CERAMENT™ G

INSTRUCTIONS FOR USE

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PRODUCT DESCRIPTION

- CERAMENT G is an implantable bone void filler (device/drug combination product) indicated for use as an adjunct to systemic antibiotic therapy and surgical debridement (standard treatment approach to a bone infection) where there is a need for supplemental bone graft.
- CERAMENT G combines gentamicin sulfate with a bone void filler, consisting of hydroxyapatite and calcium sulfate.
- By eluting gentamicin, CERAMENT G can reduce the recurrence of chronic osteomyelitis from gentamicin-sensitive microorganisms in order to protect bone healing CERAMENT G can also reduce the likelihood of infection subsequent to an open fracture.
- By combining calcium sulfate and hydroxyapatite, a balance is achieved between implant resorption rate and bone remodeling rate. Calcium sulfate acts as a resorbable carrier for hydroxyapatite. Hydroxyapatite has a slow resorption rate and high osteoconductivity providing a scaffold for new bone generation.
- The use of CERAMENT G eliminates the need to harvest autologous bone, thereby avoiding donor site morbidity (e.g., pain, infection, etc.) in patients with a diagnosed infection.
- CERAMENT G may be implanted by an injectable system. In bone infection, CERAMENT G can also be inserted as pre-set beads.

PERFORMANCE

The injecting performance is dependent upon the desired working consistency of CERAMENT G. The injection consistency is obtained at approximately 4 minutes after combining the powder and liquid components. The injection can be continued until approximately 7 minutes when using a 16 G needle.

Drilling of the material can be performed 15 minutes after start of mixing.

CERAMENT G attains final setting after 20 minutes.

The wound can be closed after approximately 15 minutes.

When using a mold to prepare beads, wait 20 minutes before removing the beads from the mold.

All times are from the start of mixing.

INDICATIONS

CERAMENT G is a resorbable, gentamicin-eluting ceramic bone void filler intended for use in defects in the extremities of skeletally mature patients as an adjunct to systemic antibiotic therapy and surgical debridement as part of the standard treatment approach to a bone infection and open fractures. By eluting gentamicin, CERAMENT G can reduce the occurrence and recurrence of bone infection from gentamicin-sensitive microorganisms in order to protect bone healing.
CERAMENT G can augment provisional hardware to help 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 G resorbs and is replaced by bone during the healing process.

CONTRAINDICATIONS

- Hypersensitivity to any amino-glycoside antibiotics
- Myasthenia gravis
- Severe renal impairment
- Pre-existing calcium metabolism disorder
- Pregnancy
- Breastfeeding

WARNINGS

- CERAMENT G is not indicated for use in the spine, such as vertebroplasty or kyphoplasty.
- Do not use in spine osteomyelitis.
- The presence of gentamicin in the product does not negate the need for systemic antibiotics.
- The safety and effectiveness of CERAMENT G have not been studied in segmental bone defects larger than 1 cm.
- Do not implant more than 30 mL of CERAMENT G in bone infection or more than 10 mL in open fracture. The safety and effectiveness and antibiotic toxicity of larger volumes of CERAMENT G is not known.
- In the clinical dataset used to support marketing of CERAMENT G, a subset of patients who did not experience a recurrence of infection exhibited radiographic evidence of CERAMENT G resorption without complete replacement by bone at timepoints 1 year post-treatment or longer. Surgeons should evaluate the need for additional treatment of these unfilled defects based on defect size, location and other patient-specific factors. While dependent on surgeon discretion and patient medical factors, patients with incomplete bone formation may need additional grafting procedures
- The clinical dataset used to support marketing of CERAMENT G did not contain demographic details related to race and ethnicity, therefore, the results of the study may not necessarily be applicable to patients of all races and ethnicities.
- The use of CERAMENT G in the absence of a proven or strongly suspected bacterial infection is unlikely to provide benefit and increases the risk of drug-resistant bacteria.

PRECAUTIONS

Practical instruction for sterile / aseptic usage

- Adhere to sterile surgical technique when preparing CERAMENT G.

Supportive therapy

- Appropriate debridement is needed.
- Low pressure irrigation should be used.
- Control active bleeding and remove blood clots and tissue fragments.
- Use of active suction drainage may lead to a decrease in effective dose of Gentamicin.

