IsoTis

DIRECTIONS FOR USE

OrthoBlast® II

Demineralized Bone Matrix with Cancellous Bone

CAUTION: Federal (U.S.) Law restricts the use of this device to sale by or on the order of a physician.

The Inner Package and its Contents are Sterile
For Single Patient Use on a Single Occasion Only
The demineralized bone matrix (DBM) in this product is derived from voluntarily donated human tissues.

INDICATIONS FOR USE
For orthopedic use, the OrthoBlast® II Paste and Putty are intended for use as an autograft extender (extremities, spine and pelvis) and as a bone void filler (extremities and pelvis) for bony voids or gaps that are not intrinsic to the stability of the bony structure. The OrthoBlast II products are indicated to be packed gently into bony defects of the skeletal system. These defects may be surgically created or from the result of traumatic injury to the bone.

DESCRIPTION
OrthoBlast II is derived from selected donated human bone tissue that has been processed into particles. The particles are subsequently demineralized using a hydrochloric acid process. The demineralized bone matrix (DBM) is combined with a reverse phase carrier, cancellous chips from the same donor, and then formulated to a paste or putty-like consistency.

OrthoBlast II is provided in a sterile, single patient use package. As biological materials, some variations in the product should be expected, such as in appearance and in handling.

CONTRAINDICATIONS
OrthoBlast II is contraindicated where the device is intended as structural support in load-bearing bone and in articulating surfaces. Conditions representing relative contraindications include:
- Severe vascular or neurological disease
- Uncontrolled diabetes
- Severe degenerative bone disease
- Uncooperative patients who will not or cannot follow postoperative instructions, including individuals who abuse drugs and/or alcohol
- Renal impairment
- Active or latent infection in or around the surgical site
- OrthoBlast II Putty contains cancellous particles up to 4 mm in size. Do not use for Dental Applications.
- Polymyxin B Sulfate, Bacitracin, Gentamicin and Iodine are used in the processing of the DBM used in OrthoBlast II Putty and Paste and trace amounts may remain. Since it is impossible to quantify the levels at which any individual may have an allergic response, this product is contraindicated in patients with known sensitivity to these compounds.

PATIENT SELECTION FACTORS
Procedures involving bone grafting can experience highly variable results. Factors to be considered in selecting the bone grafting material and the surgical technique to be utilized are as follows:
- Age of the patient
- Quality of the patient's bone
- Location of the defect
- Anticipated loading conditions
- Proximity of the graft to a suitable blood supply
- Ability to achieve direct apposition of the graft to viable host bone
- Presence/addition of autogenous bone or bone marrow at the graft site
- Elimination of gaps in the graft site
- Ability to suitably stabilize the graft site
- Complete coverage of the graft material to prevent migration

INSTRUCTIONS FOR USE
These instructions are intended as guidelines for the use of OrthoBlast II as a part of established surgical techniques. They are not intended to replace or change standard procedures for treatment of bone defects involving bone grafting and internal fixation. For best results, extreme care should be exercised to assure the correct graft material is selected for the intended application.

PREOPERATIVE PREPARATION
- Aseptic techniques must be adhered to at all times in order to minimize the risk of postoperative complications. The amount of product needed is based on the type of procedure and size of the defect being treated. When OrthoBlast II is being mixed with autograft, a ratio of 1:1 should be used. OrthoBlast II does not require rehydration prior to use.
- Radiographic evaluation of the defect site is essential to accurately assess the extent of the defect and to aid in the selection and placement of OrthoBlast II and fixation devices.
- OrthoBlast II does not possess sufficient mechanical strength to support the reduction of a graft site prior to tissue in-growth. Therefore, anatomical reduction and rigid fixation, in all planes, should be obtained independent of OrthoBlast II.
- For best results, OrthoBlast II must fill the defect and contact as much viable bone as possible.
- OrthoBlast II must not be used to repair bone defects where complete soft tissue coverage cannot be achieved.
- Only experienced surgeons who have had appropriate training and experience in the field of bone graft implant materials and surgery, should use OrthoBlast II.

REMOVING THE PRODUCT FROM PACKAGING
For Putty
1. Peel open outer package.
2. Using aseptic technique, transfer contents to a sterile field.
3. Peel open inner package and remove spatula and vial.
4. Twist off vial lid and remove putty using small spatula or other hand instrument.
5. Discard any unused portion.

For Paste
1. Peel open outer package.
2. Using aseptic technique, transfer contents to a sterile field.
3. Peel open inner package and remove syringe.
4. Remove protective cap from syringe tip.
5. Depress the plunger to extrude the implant material.
6. Discard any unused portion.

POSTOPERATIVE CARE
Postoperative patient management should follow the same regimen as similar cases utilizing autogenous bone grafting. Standard postoperative practices should be followed, particularly as applicable to defect repairs involving the use of fixation devices. The patient should be cautioned against early weight bearing and premature ambulation that could lead to loosening and/or failure of the fixators or loss of reduction.

The length of time a defect should remain in a reduced state of loading is determined by the complexity of the defect site and the overall physical condition of the patient. Hardware should not be removed until the defect is healed.

