OsteoAdapt DE

Theradaptive

ENGLISH - IMPORTANT MEDICAL INFORMATION

INVESTIGATIONAL USE ONLY - CAUTION—Investigational device. Limited by Federal law to investigational use or clinical trial use. The following contains important medical information on the use of OsteoAdapt DE.

INDICATIONS FOR USE STATEMENT

OsteoAdapt DE is a medical device indicated for localized alveolar ridge augmentations for defects associated with extraction sockets.

DESCRIPTION

The medical device, OsteoAdapt DE, consists of Adhesive variant of bone Morphogenetic Protein 2 (AMP2), a therapeutic protein containing Bone Morphogenetic Protein 2 (BMP2) which is tethered to a beta-tricalcium phosphate (β-TCP) based scaffold called ReBOSSIS-J. ReBOSSIS-J is a synthetic, resorbable bone void filler (BVF). ReBOSSIS-J is a composite material consisting of (by weight) 70% beta-tricalcium phosphate (β-TCP) and 30% lactic acid and glycolic acid copolymer (PLGA). AMP2 is osteoinductive, meaning that the protein stimulates new bone formation at the site of implantation through the same intracellular signaling process as recombinant human BMP2 (rhBMP2). AMP2 is the active osteoinductive agent in OsteoAdapt. OsteoAdapt has the appearance of a “cotton ball” with compressible fibers.

OsteoAdapt will be supplied in doses of 0.8mg AMP2 per cc of ReBOSSIS-J and 2.0mg AMP2 per cc of ReBOSSIS-J. The patient will receive the dose to which they are randomized. 0.25 cc and 0.50cc kit sizes of OsteoAdapt DE will be provided for this feasibility study. Kits will be combined by the surgeon depending on the total volume in cc he/she will need to fill the extraction socket. Table 1 below shows the OsteoAdapt Kit size available for this study. Table 2 below shows the amount of AMP2 delivered and hydration volume for the selected number of kits. Estimated extraction socket volume should be rounded up to the next 0.25 cc value to ensure that the socket is not underfilled.

Table 1 Available OsteoAdapt DE Kit Size for Feasibility Study

Size Kit (cc)	OsteoAdapt DE (cc)	OsteoAdapt DE (g)
0.25	0.25	0.033
0.5	0.50	0.067

Table 2 Available OsteoAdapt DE Kit Size for Feasibility Study

Estimated Extraction Socket Volume (cc)	OsteoAdapt DE Volume*	Amount of AMP2 Delivered (mg) 0.8 mg/cc	Amount of AMP2 Delivered (mg) 2.0 mg/cc	Hydration Volume Saline (mL)
0.25	0.25	0.2	0.5	0.3
0.5	0.5	0.4	1.0	0.5
0.75	0.75	0.6	1.5	0.6
1	1	0.8	2.0	0.8
1.25	1.25	1.0	2.5	1.0

Estimated Extraction Socket Volume (cc)	OsteoAdapt DE Volume*	Amount of AMP2 Delivered (mg) 0.8 mg/cc	Amount of AMP2 Delivered (mg) 2.0 mg/cc	Hydration Volume Saline (mL)
1.5	1.5	1.2	3.0	1.1
1.75	1.75	1.4	3.5	1.3
2	2	1.6	4.0	1.5

* The OsteoAdapt DE volume can be assembled by any combination of the available kits (0.25 and 0.5 cc)

DO NOT USE ANY PRODUCT THAT IS NOT APPROVED BY THE GOVERNING COMPETENT AUTHORITY (REGULATOR).

PATIENT INDICATIONS

1. Age ≥ 22 at time of signing informed consent.
2. Subject requires extraction of a single tooth due to extensive carious lesions, prosthetic or endodontic failure, root fracture, or other reasons with dental implant treatment planned at the site. Subjects may undergo additional tooth extractions outside the context of the study tooth, provided that: the additional extraction(s) occur in a different quadrant than the study tooth, and the timing of the extraction(s) is at least 30 days prior to, or planned for at least 30 days after, the extraction designated for study participation.
3. Tooth root in position allowing a bone core sample to be harvested within the former socket
4. 6 mm of alveolar bone height without impinging on the maxillary sinus or inferior alveolar canal
5. Dehiscence of ≤ 6 mm on the buccal bony wall at time of extraction
6. Presence of other socket walls, mesial, distal and lingual walls.
7. The subject is willing and able to be present for routine follow-up visits, comply with post-operative management program, and is able to understand and sign the informed consent form.
8. Willing to use a reliable method of contraception (for woman of childbearing potential and males with a partner who is of childbearing potential)