Device related

- Care should be taken to ensure proper placement and containment of CERAMENT G in the desired treatment area.
- Contact between CERAMENT G and living bone, and provision of normal conditions of fracture healing or bone growth, are prerequisites for good treatment outcome.
- CERAMENT G may cause an inflammatory reaction if placed into soft tissue.
- CERAMENT G is not intended for use in load bearing applications, unless it can be assured after thorough examination, that the cortical bone, surgical fixation, or in situ osteosynthesis is sufficient for load-bearing function.
- CERAMENT G should not be used in joints because its presence may cause inflammation or mechanical obstruction/damage.
- Contact with joint fluid may cause resorption of CERAMENT G.
- Overpressurization during injection should be avoided because it may lead to fat embolization or embolization of CERAMENT G into the blood stream. It may also lead to extrusion of the product beyond the desired treatment area resulting in damage to surrounding tissues.
- Do not overfill.
- Using alternative mixing solutions and/or adding other substances to the mixture is not supported by clinical data.
- When used as an alternative to autograft, please note that like many synthetic bone void fillers CERAMENT G is not designed to be osteoinductive or osteogenic.
- Intermixing with allograft or autograft before application should be avoided.
- If using CERAMENT G to augment hardware and bone alignments during surgical procedure, wait until material final setting time for optimal use.
- Use of CERAMENT G in the treatment of GA type IIIC fractures is not supported by clinical data.

Related to general use of Gentamicin

- CERAMENT G should be used with caution in elderly people and in patients with impaired renal function. Diabetes, auditory vestibular dysfunctions, otitis media, a history of otitis media, previous use of ototoxic drugs and a genetically determined high sensitivity to aminoglycoside induced ototoxicity, are other factors which may pre-dispose the patient to toxicity.
- Concurrent use of other neurotoxic and/or nephrotoxic drugs can increase the possibility of Gentamicin toxicity. Co-administration with the following agents should be avoided:
  - Neuromuscular blocking agents such as succinylcholine and tubocurarine.
  - Other potentially nephrotoxic or ototoxic drugs such as cephalosporins and methicillin.
  - Potent diuretics such as ethacrynic acid and furosemide.
  - Other aminoglycosides.
- To avoid the risk of adverse events, continuous monitoring (before, during and after) of renal function (serum creatinine, creatinine clearance), hepatic and laboratory parameters are recommended. Gentamicin serum concentrations should be closely monitored and a reduction in dose should be considered.

- Sulfites can cause allergic-type reactions, including anaphylactic symptoms and bronchospasm, in susceptible people, especially those with a history of asthma or allergy.
- Patients being treated with gentamicin should be under close clinical observation because of its potential toxicity.
- In some patients with impaired renal function, there has been a transient rise in blood-urea-nitrogen, which has usually reverted to normal during or following cessation of therapy.
- Gentamicin should be used with care in conditions characterized by muscular weakness.
- To reduce the development of drug-resistant bacteria and maintain the effectiveness of the gentamicin in CERAMENT G and other antibacterial drugs, CERAMENT G should only be used in patients where the infection has been proven or strongly suspected to be caused by susceptible bacteria.

POTENTIAL ADVERSE EVENTS

The following adverse events are related to the general use of Gentamicin:

- Ototoxicity and nephrotoxicity are the most common side effects associated with Gentamicin therapy. Both effects are related to renal impairment and, therefore, dosage alteration should be considered in such patients. In addition, there have been rare reports of changes in electrolyte balance, including hypocalcaemia and hypokalaemia, caused by renal tubular dysfunction.
- As with other aminoglycosides, toxicity is related to serum concentration. At serum levels more than 10 µg/mL the vestibular mechanism may be affected and it is advisable to check serum levels to confirm that the initial peak level does not exceed 10 µg/mL and that trough levels do not exceed 2 µg/mL.
- Other adverse reactions associated with Gentamicin therapy include the following: acute renal failure, nausea, vomiting, urticaria, reversible granulocytopenia, hypersensitivity, anaphylactic reactions, anemia, blood dyscrasia, convulsions, central nervous toxicity, abnormal hepatic function, hypomagnesaemia, stomatitis, purpura, allergic contact sensitization and neuromuscular blockade.
- Combinations of antibiotics containing Gentamicin have been associated with rare reports of Clostridium difficile diarrhea.