WARNINGS
- The product must be used prior to the expiration date.
- For single use only.
- Do not re-sterilize.
- Do not use if the packaging has been damaged and/or the product has been compromised. In the event packaging has been compromised, discard the product. Damaged packaging should be returned to the manufacturer.
- Do not use to support reduction of a defect site. Rigid fixation techniques are recommended as needed to assure stabilization of the defect in all planes. Screws must gain purchase in the host bone as opposed to the OrthoBlast II.
- Do not use to repair bone defects where soft tissue coverage cannot be achieved as complete post-operative wound closure is necessary.
- Do not overfill the graft site.

POTENTIAL ADVERSE EVENTS
Surgical procedures involving implantation of bone grafts are associated with the following risks:
- Superficial wound infection
- Deep wound infection with or without osteomyelitis
- Nonunion, delayed union and/or malunion
- Wound dehiscence
- Loss of reduction
- Refracture
- Cyst recurrence
- Hematoma
- Cellulitis

Adverse outcomes attributable to the product must be reported promptly to the manufacturer. If any dissatisfaction with the product performance or packaging occurs, notify IsoTis OrthoBiologics, Inc. immediately and promptly return product and/or packaging.

PRECAUTIONS
- OrthoBlast II is sterile for the duration of the product's shelf life, provided that the package is in its original sealed condition and that it is unopened and undamaged.

- As with all biological products, the tissue in OrthoBlast II has the potential to transmit infectious agents despite processing treatments, extensive donor screening, tissue selection and laboratory testing. To date, there have been no reports of experimental or clinical viral seroconversion attributed to the use of demineralized bone.
- As with any surgical procedure, the possibility of infection exists.
- Although the production technique is designed to eliminate antigenic properties of the product, the possibility of such a reaction is present.
- Once the container seal has been compromised, the tissue product shall be either transplanted, if appropriate, or otherwise discarded.
- Use caution when filling a closed defect. Resistance during extrusion may be an indication of over pressurization. Excessive pressurization of the device could result in fat embolization and/or embolization of the material into the bloodstream.
- When introducing OrthoBlast II, care must be taken to avoid excessive compaction.
- Appropriate placement and/or fixation are critical factors in the avoidance of potentially adverse effects.
- Overfilling the implantation site should be avoided to achieve a tension-free closure of the wound.

HUMAN TISSUE DONOR SELECTION
All tissue used in OrthoBlast II is recovered from donors and by tissue banks in the United States in accordance with regulations and standards established by the U.S. Food and Drug Administration (FDA) and the American Association of Tissue Banks (AATB). The tissue bank (as identified on the product's outer packaging) has evaluated the tissue donor and determined that the donor met suitability criteria that were current at the time. The tissue bank's evaluation included review of the tissue donor's infectious disease test results, consent documents, medical and social interview, assessment of the donor's body, available relevant medical records including previous medical history, laboratory test results, review of postmortem examination results (if applicable) and information from other sources or records which may pertain to donor eligibility including tissue procurement test results. The review did not reveal risk factors for, conditions indicating clinical and/or physical evidence of infectious disease, or communicable disease agents or diseases, including HIV (human immunodeficiency virus) or hepatitis, or risk factors for viral or prion-associated disease transmission as specified in 21 CFR 1271 Subpart C and Appendix II of the AATB standards.

SEROLOGICAL TESTING OF HUMAN TISSUE
All donated human tissue is tested per current FDA and AATB requirements at the time the donor is recovered. Donor blood samples taken at the time of recovery were tested by laboratories registered with the FDA to perform donor testing and certified to perform such testing on human specimens in accordance with Clinical Laboratory Improvement Amendments of 1988 (CLIA) and 42 CFR Part 493, or that has met equivalent requirements as determined by the Centers for Medicare and Medicaid Services (CMS), and were found negative or nonreactive using FDA licensed, cleared or approved, tests for:
- HIV antibodies type 1 and type 2 (anti-HIV-1 and anti-HIV-2)
- HIV-1 Nucleic Acid testing (HIV NAT)
- Hepatitis B Surface antigen (HBsAg)
- Hepatitis B Core Antigen [anti-HBc (IgG and IgM)]
- Hepatitis C Virus Nucleic Acid Test (HCV NAT)
- Hepatitis C Virus Antibody (anti-HCV)
- *Treponema pallidium* (Syphilis)

Additional testing may or may not include the following as applicable:
- Hepatitis B Virus Nucleic Acid Tests (HBV NAT or HIV-1/HCV/HBV NAT])
- Cytomegalovirus (CMV) [IgM anti-CMV and/or IgG anti-CMV]
- Epstein-Barr Virus (EBV) [IgM anti-VCA and/or IgG anti-VCA]
- Human T-Lymphotropic Virus type 1 and type 2 [anti-HTLV-I/II]
- West Nile Virus Nucleic Acid Test (WNV NAT)

The names and addresses of the testing laboratories, the listing and interpretation of all required infectious disease tests, a listing of the documents reviewed as part of the relevant medical records, and the name of the person or establishment determining the suitability of this human tissue are on file at the tissue bank and are available upon request. This tissue has been determined to be suitable for transplantation based on the results of screening and testing.

