CERAMENT®|BONE VOID FILLER

INSTRUCTIONS FOR USE

DEVICE DESCRIPTION

CERAMENT®|BONE VOID FILLER is a fast-setting, injectable and moldable ceramic bone graft substitute intended for filling bone voids/gaps. The material consists of a powder and a liquid component. The major constituents of the powder are hydroxyapatite and calcium sulfate hemihydrate. The liquid component (C-TRU) contains Iohexol as a radio-contrast enhancer. Mixing the components, with the combined mixing injection (CMI) device, results in a viscous material intended to set *ex vivo* or *in vivo*.

By combining hydroxyapatite and calcium sulfate a balance is achieved between implant resorption rate and bone in-growth rate. Calcium sulfate acts as a resorbable carrier for hydroxyapatite. Hydroxyapatite has a slow resorption rate, high osteoconductivity, promoting bone in-growth and gives long term structural support to newly formed bone.

The ceramic bone graft substitute is placed into the bone defect under visual inspection or under radiographic monitoring during open or percutaneous surgery. The paste may be injected into the defect, molded by hand and digitally placed into the defect, or used to prepare beads that are placed into the defect. The accompanying injection device (ID) and Tip Extenders may be used to facilitate the filling of the bone defect. When fully set *in vivo*, CERAMENT®|BONE VOID FILLER is drillable and can be used to augment hardware during the surgical procedure.

PERFORMANCE

Injectable: 3-5 minutes.

Molding by hand: Initiation between 7-9 minutes.

Beads: Fill mold cavities before 5 minutes. Release beads after 15 minutes.

Drillable: After 15 minutes.

All times are from the start of mixing. More detailed information is provided in "Directions for use".

INDICATIONS FOR USE

CERAMENT®|BONE VOID FILLER is a ceramic bone graft substitute intended for orthopedic applications as a filler for gaps and voids that are not intrinsic to the stability of the bony structure.

CERAMENT®|BONE VOID FILLER is indicated to be injected, or placed, into bony voids or gaps in the skeletal system, i.e. extremities, pelvis, and posterolateral spine (only during open surgery in spine). These defects may be the result of benign bone cysts and tumors (in adults and pediatric patients ≥ 9 years old), or osseous defects created as a result of either surgery or traumatic injury to the bone.

CERAMENT®|BONE VOID FILLER resorbs and is replaced by bone during the healing process.

CERAMENT®|BONE VOID FILLER can augment hardware and support bone fragments during the surgical procedure. The cured paste acts only as a temporary support media and is not intended to provide structural support during the healing process.
CERAMENT®|BONE VOID FILLER can be drilled and screws can be placed through it.

CONTRAINDICATIONS

- Hypersensitivity to Iohexol or to any of the excipients.
- Local infection at the site of implantation.
- Pregnancy.
- Breastfeeding.
- Known hyperthyroidism or autonomous thyroid adenoma.
- Load bearing applications.

PRECAUTIONS

- Adhere to sterile surgical technique.

Supportive therapy

- Control active bleeding and remove blood clots and tissue fragments if open surgery.
- Consult and comply with the IFU of any additional utensils.

Patient related

- Care should be taken in patients with pre-existing calcium metabolism disorders.