The following potential adverse events are associated with concomitant use of pharmaceutical agents:

- Antibacterials: increased risk of nephrotoxicity with *cephalosporins* notably *cephalothin*.
- Gentamicin has been known to potentiate anticoagulants such as warfarin and phenindione.
- Antifungals: increased risk of nephrotoxicity with *amphotericin*.
- Cholinergics: antagonism of effect of *neostigmine* and *pyridostigmine*.
- Cyclosporin, cisplatin: increased risk of nephrotoxicity.
- Cytotoxics: increased risk of nephrotoxicity and possible risk of ototoxicity with *cisplatin*.
- Diuretics: increased risk of ototoxicity with *loop diuretics*.
- Muscle relaxants: effect of non-depolarizing muscle relaxants such as *tubocurarine* enhanced. Neuromuscular blockade and respiratory paralysis have been reported from administration of aminoglycosides to patients who have received curare-type muscular relaxants during anaesthesia.
- Concurrent use of bisphosphonates may increase the risk of hypocalcaemia.
- Concurrent use of Botulinum Toxin and gentamicin may increase the risk of toxicity due to enhanched neuromuscular block.

Local interactions

The consequences of concurrent use of other locally administered drugs are not known.

The following adverse events have been associated with the use of ceramic bone void fillers:

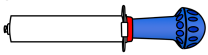
- Allergic/immune response
- Blood pressure change
- Bone fracture
- Cyst
- Death
- Decreased range of motion, loss of motor function, sensory deficit
- Delayed or nonunion, lack of osseointegration, impaired healing, inadequate bone formation
- Fluid accumulation, wound dehiscence, drainage
- Hematoma
- Material fracture, altered handling characteristics leading to failure
- Pain/discomfort, swelling, redness, fever, inflammation
- Protrusion, dislodgement, migration, or extravasation (leakage)
- Revisions and/or removals
- Superficial wound or deep wound infection
- Wound and soft tissue complications, including hematoma and drainage (calcium based bone void fillers may color wound drainage white).
- 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.

The following adverse events related to the use of CERAMENT G were reported in a clinical study:

- Delayed bone healing
- Delayed wound healing
- New sinus formation
- Non-union
- Pathologic fracture
- Recurrence of infection
- Soft tissue complications, including hematoma and drainage

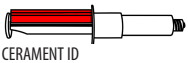
COMPONENTS AND COMPOSITIONS

CERAMENT



CERAMENT CMI

Mixing device pre-filled with ceramic bone substitute, a mixture of Calcium sulfate and Hydroxyapatite.



CERAMENT ID

Injection device (accuracy of measuring scale ± 5%).

Valve

To enable connections between CERAMENT CMI and syringes.

Tip Extender

Two Tip Extenders in different lengths to be used with CERAMENT ID facilitating paste injection.

GENTAMICIN SOLUTION

SYRINGE

Syringe with rotating adapter to use when preparing the Gentamicin solution. The red mark indicates the correct volume to take.

CERAMENT MIXING LIQUID

Sodium Chloride 9 mg/mL liquid, for dissolving the Gentamicin sulfate.

CERAMENT GENTAMICIN

Gentamicin; each dose, 1 mL paste, will contain 17.5 mg Gentamicin.

BONESUPPORT DP

Two ventilated dispensing pins to facilitate easy handling when preparing the Gentamicin solution.

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ADDITIONAL UTENSILS NEEDED

- Stopwatch

OPTIONAL UTENSILS

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

Consult and comply with the IFU of any additional utensils used.

DIRECTIONS FOR USE

- Store CERAMENT G unopened in a clean and dry environment at room temperature (15– 30°C / 59–86°F).
- 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.
- 1 mL paste contains 17.5 mg Gentamicin (provided as Gentamicin sulfate). Adjust volume of paste for sufficient dose of Gentamicin.
- The recommendation for Gentamicin intravenously is 3-6 mg Gentamicin/kg body weight.
- After the paste is in place, avoid any further adjustment.

STEP BY STEP INSTRUCTIONS FOR PREPARATION OF CERAMENT G

CERAMENT G consists of an outer cardboard box containing a plastic tray in a Tyvek pouch (sterile barrier) containing all the components. The cardboard box with content is ethylene oxide sterilized to ensure surface sterility of all components.

