Augment® Bone Graft
Package Insert – English

Augment® Bone Graft (β-TCP/rhPDGF-BB) is a synthetic graft substitute composed of beta-tricalcium phosphate granules and recombinant human platelet-derived growth factor BB.

- Beta-tricalcium phosphate (β-TCP) is a highly porous, resorbable and osteoconductive scaffold that provides a framework for bone ingrowth, aids in preventing soft tissue infiltration and promotes stabilization of the blood clot. The particle size ranges from approximately 1000 to 2000 microns in diameter.
- Recombinant human platelet-derived growth factor BB (rhPDGF-BB), also known as becaplermin, acts by stimulating the recruitment and proliferation of a variety of cell types, including bone cells and mesenchymal stem cells, while also promoting revascularization. rhPDGF-BB is a biosynthetic protein that is produced using recombinant DNA technology. rhPDGF-BB is similar in structure and activity to endogenous PDGF-BB that is naturally found in the body.

The components of Augment Bone Graft are provided in two sterile trays:

- The vial tray contains one, two or three vials, dependent on the kit configuration, aseptically filled with rhPDGF-BB solution (0.3mg/ml). The vial tray is sterilized by ethylene oxide.
- The cup tray contains a sealed cup filled with dry β-TCP granules. The volume of granules will vary depending upon the kit configuration. The cup tray is sterilized by gamma irradiation.

At time of use, the two primary components are combined in entirety, mixed and applied to the surgical site.

STORAGE CONDITIONS:
Augment Bone Graft must be stored at refrigerated temperature (2-8°C, 36-46°F). Do not freeze.

INDICATIONS FOR USE:
Augment Bone Graft is indicated for use as a substitute for autograft in foot and ankle fusion procedures that require supplemental graft material, including tibiotalar, talocalcaneal, talonavicular, calcaneocuboid, tarsometatarsal, naviculo-cuneiform, metatarsophalangeal and interphalangeal fusions.

CONTRAINDICATIONS:
- Augment Bone Graft should not be used in patients who have a known hypersensitivity to any of the components of the product or who are allergic to yeast-derived products.
- Augment Bone Graft should not be used in patients with cancer.
- Augment Bone Graft should not be used in the vicinity of a resected or active tumor.
- Augment Bone Graft should not be used in patients who are skeletally immature (<18 years of age or no radiographic evidence of closure of epiphyses).
- Augment Bone Graft should not be used in pregnant women. The potential effects of rhPDGF-BB on the human fetus have not been evaluated.
- Augment Bone Graft should not be implanted in patients with an active infection at the operative site.
- Augment Bone Graft should not be used in situations where soft tissue coverage is not achievable.
- Augment Bone Graft should not be used in patients with metabolic disorders known to adversely affect the skeleton (e.g. renal osteodystrophy or hypercalcemia), other than primary osteoporosis or diabetes.
- Augment Bone Graft should not be used as a substitute for structural graft.

WARNINGS:
- Women of childbearing potential should be advised that antibody formation to rhPDGF-BB or its influence on fetal development have not been assessed. In clinical studies to support the safety and effectiveness of Augment Bone Graft, 74 patients were evaluated for the presence of antibodies to rhPDGF-BB. Antibodies were detected in 9 out of 74 (12%) patients. However, none of the antibodies were found to be neutralizing. The clinical significance of these non-neutralizing anti-bodies is not known.
- The safety and effectiveness of Augment Bone Graft in nursing mothers has not been established. It is not known if rhPDGF-BB is excreted in human milk.
- Women of childbearing potential should be advised to avoid becoming pregnant for one year following treatment with Augment Bone Graft.
- The safety and effectiveness of Augment Bone Graft has not been established in anatomical locations other than the foot or ankle, used in surgical techniques other than open surgical approaches, or combined with autogenous bone or other bone grafting materials.
- Augment Bone Graft does not have any biomechanical strength and must be used in conjunction with standard orthopedic hardware to achieve rigid fixation.
- Augment Bone Graft should be implanted such that it does not prevent bony apposition of the articular surfaces intended for fusion. Over-packing may impair healing and prevent fusion.
- In a retrospective post-marketing study, extended daily use of Regranex® (rhPDGF-BB) in treating fully contacting diabetic foot ulcers, an increased rate of death secondary to malignancies was observed. There was no observed effect on cancer incidence.

