CERAMENT® G
with Gentamicin

VALUE ANALYSIS GUIDE

The First and Only
Injectable Antibiotic-Eluting Bone Graft

Indicated for use in management of bone infection

- PROMOTE BONE HEALING
- LOCAL ANTIBIOTIC ELUTION
- LOWER COST OF CARE

BONESUPPORT™

About BONESUPPORT

BONESUPPORT is a Swedish orthobiologics company that develops, manufactures, and markets CERAMENT® — an innovative portfolio of injectable and drug-eluting bone void fillers with a proven ability to remodel into bone[4] and reliably elute local broad spectrum antibiotics.[8-10, 13]

Backed by more than 240 peer reviewed studies and publications, our products are effective in the management of patients with bone voids and infections caused by trauma, disease or related surgery.

Advances in Bone Infection

The best protection against bone infection is healthy bone. The traditional way of managing osteomyelitis (bone infection) is to first clear the infection site of any dead and/or poorly perfused bone by surgical debridement, leaving an empty void. For optimal management of bone voids and gaps, we created CERAMENT® G.

- **Proven bone remodeling[4]**
- **Local, broad spectrum antibiotic elution**
- **96% success in eradication of infection**
- **Supports a single-stage treatment pathway**
- **Lowers cost of care while improving patient quality of life[20]**
- **Consistent antibiotic elution that is safe and reliable**

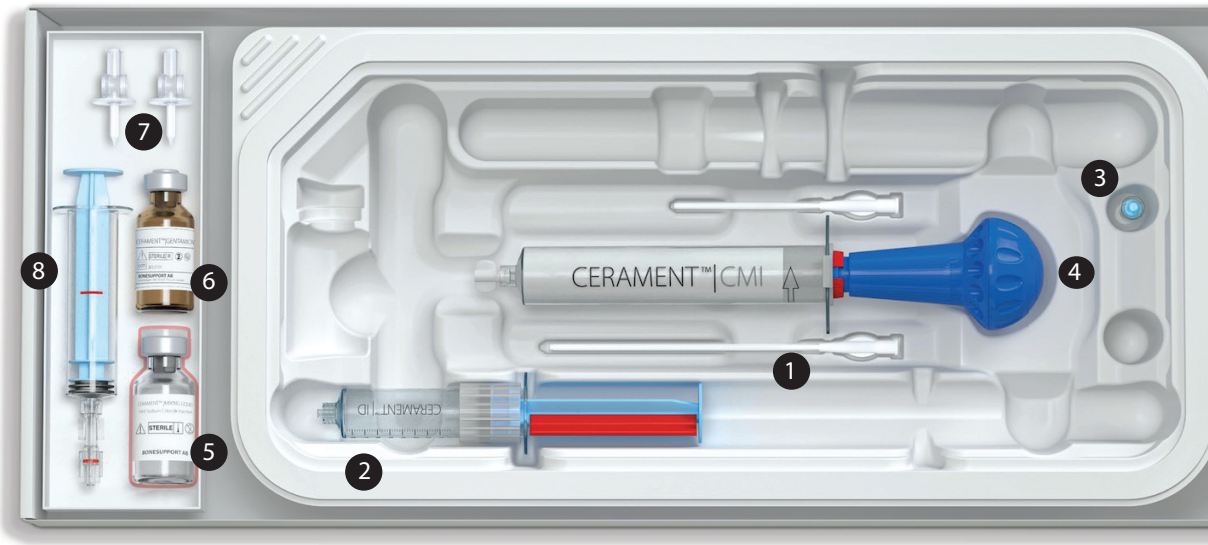
Our Mission - Restoring health to improve the quality of life for patients with bone disorders.

The FDA designated CERAMENT® G a Breakthrough Device

Reserved for therapies that treat serious and life-threatening conditions and which have demonstrated substantial improvement over other therapies and/or is the first of its kind.

One complete kit

1. 2 x 11G tip extenders with tapered ends in 50mm & 100mm lengths
2. Injection Device (ID) syringe
3. Valve
4. Combined Mixing and Injection (CMI) syringe pre-filled with hydroxyapatite (HA)/calcium sulfate (CaS) powder
5. Mixing Liquid, sodium chloride 9 mg/mL liquid
6. Gentamicin sulfate, provides 17.5 mg gentamicin/mL paste
7. Dispensing pins
8. Syringe for preparing the gentamicin solution



CERAMENT G® with Gentamicin

CERAMENT® G is the firstc ombination bone graft substitute and antibiotic indicated as part of the management of osteomyelitis. Unlike other treatment options, CERAMENT® G is injectable and can be delivered in a single-stage procedure because of its unique ability to simultaneously remodel into bone and elute an antibiotic to protect bone healing. With a 96% success rate in reducing chronic osteomyelitis, healthcare resources and costs are reduced while clinical outcomes are improved.[5]

Challenges of Bone Infection

Osteomyelitis is an infection of the bone that can arise from fractures, placement of orthopedic implants, and diabetic foot ulcers.