Device related

- Contact between CERAMENT®|BONE VOID FILLER and living bone, and provision of normal conditions of fracture healing or bone growth, are prerequisites for good treatment outcome.
- May cause inflammatory reaction if present in soft tissue.
- Not intended for load bearing areas, unless it can be assumed after thorough examination that the cortical bone, surgical fixation, or in situ osteosynthesis is sufficient for load bearing function.
- CERAMENT®|BONE VOID FILLER should not be used in joint spaces since its presence may cause inflammation or mechanical obstruction.
- Contact with joint fluid may cause resorption of CERAMENT®|BONE VOID FILLER.
- Overpressurization during injection should be avoided as intra-medullar injection with any bone void filler may lead to fat embolization or embolization of CERAMENT®|BONE VOID FILLER into the blood stream.
- Overpressurization of the device may lead to extrusion of the device beyond the site of its intended application and damage the surrounding tissues.
- Inject carefully under visual inspection or radiographic monitoring to avoid spreading of product outside of the intended injection site.
- Do not overfill.
- In Aneurysmal bone cysts (ABCs) and other bone cysts prone to producing large volumes of fluid, there is increased risk of wound drainage, soft-tissue inflammation and wound breakdown if treated by open surgery. Use CERAMENT®|BONE VOID FILLER in bead form rather than complete void filling for these indications.
- Using alternative mixing solutions and/or adding other substances to CERAMENT®|BONE VOID FILLER may affect the product setting in an uncontrolled manner, and may affect the safety and effectiveness of the product.
- When using as alternative to autograft, be aware that CERAMENT®|BONE VOID FILLER is not osteoinductive.
- Do not use if the CERAMENT®|C-TRU liquid is discolored or contains a precipitate.

Related to general use of Iohexol

These precautions have been established for the intravenous use of iohexol-containing radiocontrast agents

Hypersensitivity

- A positive history of allergy, asthma, or untoward reactions to iodinated contrast media indicates a need for special caution. Any application of contrast media should, therefore, be preceded by a detailed medical history. In patients with allergic diathesis and in patients with known hypersensitivity reactions a very strict indication is required.
- Premedication with corticosteroids or histamine H1 and H2 antagonists might be considered in patients at risk for intolerance, they may not, however, prevent anaphylactic shock, they may actually mask initial symptoms. In patients with bronchial asthma, especially the risk for bronchospasm is increased.
- The risk of serious reactions in connection with use of Iohexol is regarded as minor. However, iodinated contrast media may provoke serious, life threatening, fatal anaphylactic reactions or other manifestations of hypersensitivity.
- Independent of quantity and route of administration, symptoms such as angio-oedema, conjunctivitis, coughing, pruritus, rhinitis, sneezing and urticaria may be indicative of a serious anaphylactoid reaction requiring treatment. A course of action should therefore be planned in advance, with necessary drugs and equipment available for immediate treatment, should a serious reaction occur. In imminent state of shock, administration of the contrast medium must be terminated immediately and - if necessary – specific intravenous treatment must be initiated.

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- Patients using β-blockers may present with atypical symptoms of anaphylaxis which may be misinterpreted as vagal reaction.

Hydration

- Adequate hydration should be assured before and after contrast media administration. If necessary, the patient should be hydrated intravenously until excretion of the contrast medium is complete. This applies especially to patients with dys- and paraproteinaemias like multiple myeloma, diabetes mellitus, renal dysfunction, hyperuricaemia, as well as to elderly patients and patients in bad general condition. In patients at risk, the water and electrolyte metabolism must be controlled and symptoms of a dropping serum calcium level must be taken care of. Due to the risk of dehydration induced by diuretics, at first, water and electrolyte rehydration is necessary to limit the risk of acute renal failure.

Cardio-circulatory reactions

- Care should also be taken in patients with serious cardiac disease / cardio-circulatory disease and pulmonary hypertension, as they may develop hemodynamic changes or arrhythmias.
- Patients with cardiac insufficiency, severe coronary heart disease, instable angina pectoris, valvular diseases, previous myocardial infarction, coronary bypass and pulmonary hypertension are especially predisposed for cardiac reactions.
- In elderly patients and patients with pre-existing cardiac diseases, reactions with ischemic changes in the ECG and arrhythmia occur more frequently.

CNS disturbances

- Patients with acute cerebral pathology, tumors or a history of epilepsy are predisposed for seizures and merit particular care. Alcoholics and drug addicts have an increased risk for seizures and neurological reactions.