CONTRAINDICATIONS

1. Active localized or systemic infection. Subjects presenting with a chronic tooth infection requiring extraction may be considered eligible if the following conditions are met: Prophylactic antibiotics are administered as clinically appropriate, and the extraction procedure includes complete removal of the infected tissue.
2. Untreated periodontal disease
3. Presence of a fenestration larger than 7 mm in diameter in the buccal wall at the time of extraction
4. Inadequate bone dimensions or restorative space to place a dental implant
5. The subject uses, or has used within 45 days of surgery, tobacco or nicotine or is prescribed steroids such as cortisone.
6. Presence or history of malignancy (excludes surgically resected skin squamous cell or basal cell carcinoma), radiotherapy, or chemotherapy for any malignancy within the last 5 years. History of malignancy may include multiple exostoses syndrome ((also known as multiple osteochondromas syndrome), an inherited condition associated with bumps of cartilage on the bones, has been associated with an increased risk of chondrosarcoma); individuals with hereditary cancer syndromes are excluded.
   Examples of hereditary cancer syndromes are hereditary breast and ovarian cancer syndrome, Li-Fraumeni syndrome, Cowden syndrome, and Lynch syndrome. Also called family cancer syndrome and inherited cancer syndrome individuals who have undergone any transplant surgery and are on immunosuppressant therapy.

7. Has history of any endocrine or metabolic disorder known to affect osteogenesis (e.g.: Paget's disease, renal osteodystrophy, Ehler-Danlos syndrome, or osteogenesis imperfecta).
8. Insulin dependent diabetes.
9. History of exposure to any recombinant proteins or peptides used for bone formation (i.e., Infuse Bone Graft, AUGMENT Bone Graft, GEM21S, i-FACTOR Peptide Enhanced Bone Graft, or PepGen P-15 Synthetic Bone Graft).
10. Hypersensitivity or allergy to any components of the study treatments including, but not limited to, bone morphogenetic proteins (BMPs); tricalcium phosphate (TCP); PLGA polymer.
11. History of any allergy resulting in anaphylaxis.
12. Treatment with an investigational therapy (drug, device, and/or biologic) within 120 days (or 5 half-lives, whichever is greater) prior to implantation surgery, or such treatment is planned during the 24-month period following implantation of the study treatment; prior or planned use of rhBMP-2.
13. Pregnant at final Screening evaluation prior to Day 0 pre-procedure or interested in trying to conceive a child (both females and males) in the next 12 months or nursing. Any condition that would interfere with the subject's ability to comply with study instructions or prohibit Radiographic assessments that might confound the interpretation of the study or put the subject at risk.
14. Patients currently taking any drug known to interfere with bone/soft tissue healing. See “Medication Protocol” section of the Investigator’s Brochure. See note below containing the Medication Protocol language.
15. Any other condition or prior therapy that in the opinion of the Investigator would make the volunteer unsuitable for this study, including inability to cooperate fully with the requirements of the study protocol or likelihood of noncompliance with any study requirements.

***Medication Protocol:*
If possible, patients should titrate down all opioid medications prior to surgery according to the physician’s orders. Stopping opioids three months prior to surgery is ideal, to reduce the risk of postoperative complications and continued opioid usage. If the patient’s pain is not able to be controlled, the patient should be titrated down to no more than 10 morphine equivalents per day, unless specifically instructed by the treating physician. NSAIDS should be stopped 5 days preoperatively, and steroid use should be stopped 3 weeks preoperatively, unless specifically instructed by treating physician. Additionally, all supplements (including herbal/vitamins) should be stopped 2 weeks preoperatively, unless deemed medically necessary.

WARNINGS

1. OsteoAdapt DE is designed for single patient use only. Attempting to reuse will adversely affect product sterility and physical handling characteristics. DO NOT attempt to re-sterilize or re-use. Discard unused contents.
2. The safety and effectiveness of OsteoAdapt DE when mixed with any additional components, e.g., other bone grafting materials or bone marrow aspirate, has not been established.
3. The safety and effectiveness of OsteoAdapt DE in patients with hepatic or renal impairment has not been established.
4. The safety and effectiveness of OsteoAdapt DE in patients with metabolic bone disease has not been established.
5. As with any surgical procedure, care should be exercised in treating individuals with pre-existing conditions that may affect the success of the surgical procedure.
6. OsteoAdapt DE should not be used in female patients that are pregnant or planning to become pregnant, or males trying to conceive a child with their female partner. Double contraception should be used by both male and females as reproductive toxicity for OsteoAdapt has not been established.
7. Immunogenic effects of OsteoAdapt DE are unknown at this time, presenting an additional risk. This study will evaluate patient antibody response to AMP2.

