* Biomaterials 1999; 20: 2287–2303.

Notes

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