Renal reactions

- Use of iodinated contrast media may cause contrast induced nephropathy, impairment of renal function or acute renal failure. To prevent these conditions following contrast media administration, special care should be exercised in patients with preexisting renal impairment and diabetes mellitus as they are at risk.
- Other predisposing factors are preceding renal failure following application of contrast media, a history of renal disease, age over 60 years, dehydration, advanced arteriosclerosis, decompensated cardiac insufficiency, high doses of contrast media and multiple injections, exposition to further nephrotoxins, severe and chronic hypertension, hyperuricaemia, paraproteinemias (myelomatosis and Waldenström's macroglobulinemia, plasmocytoma) or dysproteinemias.

Hepatic reactions

- A potential risk of transient hepatic dysfunction exists. Particular care is required in patients with severe disturbance of both renal and hepatic function, as they may have significantly delayed contrast media clearance.

Myasthenia gravis

- The administration of iodinated contrast medium may aggravate the symptoms of myasthenia gravis.

Phaeochromocytoma

- In patients with phaeochromocytoma undergoing interventional procedures, alpha blockers should be given as prophylaxis to avoid hypertensive crisis.

Disturbed thyroid function

- Due to free iodide in the solutions and additional iodide released by deiodination, iodinated contrast media influence thyroid function. This may induce hyperthyroidism or even thyrotoxic crisis in predisposed patients.
- Patients with manifest but not yet diagnosed hyperthyroidism are at risk, patients with latent hyperthyroidism (e.g. nodular goitre) and patients with functional autonomy (e.g. elderly patients, especially in regions with iodine deficiency) should therefore have their thyroid function assessed before examination if such conditions are suspected.
- Before administering an iodinated contrast agent, make sure that the patient is not about to undergo thyroid scan or thyroid function tests or treatment with radioactive iodine, as administration of iodinated contrast agents, regardless of the route, interferes with hormone assays and iodine uptake by the thyroid gland or metastases from thyroid cancer until urinary iodine excretion returns to normal.
- Following injection of an iodinated contrast agent, there is also a risk of induction of hypothyroidism.

Further risk factors

- Among patients with autoimmune diseases, cases of serious vasculitis or Stevens-Johnson-like syndromes have been observed.
- Severe vascular and neurological diseases, especially in elderly patients are risk factors for reactions to contrast media.

WARNINGS

- Only to be used for voids or gaps not intrinsic to the stability of the bone structure and should not be used in load bearing applications, such as vertebroplasty or kyphoplasty.
- The device cannot be used for prophylactic use (e.g. pending fragility fractures).

POTENTIAL ADVERSE EVENTS

The following complications have been reported to result from ceramic bone graft substitutes

- Calcium based bone void fillers may color wound drainage white. This should not be a concern, however, be aware of the risk of infection when drainage occurs.
- There have been reports in the literature on idiosyncratic reactions (laryngospasm and tachyarrhythmia) in children up to the age of 15 treated with ceramic bone graft substitute containing 75-100% calcium sulfate and 0-25% calcium phosphate.
- Revisions and/ or removals.
- Delayed or nonunion, lack of osseointegration, impaired healing, inadequate bone formation.

Possible complications related to any surgery

- In cases where it is not possible to establish a sufficient wound closure there might be a risk of skin inflammation reaction and/ or prolonged wound drainage.
- Bone fracture and wound complications, including hematoma, site drainage, infection and other complications are possible side-effects of surgery.
- Blood pressure change.

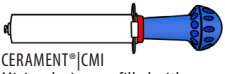
INTERACTIONS

Related to general use of Iohexol

These interactions have been established for the intravenous use of iohexol-containing radiocontrast agents

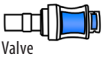
- There is a risk of the development of lactic acidosis when iodinated contrast agents are administrated to diabetic patients treated with metformin, particularly in those with impaired renal function.
- Patients treated with Interleukin - 2 less than two weeks previously have been associated with an increased risk of delayed reactions (flu-like symptoms or skin reactions).
- The concomitant use of certain neuroleptics or tricyclic antidepressants can reduce the seizure threshold and thus increase the risk of contrast medium-induced seizures.
- Treatment with β-blockers may lower the threshold for hypersensitivity reactions, as well as necessitating higher doses of β-agonists when treating hypersensitivity reactions.
- Beta-blockers, vasoactive substances, angiotensin-converting enzyme inhibitors and angiotensin receptor antagonists may reduce efficacy of cardiovascular compensation mechanisms of blood pressure changes.
- All iodinated contrast media may interfere with tests on the thyroid function, thus the iodine binding capacity of thyroid may be reduced for up to several weeks.
- High concentrations of contrast media in serum and urine can interfere with laboratory tests for bilirubin, proteins or inorganic substances (e.g. iron, copper, calcium and phosphate).