PRECAUTIONS

1. OsteoAdapt DE should only be used by clinicians who are experienced with bone grafting procedures associated with extraction sockets and are familiar with the implant components, instruments, appropriate selection criteria, and risks associated with such procedures. A lack of adequate experience and/or training may lead to a higher incidence of adverse events.
2. DO NOT USE IF STERILE PACKAGING IS OPENED OR DAMAGED. Discard or return damaged packaging and all contents.
3. Do not use after the printed expiration date on the label.
4. OsteoAdapt DE should only be used in procedures where it can be adequately contained in the extraction socket. Avoid overfilling the extraction socket. Inadequate containment of OsteoAdapt DE could result in product migration from the intended treatment site. If product migration occurs, clinical outcomes may be compromised by the lack of bone graft material in the appropriate space, or the migration of material outside of the intended treatment site. Potential adverse events caused by inadequate containment and migration of OsteoAdapt DE may require revision surgery.

POTENTIAL ADVERSE EVENTS

A list of potential adverse events associated with OsteoAdapt:

- Allergic reaction
- Anaphylactic reaction
- Antibody Formation
- Difficult to control or uncontrolled bleeding
- Bone fracture
- Bone resorption, which may be transient
- Cardiovascular problems, including heart dysfunction, arrhythmia (change in heart rhythm), and arrest
- Cellulitis
- Cessation of potential growth at the operative site
- Cognitive changes (confusion, hallucination, memory loss or other changes to mental status)
- Cyst or Encapsulated fluid collection
- Damage to internal organs and connective tissue
- Death
- Development of respiratory problems
- Dizziness
- Edema (swelling)
- Elevated erythrocyte sedimentation rate
- Embolism (detached clot in the blood vessels) that can cause additional body damage
- Erythematous tissue
- Fainting
- Fetal development complications/reproductive toxicity
- Foreign body reaction
- Graft extrusion or migration
- Graft rejection/failure
- Headache
- Hematoma
- Heterotopic and/or exuberant bone formation
- Hyper or hypo tension (high or low blood pressure)
- Incisional complications
- Increased tooth mobility
- Infection
- Inflammation
- Itching
- Nerve anesthesia including permanent paresthesia or anesthesia
- Pain
- Scar formation
- Seroma or fluid accumulation
- Sinusitis
- Sterile abscess
- Stroke
- Swelling
- Thrombosis (blood clots in the blood vessels) that can cause additional body damage
- Tissue or nerve damage
- Wound Dehiscence

HOW SUPPLIED

OsteoAdapt DE is supplied sterile (15.4 - 22.5 kGy ebeam sterilization) and non-pyrogenic in 0.25cc and 0.50cc kit sizes. Multiple kits can be combined to achieve the appropriate total volume based on the volume of the extraction socket

STORAGE CONDITIONS

Store the OsteoAdapt DE at 2-8° C.

DOSAGE AND ADMINISTRATION

OsteoAdapt DE is prepared immediately prior to use in surgery. OsteoAdapt DE contains AMP2 at a dose of 0.8mg/cc or 2.0 mg/cc. The size of the OsteoAdapt DE kit and the volume OsteoAdapt DE component to be implanted are determined by the internal volume of the extraction socket. Only store the OsteoAdapt DE kits in the manner described on the package. Only mix the components in the manner described in the Directions for Use, and only use in the quantity and indication specified in the package insert. Any other storage, mixture, or administration may cause unanticipated adverse events.

DIRECTIONS FOR USE

OsteoAdapt DE is prepared at the time of surgery by hydrating the OsteoAdapt DE with saline in concordance with Table 2 above. When combining kits to reach the desired volume, hydrate the total volume of OsteoAdapt DE after combining all dry kits to meet the recommended grafting volume. The OsteoAdapt DE component is then inserted into the prepared extraction socket. The extraction socket is covered with the prescribed resorbable collagen barrier membrane according to the instructions for use for the barrier membrane and routine standard of care for this procedure.

Step 1. Inspect box for damage, if damaged send back. Open the foil pack and discard desiccant (DO NOT USE THE DESSICANT IN PROCEDURE). In a sterile environment, using the tab of the Tyvek, peel back the Tyvek cover to expose the OsteoAdapt DE. Inspect the product for damage or unknown particles/material.

Step 2. Determine number of OsteoAdapt DE kits and saline needed from Table 2.

Step 3. Open OsteoAdapt DE packaging and combine all kits into one tray, using forceps, for hydration step. Collect as many as possible of the stray fibers.

Step 4. Add saline as the hydration fluid using a syringe for appropriate volume determination and inject on top of OsteoAdapt DE.

