CERAMENT™ G

INSTRUCTIONS FOR USE

DEVICE DESCRIPTION AND CLINICAL BENEFIT

CERAMENT G is an injectable ceramic bone graft substitute, consisting of Calcium sulfate (60%), Hydroxyapatite (40%), Sodium chloride (5 mg/mL paste) and Gentamicin sulfate. CERAMENT G delivers 17.5 mg Gentamicin/mL paste.

By combining Calcium sulfate and Hydroxyapatite an optimal balance is achieved between implant resorption rate and bone ingrowth 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 the newly formed bone.

By adding Gentamicin, colonization with Gentamicin sensitive microorganisms can be prevented in order to protect bone healing.

INTENDED USERS

Medical professionals.

INTENDED PATIENT POPULATION

Skeletally-mature patients who require surgery for bone voids which are at risk of bacterial colonization.

PERFORMANCE

The injecting performance is dependent upon the desired working consistency of the CERAMENT G.

Injectable: Approximately 4-7 minutes.

Final setting: The wound can be closed at approximately 15 minutes. CERAMENT G attains final setting at 20 minutes.

Beads: Fill mold cavities before 6 minutes. Release beads after 20 minutes.

Drilling: Drilling of the material can be performed at 15 minutes.

After implantation: CERAMENT G is resorbed and remodeled into new bone within 6-12 months after implantation.

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

INTENDED USE

CERAMENT G is a resorbable ceramic bone graft substitute intended to fill gaps and voids in the skeletal system to promote bone healing.

CERAMENT G provides a void/gap filler that during the surgical procedure can augment hardware and bone alignments.

Gentamicin is included in CERAMENT G to prevent colonization of Gentamicin sensitive microorganisms in order to protect bone healing.

INDICATIONS

CERAMENT G is indicated to be placed into bone voids or gaps in the skeletal system, i.e. extremities and pelvis (only during acetabular revision), that are not intrinsic to the stability of the bony structure.

These osseous defects may be:
In skeletally mature patients: spontaneously occurring, surgically created, resulting from traumatic injury to the bone, identified during primary surgery and revision surgery, or osseous defects identified around hardware devices.

MODE OF ACTION

The device CERAMENT G has two modes of action:

- Primary mode of action is to be a resorbable ceramic bone graft substitute intended to fill gaps and voids in the skeleton system to promote bone healing. CERAMENT G provides a void/gap filler that during the surgical procedure can augment hardware and bone alignments.
- Secondary mode of action is to prevent colonization of Gentamicin sensitive microorganisms in order to protect bone healing.

CONTRAINDICATIONS

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

WARNINGS

- Addition of Gentamicin does not negate the need for systemic antibiotics.

PRECAUTIONS

Practical instruction for sterile / aseptic usage

- Adhere to sterile surgical technique when preparing the CERAMENT G paste.

Supportive therapy

- Appropriate debridement is needed if pre-existing infection has been identified.
- Control active bleeding and remove blood clots and tissue fragments if open surgery.
- Use of active suction drainage may lead to a decrease in effective dose of Gentamicin.
- Consult and comply with the IFU of any additional utensils used.

Device related

- Contact between CERAMENT G and vital bone, and provision of normal conditions of fracture healing or bone growth as described in this section, is a prerequisite for good treatment outcome.
- 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 G should not be used in joints since its presence may cause inflammation or mechanical obstruction/damage. When used in the vicinity of joints, care should be taken to ensure that bone voids implanted with CERAMENT G are not in continuity with joint spaces, for example by ensuring adequate fracture reduction and/or by using fluoroscopic guidance (as determined by best surgical practice).
- Contact with joint fluid may cause resorption of CERAMENT G.
- Overpressurization during injection should be avoided as intra-medullar injection with any bone void filler may lead to fat embolization or embolization of device into the blood stream.
- 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 G in bead form rather than complete void filling for these indications.
- No clinical experience with additives in CERAMENT G. Using alternative mixing solutions and/or adding other substances to the mixture may affect the product setting in an uncontrolled manner, and may affect the safety and effectiveness of the product.
- 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.
- If using CERAMENT G in conjunction with allograft or autograft, apply each component separately, without intermixing before application, since intermixing may affect the setting time in an uncontrolled manner.
- If using the CERAMENT G to augment hardware and bone alignments during surgical procedure, wait until material final setting time for optimal use.

