SeaSpine

DIRECTIONS FOR USE

OsteoStrand™

For Single Patient Use on a Single Occasion Only

The Inner Package and its Contents are Sterile
This allograft product is derived from voluntarily donated human tissue.

INDICATIONS FOR USE
Demineralized Bone Fibers is 100% human tissue and is regulated as a 361 Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/P). It is restricted to homologous use for the repair, replacement, or reconstruction of bony defects.

DESCRIPTION
Demineralized Bone Fibers is composed of 100% human tissue in the form of fibers provided in a sterile, single use package. Demineralized Bone Fibers are freeze-dried.

Demineralized Bone Fibers is human bone, and as a biological material some variations in the product should be expected, such as in appearance and handling.

Tissue Donor Selection, Screening and Testing (Summary of Records): Demineralized Bone Fibers is recovered 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 has evaluated the tissue donor and determined that the donor met eligibility criteria that were current at the time of tissue recovery. The tissue bank's evaluation included review of the tissue donor's infectious disease test results, consent documents, donor medical history and behavior risk assessment, available relevant medical records including previous medical history; laboratory test results; existing autopsy or coroner reports (if applicable) and information from other sources or records which may pertain to donor eligibility including tissue procurement microbiological test results. The donor review did not reveal risk factors for, or clinical or physical evidence of significant active infection including HIV (human immunodeficiency virus) or hepatitis infection, 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: 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 non-reactive 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.

OSTEOINDUCTIVE POTENTIAL
Demineralized Bone Fibers or representative finished product is verified for osteoinductive potential using an in vivo assay in athymic nude rodents for bone formation and/or in-vitro assay for endogenous BMP-2. It is unknown how osteoinductive potential assessments correlate with human clinical performance.

INSTRUCTIONS FOR USE
These instructions are intended as guidelines for the use of Demineralized Bone Fibers 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. 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

For best results, extreme care should be exercised to assure the correct graft material is selected for the intended application.

TO OPEN:

1. Inspect for package integrity and expiration date prior to opening.
2. Peel open package.
3. Using aseptic technique, remove the product syringe and transfer contents to a sterile field.
4. Remove clear protective cap from syringe cap.
5. Using a sterile male Luer syringe, draw the hydration fluid and connect to the female syringe cap of the product syringe.
   - Demineralized Bone Fibers may be hydrated with either blood, bone marrow aspirate or any isotonic solution prior to implantation.

Product Size	Hydration Volume (ml)
X-small	0.8
Small	2
Medium	4
Large	8

6. Hold coupled units vertically with Luer end of product syringe in vertical position.
7. Dispense hydration fluid into the product syringe by pressing down on the hydration syringe plunger.
8. Release the hydration syringe plunger after each pump, allowing plunger to move vertically – repeat 20 times.
9. Unscrew syringe cap from product syringe.
10. Depress the plunger to extrude the implant material from the syringe prior to implantation. The syringe is NOT to be used as a delivery device to implant material directly into the patient. The syringe may be directly attached to a RAPID® graft tube to fill the graft tube prior to implantation using RAPID.
    - Demineralized Bone Fibers may also be combined with other bone grafting materials such as autologous or allograft bone materials.
11. It is acceptable to add additional hydration fluid after extrusion to achieve the desired handling characteristics.
12. Discard any unused portion.

PREOPERATIVE PREPARATION
Aseptic techniques must be adhered to at all times in order to minimize the risk of post-operative complications. The amount of product needed is based on the type of procedure and size of the defect being treated.

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 Demineralized Bone Fibers and fixation devices.

Demineralized Bone Fibers do 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 Demineralized Bone Fibers.

For best results, Demineralized Bone Fibers must fill the defect and contact as much viable bone as possible.

Demineralized Bone Fibers must not be used to repair bone defects where complete soft tissue coverage cannot be achieved.

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 which 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.

CONTRAINDICATIONS
Demineralized Bone Fibers 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
- Iodine, ethanol and hydrogen peroxide may have been used in processing 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.

WARNINGS AND PRECAUTIONS
Demineralized Bone Fibers is sterile during the stated shelf life in an unopened and undamaged package. The product must be used prior to the expiration date.

Do not use if the packaging has been damaged and/or the product has been compromised. In the event of packaging has been compromised, discard the product. Damaged packaging should be returned to the manufacturer.

Appropriate placement and/or fixation are critical factors in the avoidance of potentially adverse effects. As with all biological products, Demineralized Bone Fibers has the potential to transmit infectious agents despite processing treatments, extensive donor screening, tissue selection and laboratory tests.

As with any surgical procedure, the possibility of infection exists.

As with all demineralized bone grafts, there is risk of nonunion, delayed union and/or malunion.

Although thorough screening and testing is used, tissue may transmit infectious agents such as human immunodeficiency virus or hepatitis infection.

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

STERILIZATION
Demineralized Bone Fibers 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 should not be re-sterilized. The product must not be used beyond the stated expiration date. If it appears that the product or its packaging has been compromised, both the product and the packaging should be returned to IsoTis Orthobiologics.

DO NOT RE-STERILIZE

STORAGE
Do not expose to extreme heat. Store at ambient temperature (up to 30ºC) in a clean, dry environment. The product has been validated to withstand temperatures between -10^{o}C to 35^{o}C during transit. 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.

CAUTION: Federal Law restricts the use of this product to sale by or on the order of a physician. This product is restricted to use by a licensed clinician.

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.

STERILE R	Sterilized using irradiation
	Consult Instructions for Use
	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
REF	Catalog number
LOT	Lot number
	Manufacturer
	Do not use if package is damaged
	Do not re-sterilize

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

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L03-1100 Rev. A (3/2019)