COMPONENTS, COMPOSITIONS & PARTS



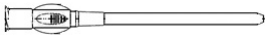
CERAMENT®|CMI
Mixing device pre-filled with ceramic bone graft substitute, a mixture of hydroxyapatite and calcium sulfate.

CERAMENT®|C-TRU
Pre-filled syringe with iodine based mixing liquid. A water-soluble, radio-contrast enhancer (Iohexol) with the iodine concentration of 180 mg I/mL.



Valve
To connect CERAMENT®|C-TRU and CERAMENT®|ID to CERAMENT®|CMI.

CERAMENT®|ID
Injection device (accuracy of measuring scale ± 5%). For the 18 mL product, two injection devices are included.



Tip Extender
Two Tip Extenders in different lengths for use with CERAMENT®|ID facilitating paste injection.

ADDITIONAL UTENSILS NEEDED

- Stopwatch

OPTIONAL UTENSILS

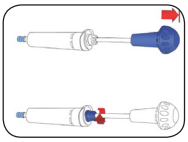
- A cannula or needle with a minimum diameter of 16G
- Bead mold

DIRECTIONS FOR USE

When handling CERAMENT®|BONE VOID FILLER adhere to sterile surgical techniques.

Preparation of the paste - Step by step instructions

1. Retract the blue handle on the CERAMENT®|CMI and remove the red plunger stop ring.
2. Remove the plug on CERAMENT®|CMI and attach the Valve with the clear end to CERAMENT®|CMI by turning it clockwise.
3. Remove the plug from the liquid filled syringe (CERAMENT®|C-TRU) using the tool embedded in the blister tray bottom by pushing the syringe-plug into the tool and turn the syringe counter-clockwise. After removing the plug, press the CERAMENT®|C-TRU through the blue membrane of the Valve and attach it by turning it clockwise.
4. Empty the syringe with CERAMENT®|C-TRU into the CERAMENT®|CMI completely. Keep the plunger pushed to the bottom to avoid back flush. Detach CERAMENT®|C-TRU syringe from the Valve.
5. Start the stop watch (t = 0 seconds). Mix in a tipped down position for 30 seconds with a frequency of approximately one complete stroke per second. Rotate the blue handle at the end positions.
6. Finish the mixing:
   - Fully retract the blue handle into its back position.
   - Lock the plunger by turning the blue collar clockwise 180° until a "click" is heard.



7. Attach the CERAMENT®|ID to the Valve by pressing it through the blue membrane and turning clockwise. Transfer the paste from the CERAMENT®|CMI immediately, with the grading on the CERAMENT®|ID facing the user. For the 18 mL product, the second syringe should be filled immediately after the first syringe. When the CERAMENT®|ID is completely filled, excess paste will begin to ooze from under the sleeve. Stop filling when this occurs.
8. Detach the filled CERAMENT®|ID from the Valve and remove the red plunger stop rod. The paste is now ready to use. If applicable, attach Tip Extender or an optional sterile needle (minimum 16G) to the CERAMENT®|ID.

Filling of the bone void/gap - 3 different options

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Injection

- Wait until 3 minutes after start of mixing; carefully inject into the bone void/gap under visual inspection and/or by radiographic monitoring.
- Proceed until the void/gap is filled with an adequate amount of paste, as judged by the responsible physician.
- The paste is injectable between 3-5 minutes when using a 16 G needle.
- After the paste is *in situ*, allow to set for a few minutes before any adjustments are done or the wound is closed, especially if bleeding occurs.
- Close the wound(s) meticulously to avoid leakage into the soft tissue.
- Follow accepted clinical practice for postoperative care.