PRECAUTIONS:
- Augment Bone Graft should only be used by surgeons who are familiar with bone grafting techniques used in foot and ankle surgery.
- In order to enhance the formation of new bone, Augment Bone Graft should be placed in direct contact with well-vascularized bone. Cortical bone may be perforated prior to placement of the material. In order to optimize bony fusion, Augment Bone Graft should be implanted such that it does not prevent bony apposition of the articular surfaces intended for fusion.
- The β-TCP component is radiopaque, which must be considered when evaluating radiographs as it may mask underlying pathological conditions.
- The safety and effectiveness of repeat applications of Augment Bone Graft has not been established.
- Careful consideration should be given to alternative therapies prior to performing bone grafting in patients who have severe endocrine-induced bone diseases (e.g. hyper-parathyroidism); who are receiving immunosuppressive therapy; or who have known conditions that may lead to bleeding complications (e.g. hemophilia).
- The safety and effectiveness of Augment Bone Graft in pediatric patients below the age of 18 years has not been established.
- Augment Bone Graft is supplied as a single use only kit. Discard any unused material. The individual components of this product should not be used separately. Use a new device for subsequent applications.
- Prior to use, inspect the packaging, vial and stopper for visible damage. If damage is visible, do not use the product. Retain the packaging and contact a representative of BioMimetic Therapeutics, LLC.
- Do not use after the expiration date located on the product carton. The product expires on the last day of the month indicated on the carton label.
- IMMUNOGENICITY: As with all therapeutic recombinant proteins, there is a potential for immune responses to be generated to the rhPDGF-BB component of Augment Bone Graft. The immune response to rhPDGF-BB was evaluated in 74 patients receiving foot and ankle fusions in conjunction with application of the product. In this study population, anti-bodies were detected in 9 out of 74 patients (12%) treated with Augment Bone Graft, but no antibodies were found to be neutralizing. The clinical significance of these antibodies is not known. Antibody levels returned to baseline at follow up visits. The incidence of antibody detection is highly dependent on the sensitivity and specificity of the assay. Additionally the incidence of antibody detection may be influenced by several factors including sample handling, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to Augment Bone Graft with the incidence of antibodies to other products may be misleading.

ADVERSE EVENTS:
- No serious adverse events (SAE's) attributable to Augment Bone Graft have been reported in clinical studies with the product, however patients may experience any of the following adverse events that have been reported in the literature with regard to the use of autograft or bone graft substitute products: swelling, pain, bleeding, hematoma, superficial or deep wound infection, cellulitis, wound dehiscence, incomplete or lack of osseous ingrowth, transient hypercalcemia, neuralgia and loss of sensation locally and peripherally and anaphylaxis.
- Occurrence of one or more of these conditions may require an additional surgical procedure and may also require removal of the grafting material.

The following table (Table 1) was compiled using pooled data obtained from two multi-center clinical studies of Augment Bone Graft conducted in the United States (randomized, controlled 2:1 with autologous bone graft) and Canada (open-label) in patients undergoing foot and ankle fusion procedures. This table contains all of the reported events that were available as of May 1, 2008.

Table 1 – Summary of Adverse Events for All Patients in the Foot and Ankle Fusion Clinical Studies

Body System	Augment N=74	Autograft N=6
Cardiac Disorders	1 (1%)	0 (0%)
Gastrointestinal Disorders	3 (4%)	0 (0%)
General disorders and administration site condition	63 (85%)	4 (67%)
Immune System Disorders	1 (1%)	0 (0%)
Infections and Infestations	12 (16%)	0 (0%)
Investigations	1 (1%)	0 (0%)
Musculoskeletal and connective tissue disorders	16 (22%)	2 (33%)
Neoplasms benign, malignant and unspecified	1 (1%)	0 (0%)
Nervous system disorders	10 (14%)	2 (33%)
Procedural complications	39 (53%)	0 (0%)
Psychiatric disorders	1 (1%)	0 (0%)
Renal and urinary disorders	3 (4%)	0 (0%)
Reproductive system and breast disorders	1 (1%)	0 (0%)
Respiratory, thoracic and mediastinal disorders	2 (3%)	0 (0%)
Skin and subcutaneous tissue disorders	4 (5%)	2 (33%)
Surgical and medical procedures	2 (3%)	0 (0%)
Vascular disorders	1 (1%)	0 (0%)

Due to the small size of the control group relative to the treatment group, direct comparisons cannot be relied upon to determine the relative incidence of adverse events between the two groups.