Patient related

- Careful examination of patient medical history is recommended.

Related to the use of Gentamicin

- CERAMENT G should be used with caution in elderly people and generally 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 main 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.

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- 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.
- Sulfites can cause allergic-type reactions including anaphylactic symptoms and bronchospasm in susceptible people, especially those with a history of asthma or allergy.
- Patient 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.
- In cases of significant obesity gentamicin serum concentrations should be closely monitored and a reduction in dose should be considered.

Potential interactions with concomitant use of pharmaceutical agents

(i) Antibacterials: increased risk of nephrotoxicity with *cephalosporins notably cephalothin.*
(ii) Gentamicin has been known to potentiate anticoagulants such as warfarin and phenindione.
(iii) Antifungals: increased risk of nephrotoxicity with *amphotericin.*
(iv) Cholinergics: antagonism of effect of *neostigmine* and *pyridostigmine.*
(v) Cyclosporin, cisplatin: increased risk of nephrotoxicity.
(vi) Cytotoxics: increased risk of nephrotoxicity and possible risk of ototoxicity with *cisplatin.*
(vii) Diuretics: increased risk of ototoxicity with *loop diuretics.*
(viii) 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.
(ix) Concurrent use of bisphosphonates may increase the risk of hypocalcaemia.
(x) Concurrent use of Botulinum Toxin and gentamicin may increase the risk of toxicity due to enhanched neuromuscular block.

Local interactions

Consequences of concurrent use of other locally administered drugs are not known.

SIDE EFFECTS

The following side effects have been reported to result from ceramic bone 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.
- May cause inflammatory reaction if present in soft tissue.
- 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 substitute containing 75-100% Calcium sulfate and 0-25% Calcium phosphate.

Known side effects related to the systemic use of Gentamicin

These side effects are side effects reported related to systemic gentamicin, but which are not known to be associated with the use of CERAMENT G. Nevertheless, it is recommended that users familiarize themselves with the potential side effects associated with the systemic 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. Vestibular damage and ototoxicity is usually reversible.
- As with other aminoglycosides toxicity is related to serum concentration. At serum levels more than 10 µg/mL the vestibular mechanism may be affected.
- Other adverse reactions associated with Gentamicin therapy include 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.

DISCLAIMER

- 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.

COMPONENTS AND COMPOSITIONS

Preparation of Gentamicin solution

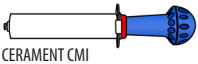
SYRINGE
Syringe to use when preparing the Gentamicin solution. The red mark indicates the correct volume to take.

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

CERAMENT GENTAMICIN
Gentamicin sulfate, 1 mL of CERAMENT G paste will contain 17.5 mg Gentamicin.

BONESUPPORT DP
2 pcs of ventilated dispensing pins to facilitate easy handling when preparing the Gentamicin solution.

Preparation of CERAMENT G paste



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 length 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

- 1 mL paste contains 17.5 mg Gentamicin (provided as Gentamicin sulfate). Adjust volume of paste for appropriate 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

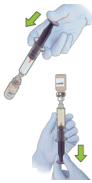
CERAMENT G consists of an outer cardboard box containing a plastic tray in a Tyvek pouch (sterile barrier) containing all the components. The cardboard box with content is ethylene oxide sterilized to ensure surface sterility of all components.

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 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.

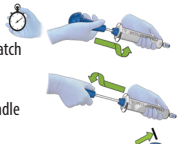
5. Withdraw all Gentamicin solution back into the SYRINGE. The Gentamicin solution is now ready to be injected into CERAMENT CMI.