Molded by hand

- Wait until approximately 3 minutes after start of mixing; extrude the paste to a solid mass of suitable size on sterile surface and wait until desired consistency for molding. The extrusion should be performed before 5 minutes.
- Molding of the paste by hand can be initiated between 7-9 minutes (the paste is moldable for a period of 1 minute).
- Place the molded product in the bone void or gap.
- Gently pack the molded material.
- Close the wound(s) meticulously to avoid leakage into the soft tissue.
- Follow accepted clinical practice for postoperative care.

Molded with the use of Bead Mold Trays

- Select the size of beads needed.
- Fill the cavities in the mold before 5 minutes (from start of mixing).
- Allow paste to cure undisturbed for at least 15 minutes from start of mixing, before the beads are released from the mold.
- Flex mold to release the beads.
- Gently pack the beads in the bone void or gap.
- Close the wound(s) meticulously to avoid leakage into the soft tissue.
- Follow accepted clinical practice for postoperative care.

STERILITY

CERAMENT®|BONE VOID FILLER is supplied sterile. The CERAMENT®|CMI is sterilized by gamma irradiation, the CERAMENT®|C-TRU is sterilized by steam and the surface sterilization of the complete device is by ethylene oxide.

The product is intended only for single use and cannot be re-sterilized by any method and shall not be re-used due to contamination risks.

RESTRICTIONS

CERAMENT®|BONE VOID FILLER may only be sold and distributed for professional use.

Store CERAMENT®|BONE VOID FILLER unopened in a clean and dry environment at room temperature (15– 30°C / 59–86°F).

The contents of this document may not be duplicated without written permission from BONESUPPORT AB.

Do not use if any of the packages are open or damaged or if the expiration date has been exceeded.

Excess material and opened but unused items must be discarded. Used material should be discarded in accordance with hospital procedures.

The products are protected by patents, see:
http://bonesupportpatents.com

CAUTION

Federal (US) law restricts this device to sale by or on the order of a physician.

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MANUFACTURED BY:
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REF

A 0210-11 (18 mL) CERAMENT®|BONE VOID FILLER 18 mL
A 0210-08 (10 mL) CERAMENT®|BONE VOID FILLER 10 mL
A 0210-09 (5 mL) CERAMENT®|BONE VOID FILLER 5 mL

Comments regarding the performance of this device in the USA can be directed to

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Symbol glossary

Symbol	Title and reference number*	Description of symbol
	5.1.1 Manufacturer	Indicates the medical device manufacturer.
	5.1.4 Use-by date	Indicates the date after which the medical device is not to be used.
	5.1.5 Batch code	Indicates the manufacturer´s batch code so that the batch or lot can be identified.
	5.1.6 Catalogue number	Indicates the manufacturer´s catalogue number so that the medical device can be identified.
	5.2.3 Sterilized using ethylene oxide	Indicates a medical device that has been sterilized using ethylene oxide.
	5.2.4 Sterilized using irradiation	Indicates a medical device that has been sterilized using irradiation.
	5.2.5 Sterilized using steam or dry heat	Indicates a medical device that has been sterilized using steam or dry heat.
	5.2.8 Do not use if package is damaged	Indicates a medical device that should not be used if the package has been damaged or opened.
	5.3.7 Temperature limit	Indicates the temperature limits to which the medical device can be safely exposed.
	5.4.2 Do not re-use	Indicates a medical device that is intended for one use, or for use on a single patient during a single procedure.
	5.4.3 Consult instructions for use	Indicates the need for the user to consult the instructions for use.
	5.4.4 Caution	Indicates the need for the user to consult the instructions for use for important cautionary information such as warnings and precautions that cannot, for a variety of reasons, be presented in the medical device itself.

*According to: ISO15223-1:2016 *Medical devices- Symbols to be used with medical device labels, labelling and information to be supplied*