Osteomyelitis is a devastating disease that can be irreversibly debilitating and can lead to limb amputations.[11] Patient comorbidities play an important role in the propagation of the infection, and the disease requires substantial dedication from the patient and the entire multi-disciplinary medical care team to eradicate.[12,5] The overall healthcare burden to patients, providers and payers is significant.

CONSIDER THE IMPACT OF BONE INFECTION

CHRONIC OSTEOMYELITIS

Underlying osteomyelitis due to trauma may present itself post-surgery. While the infected bone is removed through surgery, the infection often recurs.

~2 PER 10,000

People diagnosed annually with osteomyelitis in the US[11]

20-30%

Long term recurrence rate (despite antibiotic/surgical advancements)[15, 16]

FRACTURE-RELATED INFECTIONS

Infection can quickly establish itself after a fracture. For Gustilo-Anderson type III open tibial fractures, the estimated rate of infection is 12.3% for IIIB and 16.1% for IIIC.[30]

UP TO 30%

Infection rate after open fractures[31]

3-5%

Amputation rate to treat FRI[17]

DIABETIC FOOT OSTEOMYELITIS

Diabetic foot ulcers are the consequence of neuropathy and vascular disease. They are worsened by infection which, if it reaches the bone, may require surgical resection or amputation.

20%

Diabetic patients with infected foot ulcers have underlying osteomyelitis[18]

15%

Patients will require amputation[19]

1 OF 5

Patients will be readmitted within 30 days of lower extremity amputation(s)[21]

Osteomyelitis Treatment and Limitations

Surgical management of bone infection consists of debridement, tissue sampling and excision of dead/necrotic (infected) bone. The resulting dead space requires management to regenerate the lost bone and mitigate reinfection.[12]

Common practice is a two-stage or multi-stage surgical approach in which the first stage incorporates antibiotic-loaded polymethyl methacrylate (PMMA) beads. The beads are then removed in a subsequent surgery and replaced with a resorbable bone graft to fill the dead space.[23]

Clinical advancements have cleared the path for a single-stage surgery, but typically entails off-label manual mixing of calcium sulfate with antibiotics. This results in inconsistent and unpredictable local antibiotic delivery and little bone remodeling due to fast absorbing calcium sulfates.

The lack of a standard of care along with improvised treatment options contribute to the high rates of reinfection, amputations, increased mortality and associated healthcare costs.

Survey Results: Hospital Admins & Surgeons

26% Reported reinfection rate[23]

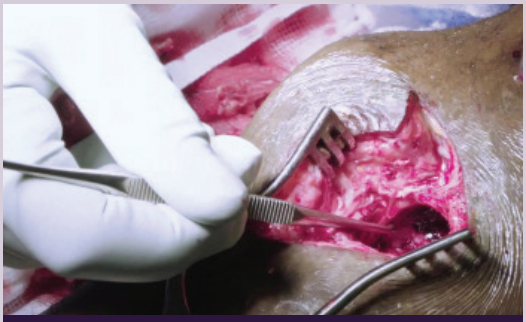
33% Patients present needing amputation[23]

94% Want a better bone graft option[3]

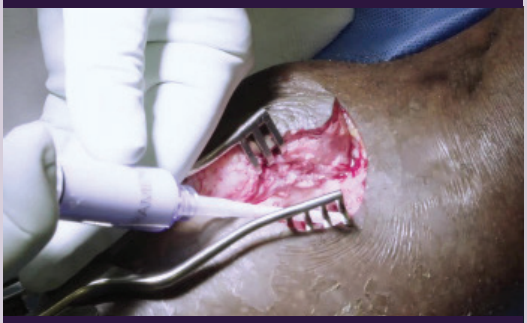
92% Prefer a single stage treatment[23]

FILLING A BONE VOID WITH CERAMENT® G AFTER SURGICAL DEBRIDEMENT IN A SINGLE-STAGE PROCEDURE

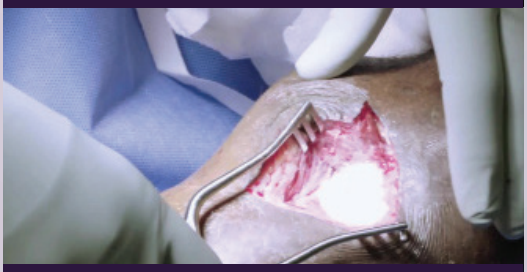
CERAMENT® G's dual mode of action provides bone remodeling with predictable elution of gentamicin in a single-stage procedure.