DIRECTIONS FOR USE:
1) Using sterile technique, transfer the cup (containing the β-TCP granules) and the vial(s) (containing the rhPDGF-BB solution) to the sterile field.
2) Open the cup and transfer the β-TCP granules to a sterile surgical bowl.
3) Using a syringe and needle, draw up the contents of the vial(s) in entirety and transfer all of the fluid to the surgical bowl containing the β-TCP granules. If multiple kits are used (not to exceed 9cc), the contents may be combined.
4) Gently stir the two components together for approximately 30 seconds using a spatula, curette or similar instrument.
5) The mixture should be left undisturbed for 10 minutes before being implanted to ensure optimal saturation the β-TCP particles.
6) The product should be implanted within one (1) hour after mixing the two components.

Any unabsorbed rhPDGF-BB solution should be drawn into a sterile syringe and applied to the surgical site prior to the release of the tourniquet to ensure the graft remains hydrated.

RECOMMENDED TECHNIQUE:
- Debride and decorticate the joint surfaces to expose viable bone.
- Where practical, complete surgical manipulations of the graft site prior to implanting the graft material.
- Irrigate the surgical site.
- Manually pack Augment Bone Graft into all subchondral voids and surface irregularities throughout the joint. NOTE: Overfilling of the osseous defect(s) should be avoided in order to achieve adequate fixation, closure and containment of the material.
- Reduce the joint and apply rigid fixation.
- Pack any remaining Augment Bone Graft around the perimeter of the joint.
- Apply all remaining rhPDGF-BB solution to the surgical site to ensure the graft remains hydrated.
- Carefully layer the periosteal and overlying soft tissue to enclose and contain the graft material. NOTE: Do not irrigate the graft site following implantation of Augment Bone Graft.
- Apply the self-adhesive labels that indicate the lot number of each device to the patient's permanent records.

CLINICAL EXPERIENCE:
In a multi-center clinical study conducted in Canada, 60 patients requiring ankle, hindfoot or midfoot fusion surgery were treated with Augment Bone Graft to facilitate bony healing and union. Success rates for clinical and radiographic endpoints are shown in Table 2 below. Radiographic success, at 9 months, was defined as bridging on at least 2 of 4 radiologic aspects from plain film radiographs. Clinical success indicates that patients did not require and were not recommended for revision surgery within 12 months of the index surgery.

Table 2 – Summary Foot/Ankle Fusion Study Results Canada

	Augment N=60
Radiographic	52/60 (87%)
Clinical	54/60 (90%)

In the United States, a similar multi-center study was conducted. In this investigation, 20 patients requiring hindfoot and ankle fusion surgery were treated with either Augment Bone Graft or autograft in a 2:1 ratio. Success rates for clinical and radiographic endpoints at 9 months are shown in Table 3 below. Radiographic success was defined as bridging on at least 3 of 4 radiologic aspects from plain film radiographs and CT scans. Clinical success is the number and percentage of subjects judged to have complete clinical union.

Table 3 – Summary Foot/Ankle Fusion Study Results United States

	Augment N=14	Autograft N=6
Radiographic	10/14 (71%)	3/4 (75%)
Clinical	11/13 (85%)	6/6 (100%)

SYMBOLS:


Attention, See Instructions for Use


Single Use Only


Expiration Date


Prescription Only


Store at Refrigerated Temperature


Manufacturer


Do Not Use If Package Is Open Or Damaged

Reorder Number

Lot Number

Sterilized by Irradiation

Sterilized by Ethylene Oxide

Sterilized by Aseptic Techniques


Peel Here

Catalog (REF) Numbers

REF	Product
K200-015-00	Augment Bone Graft 1.5 cc Kit
K200-030-00	Augment Bone Graft 3.0 cc Kit
K200-060-00	Augment Bone Graft 6.0 cc Kit
K200-090-00	Augment Bone Graft 9.0 cc Kit

This product is covered by the following Canadian patent: 1,340,846. Other Canadian patents pending.

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Regranex® Gel is a topical ointment containing rhPDGF-BB indicated for the daily treatment of diabetic foot ulcers. Regranex® is a registered trademark of Smith and Nephew pcl.

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