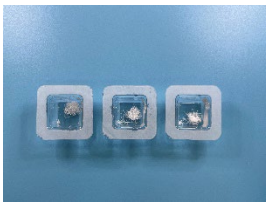
Step 5. Using forceps, move the OsteoAdapt DE around the bottom of the tray well to sop up the saline. Flip the piece of OsteoAdapt DE over a few times while sopping up the saline. Lightly pressing the partially hydrated OsteoAdapt against the side of the tray will promote wetting. When fully hydrated, move the wet OsteoAdapt DE around the perimeter of the tray well to “mop up” any stray fibers and remaining saline. When hydrated, OsteoAdapt DE may be removed from the tray and formed lightly with forceps to desired shape.

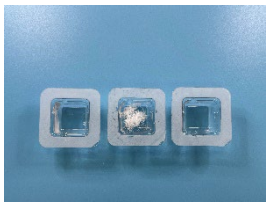
Step 6. Gently slide the OsteoAdapt DE into the extraction socket. Make sure it is in direct contact with the bottom and sides of the extraction socket and flush with the top. If there are any gaps, use forceps to pull the OsteoAdapt to fill the gaps. The prepared OsteoAdapt DE must be implanted within 2 hours of hydration to prevent excessive evaporation of the saline and drying of the material.

NOTE: Recommended not to add more than the recommended amount of saline but rather focus on working the available saline into the tuft of OsteoAdapt DE with light pressure, flipping, and mopping action.

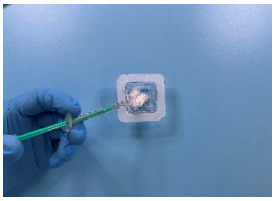
Assembly of required OA

Open required number of kits



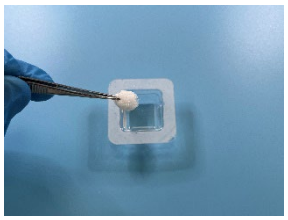


Combine kits to a single tray

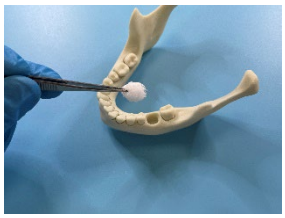


Hydrate material with appropriate amount of saline from Table 2

Work the OsteoAdapt DE around the tray until fully hydrated



From a "ball" with the hydrated OA



Place the OsteoAdapt DE inside the extraction socket

PRODUCT ADVERSE EVENTS AND MALFUNCTIONS

To report product adverse events or malfunctions, contact the Sponsor or Sponsor's representative. When filing a complaint, please provide the site name, country, Patient ID, and the nature of the incident.

Product adverse events and malfunctions are reported in accordance with the Protocol and Clinical report forms. Where appropriate, reports to Competent Authorities and Regulatory Agencies will be made in accordance with local regulation. These are reported in the appropriate Clinical Report Forms. If there any doubt, please contact the Sponsor's Clinical Program Manager as defined in the Adverse Event Clinical Report Form. Issues or dissatisfaction, not defined in the protocol or the associated material – including the Investigator's Brochure (IB), are reported to the clinical program manager or representative for evaluation and action if appropriate.

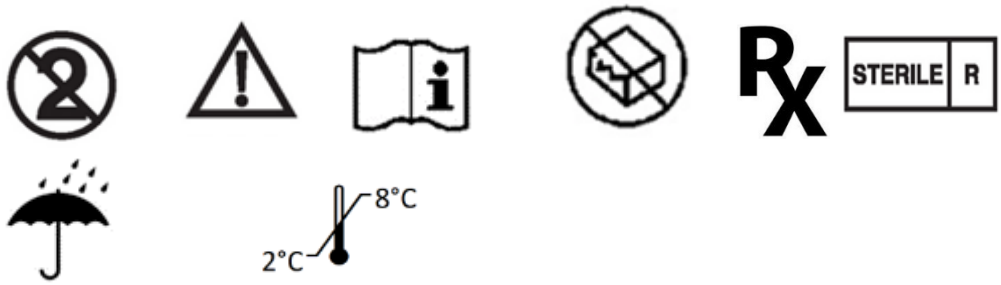
DEVICE RETRIEVAL EFFORTS

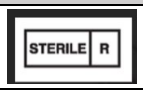
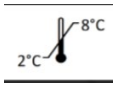
Should it be necessary to remove the OsteoAdapt DE, please contact Theradaptive prior to the scheduled surgery to receive instructions regarding data collection, including histopathological, mechanical, and adverse event information.

FURTHER INFORMATION:

If further information is required, please contact Theradaptive at the address below.

Theradaptive
7495 New Horizon Way, Suite 240
Frederick, MD 21703
+1 240 415 9776



Symbol	Meaning
	**Sterilized using irradiation**
	**Non-pyrogenic**
	**Fragile, handle with care**
	**Temperature limit**
	**Medical Prescription**
	**Keep dry**
	**Caution**
	**Do not resterilize**
	**Consult instructions for use**
	**Do not use if package is damaged and consult instructions for use**