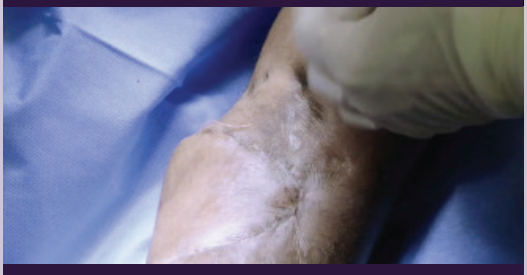
1. Dead bone is removed leaving a void



2. CERAMENT injected into bone void



3. Bone void is completely filled



4. CERAMENT has set and wound is closed

Reprinted with kind permission of the Oxford Bone Infection Unit

A New Pathway for Bone Infection

CERAMENT® G provides a pathway for a one-stage approach to the management of osteomyelitis with its unique dual mode of action that delivers proven bone remodeling with reliable elution of a local broad spectrum antibiotic.[5]

CERAMENT® G is an implantable device/drug combination bone void filler and was granted Breakthrough Device Designation by the Food and Drug Administration (FDA). This important designation is reserved for devices that provide for more effective treatment or diagnosis of life-threatening or irreversibly debilitating human disease or conditions and are first of its kind.

Additional Surgical Option for Diabetic Foot Infection

CERAMENT G can enable a surgical pathway for challenging diabetic patients. It is an additional option available to preserve limb length, saving mobility and reducing costs by averting amputations.

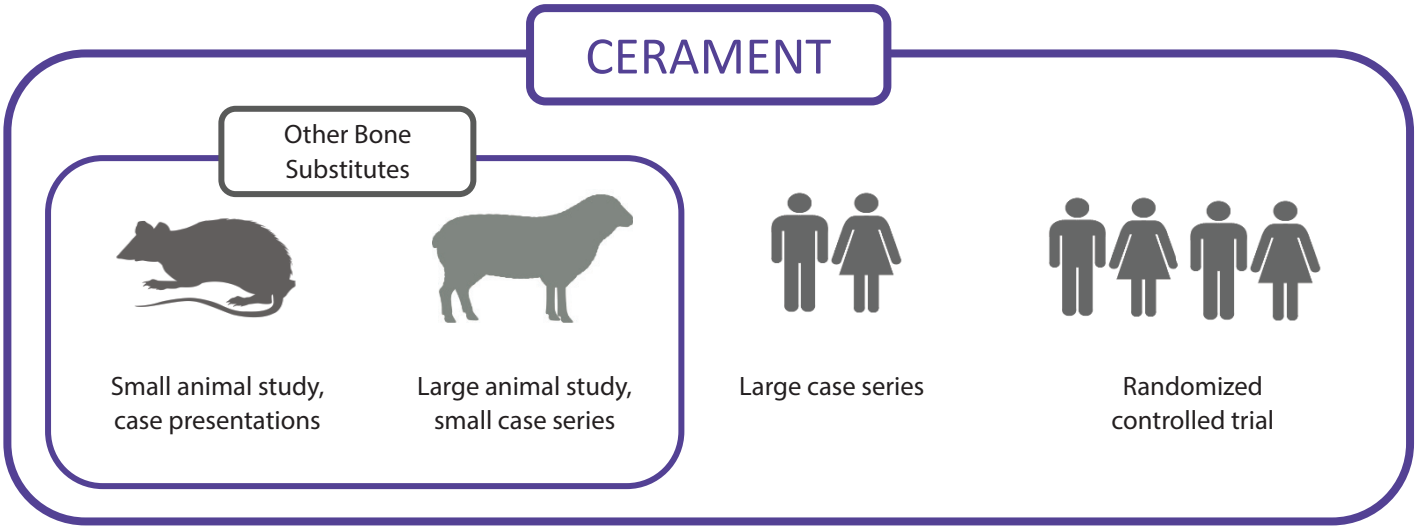
The high costs of treating diabetic foot patients is well documented, beginning with an average of $17,245 for management of a diabetic foot ulcer. This can escalate quickly if amputation is needed, ranging from $43,000 to over $63,000 per event.[28]

Limb salvage attempt: debridement and filling with CERAMENT® G

CERAMENT® G offers a surgical option for diabetic patients progressing towards amputation.