VIRAL INACTIVATION
The methods for processing of the DBM contained in OrthoBlast II were evaluated for their viral inactivation potential. A selected panel of viruses representing various virus types, sizes, shapes and genomes were evaluated. The viral inactivation testing demonstrated suitable inactivation potential of the processing methods for a wide range of potential viruses. The OrthoBlast II product contains cancellous bone which has been added to the demineralized bone matrix. Since the cancellous bone chips are not demineralized, the degree of viral inactivation of this component is not fully known. The cancellous bone has been processed in antimicrobial, antiviral, and antiseptic solutions for reduction of the risk of transmissible viral diseases from human tissue products. The risk of disease transmission with the cancellous bone component remains low due to multiple safeguards including donor screening, serologic testing, tissue cleaning process, and terminal sterilization of the finished device

OSTEOINDUCTIVE POTENTIAL
The osteoinductive potential of the Demineralized Bone Matrix (DBM) used in OrthoBlast II Putty and Paste is determined via an in vitro assay. Results from the assay were correlated with results from implantation of DBM into an athymic mouse muscle pouch. Analysis of these results shows that the in vitro assay has been validated against the in vivo athymic mouse model and predicts with at least 95% confidence the in vivo osteoinductivity of the test material.

Each lot of DBM incorporated in OrthoBlast II Putty and Paste is evaluated for osteoinductive potential using an in vitro assay. Testing each lot of DBM assures that only DBM with osteoinductive potential is used in OrthoBlast II Putty and Paste. Although DBM used in the final product has been shown to be osteoinductive using an in vitro assay, the combination of DBM, poloxamer and cancellous bone chips has not been evaluated for osteoinductivity; therefore, it is unknown to what extent the formulation components may alter the osteoinductivity of the DBM. Additionally, it is unknown how osteoinductivity of the DBM component, measured via the in vitro assay, will correlate with human clinical performance of OrthoBlast II Putty and Paste.

STERILIZATION
OrthoBlast II has been sterilized by electron beam irradiation. The inner package and its contents are sterile. The package should be inspected prior to use to ensure the sterility barrier has not been compromised. This product is for single use only and must not be re-sterilized. The product must not be used beyond the stated expiration date.

DO NOT RE-STERILIZE

STORAGE
- Store at ambient temperature (15°C to 30°C) in a clean, dry place. The product has been validated to withstand temperatures between -10°C to 35°C during transit.
- Do not refrigerate or freeze.
- Do not expose to extreme heat.
- It is the responsibility of the tissue dispensing service and user (facility/clinician) to maintain the product under appropriate conditions prior to use.
- Discard any unused product.

RECIPIENT TRACING
The FDA requires that allograft tissue be traceable from the donor to the recipient. The tissue bank is responsible for traceability from the donor to the consignee (transplantation facility, clinician or hospital), and the transplantation facility is responsible for traceability to the recipient. A Graft Tracing Record and pre-printed peel-off labels are included with each package of tissue. Record the patient name or ID number, the transplantation facility name and address, the allograft tissue identification information (using the peel-off stickers) and comments regarding the use of the tissue on the Graft Tracing Record. Return the completed form to IsoTis OrthoBiologics and retain a copy in the patient medical record. If the tissue has been discarded, please return the Graft Tracing Record to IsoTis OrthoBiologics with the graft identification information and reason for discard.

PRODUCT INFORMATION DISCLOSURE
IsoTis OrthoBiologics, Inc ("IsoTis") HAS EXERCISED REASONABLE CARE IN THE SELECTION OF MATERIALS AND THE MANUFACTURE OF THESE PRODUCTS. IsoTis EXCLUDES ALL WARRANTIES, WHETHER EXPRESSED OR IMPLIED, INCLUDING BUT NOT LIMITED TO, ANY IMPLIED WARRANTIES OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE. IsoTis SHALL NOT BE LIABLE FOR ANY INCIDENTAL OR CONSEQUENTIAL LOSS, DAMAGE, OR EXPENSE, DIRECTLY OR INDIRECTLY ARISING FROM USE OF THIS PRODUCT. IsoTis NEITHER ASSUMES NOR AUTHORIZES ANY PERSON TO ASSUME FOR IT ANY OTHER OR ADDITIONAL LIABILITY OR RESPONSIBILITY IN CONNECTION WITH THESE PRODUCTS. IsoTis INTENDS THAT THIS DEVICE SHOULD BE USED ONLY BY PHYSICIANS HAVING RECEIVED PROPER TRAINING IN THE USE OF THE DEVICE.

An explanation of the symbols used on product labeling is provided below.

Sterilized using irradiation

Consult Instructions for Use
www.seaspine.com/eifu

Expiration date (YYYY-MM-DD)

Do not re-use

Temperature limitation

Rx ONLY

Caution: Federal (USA) law restricts this device to sale by or on the order of a physician or practitioner

Catalog number

Lot number

Manufacturer

Do not use if package is damaged

Not made with natural rubber latex

Do not re-sterilize

IsoTis OrthoBiologics, Inc. is a member of the SeaSpine Orthopedics Corporation family of companies.

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