Preparation of CERAMENT G paste

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

7. Remove the plug on the CERAMENT CMI and attach the Valve with the clear end to the CERAMENT 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 CERAMENT 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 CERAMENT CMI and immediately start the stop watch (t = 0 seconds). Mix in a tipped down position for 30 seconds with a frequency of approximately 1 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 CERAMENT ID to the Valve and transfer the paste immediately with a light pressure and with the CERAMENT ID plunger pointing upwards. The grading on the CERAMENT ID should be facing the user. When the CERAMENT ID is completely filled, excess paste will begin to ooze from under the sleeve. Stop the transfer when this occurs.

12. Detach the filled CERAMENT 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 CERAMENT ID.

Implantation of CERAMENT G

13. Wait until the paste has reached the desired consistency at approximately 4 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.

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 risk.

INFORMATION TO BE GIVEN TO THE PATIENT

Implant card

The included implant card shall be provided to the patient. The information on the front side of the card should be completed and label A0550 be attached on the back side before it is handed over to the patient.

Patient leaflet

The information in this section shall be conveyed to the patient. The patient information is also available as a leaflet on the web page www.BONESUPPORT.com/patientinfo (indicated on implant card).

What is CERAMENT G?

CERAMENT G is a synthetic bone graft substitute, containing Calcium sulfate (60%), Hydroxyapatite (40%), Sodium chloride (5 mg/mL paste) and Gentamicin sulfate. CERAMENT G delivers 17.5 mg Gentamicin/mL paste.

What is CERAMENT G used for?

CERAMENT G is used for patients that have a bone void/defect, in order to fill the bone void/defect to support bone healing and prevent infection.

How does CERAMENT G work?

Over time, CERAMENT G is resorbed and remodeled into new bone within 6-12 months after implantation. The gentamicin helps prevent colonization.

Is any special follow-up or monitoring required if you have CERAMENT G implanted?

No further surgical treatment or monitoring is required, you will have the routine follow-up appointments after your surgery.

Does the Gentamicin in CERAMENT G mean I don't have to take antibiotics separately?

No. If you have been prescribed antibiotics following your surgery, you must take them, as the Gentamicin in CERAMENT G does not replace the need for oral or intravenous antibiotics.

Adverse effects

Implanting CERAMENT G carries the same risks associated with every surgery such as infection, pain, bruising, swelling and bleeding at surgery site.

If CERAMENT G was used in proximity to a joint, this might cause an inflammation (redness, swelling, pain) of the joint.

Within soft tissue, CERAMENT G may cause an inflammatory reaction (redness, swelling, pain).

In rare cases CERAMENT G can lead to a collection of fluid or fluid that leaks from the wound, which is white in color. This "white wound drainage" resolves in most cases within two-three weeks without further treatment.

Seek medical advice if you experience any of these symptoms.

Do you use other medicines?

Tell your surgeon if you are using, have recently used or might use any other medicines.

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RESTRICTIONS

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

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http://www.bonesupportpatents.com/

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https://www.bonesupport.com/trademarks.html

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 unintentionally opened 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.

SUMMARY OF SAFETY AND CLINICAL PERFORMANCE

A summary of safety and clinical performance (SSCP) will be available in the European database on medical devices (EUDAMED), where it is linked to the Basic UDI-DI number of the product, 07350055430475 3.

https://ec.europa.eu/tools/eudamed

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

MANUFACTURED BY:

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ORDERING INFORMATION

Art. Number / Item

REF

A 0535-01 (10 mL) CERAMENT G 10 mL
A 0535-02 (5 mL) CERAMENT G 5 mL

CE 2797

Symbol glossary

Symbol	Description of symbol	Symbol	Description of symbol
	Time, measured from start of mixing		Do not use if package is damaged and consult instructions for use
UDI	Unique Device Identifier (UDI)		Information website for patients
	Indicates that the device contains or incorporates a medicinal substance		Patient name or patient ID
BIO	Indicates that the device contains or incorporates tissues or cells of animal origin, or their derivatives		Name and address of the implanting healthcare institution/provider
MD	Indicates that the device is a medical device	31	Date of implantation
	Indicates the sterile barrier system