Preparation of Gentamicin solution

1. Remove the transparent cap from the CERAMENT MIXING LIQUID and the protective cover from one of the BONESUPPORT DPs and push the BONESUPPORT DP through the membrane of the CERAMENT MIXING LIQUID vial while keeping the vial stable.

2. Attach the SYRINGE to the BONESUPPORT DP, turn it upside down and withdraw liquid to the red mark on the SYRINGE barrel. Disconnect thereafter the SYRINGE from the BONESUPPORT DP.

3. Remove the lid from the CERAMENT GENTAMICIN vial and the protective cover from the second BONESUPPORT DP and push the BONESUPPORT DP through the membrane of the CERAMENT GENTAMICIN vial while keeping the vial stable.

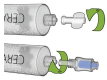
4. Attach the SYRINGE to the BONESUPPORT DP on the CERAMENT GENTAMICIN vial and inject the liquid to dissolve the Gentamicin powder.

5. Withdraw all Gentamicin solution back into the SYRINGE. The Gentamicin solution is now ready to be injected into CERAMENT CMI.

Preparation of CERAMENT G paste

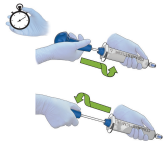
6. Retract the blue handle on the CMI and remove the red plunger stop.

7. Remove the plug on the CMI and attach the VALVE with the clear end to the CMI by turning it clockwise.



8. Attach the SYRINGE with Gentamicin solution to the blue end of the VALVE by pressing its tip through the blue membrane and turning it clockwise. Inject all Gentamicin solution into the CMI. Empty the SYRINGE completely and avoid back flush by keeping the plunger pushed to the bottom before detaching it.

9. Detach the SYRINGE from the VALVE on the CMI and immediately 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.



10. Fully retract the blue handle into its back position and lock the plunger by turning the blue collar clockwise until a "click" is heard.

11. Attach the ID to the VALVE and transfer the paste immediately with the grading on the ID facing the user and the ID plunger pointing upwards. When the ID is completely filled, excess paste will begin to ooze from under the sleeve. Stop the transfer when this occurs.

12. Detach the filled ID, remove the red plunger stopper and the paste is now ready to use. If applicable attach TIP EXTENDER or an optional needle (minimum 16G) to the ID.

Implantation of CERAMENT G

13. Wait until the paste has reached the desired consistency at approximately 4-7 minutes after start of mixing; carefully inject material from CERAMENT ID into the bone gap/void under visual inspection.

14. Proceed until the gap/void is filled with an adequate amount of paste, as judged by the responsible physician.

15. After the paste is in situ, allow to set and avoid adjustments for approximately 15 minutes, especially if bleeding occurs.

16. Close the wound meticulously to avoid leakage into soft tissue. Follow accepted clinical practice for postoperative care.

RESTRICTIONS

CERAMENT G may only be sold, distributed, and used in accordance with the intended use.

Only for professional use.

STERILITY

CERAMENT G is supplied sterile. Method for sterilization is by gamma irradiation, steam and ethylene oxide.

CERAMENT G is disposable and intended only for single use; the product should not be re-sterilized by any method and should not be re-used due to contamination risks.

MRI SAFETY INFORMATION

CERAMENT G is MR safe.

CAUTION

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

MANUFACTURER

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If you experience a serious incident in relation to CERAMENT G, report it immediately to both the manufacturer and the competent authority of your country.

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

BONESUPPORT Inc.
117 4th Ave, Suite 202
Needham, MA 02494
Email: us.sales@bonesupport.com
Email: complaint@bonesupport.com (for incident reporting)
Phone: 1-877-719-6718

ORDERING INFORMATION

Art. Number / Item

REF

A0535-05 CERAMENT G 10 mL
A0535-06 CERAMENT G 5 mL

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Symbol glossary

Symbol	Description	Symbol	Description
	Manufacturer	STERILE	Sterilized using steam or dry heat
	Use-by date		Do not use if package is damaged
LOT	Batch code		Caution
REF	Catalogue number		Do not re-use
STERILE EO	Sterilized using ethylene oxide		Consult instructions for use
STERILE R	Sterilized using irradiation	Rx Only	Device restricted to sale by or on the order of a physician
	Indicates the single sterile barrier system		Temperature limit

ISO 15223-1:2021 symbols used as applicable

Time, measured from start of mixing