Only CERAMENT® is backed by a robust body of data

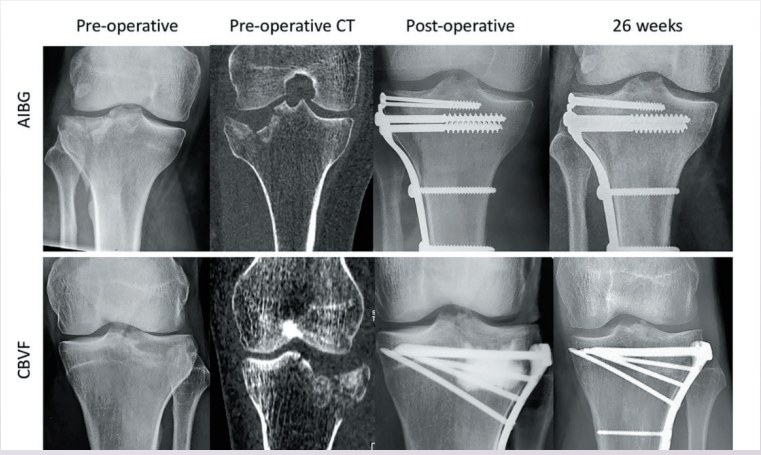
CERAMENT® has the largest amount of animal and clinical data to prove bone remodeling and is the only bone graft substitute with patient reported outcome measures (PROMs) data. No other bone graft offers this level of clinical data.



A LEVEL 1 STUDY COMPARING CERAMENT® BONE VOID FILLER TO "GOLD STANDARD" AUTOGRAFT

ABOUT THE STUDY

Published in the *Journal of Bone and Joint Surgery American* (2020), CERTiFY is a Level I, multi-center, prospective, randomized controlled trial of patient-reported outcome measures (PROMs) in 135 patients[24]



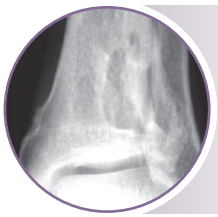
RESULTS

- CERAMENT was found to be as good as autograft
- Proven bone remodeling with CERAMENT
- Less post-op pain with CERAMENT
- Less blood loss with CERAMENT
- Results confirmed by PROMS and radiographs

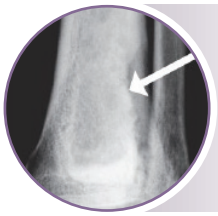
CERAMENT® G
Dual Mode of Action

PROMOTE BONE HEALING

- Proven bone remodeling



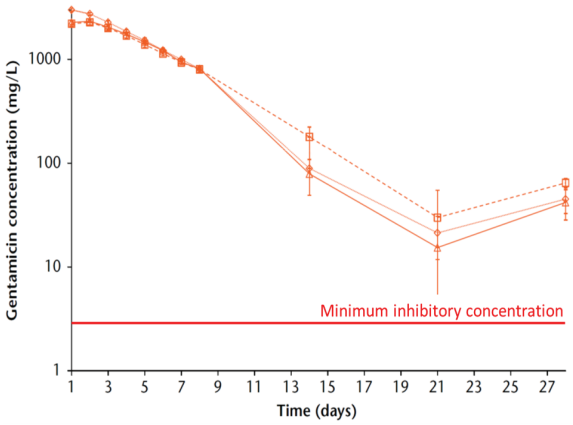
Debridement and injection of CERAMENT G: CERAMENT is highly flowable to completely fill voids and cracks.



The bone is healed at 6-12 months: The CaS in CERAMENT is fully resorbed, HA is embedded in bone and natural bone building continues increasing mechanical strength

PROTECT BONE HEALING

- High burst of a local broad spectrum antibiotic.
- Sustained release above MIC* for 28 days.
- Serum levels well below systemic toxicity levels.[8]
- Consistent elution independent of surface area as demonstrated on the graph below.[8]



*The minimum inhibitory concentration (MIC) is the lowest concentration of a chemical, usually a drug, which prevents visible growth of bacterium.[14]

Managing bone infections is simplified with CERAMENT G

TRADITIONAL TREATMENT

Multi-stage surgery plus systemic antibiotics to manage infection

0-2 WEEKS | 3-4 WEEKS | 5-6 WEEKS | 7+ WEEKS

MULTIPLE STAGES | **HEALING STARTS**

1st surgical procedure
Placement of non-resorbable antibiotic carrier

Subsequent procedure
Harvest bone graft (for autograft), removal of non-resorbable antibiotic carrier plus bone transplantation.

WITH CERAMENT G

Single-stage surgery to manage infection

HEALING STARTS

Single surgical procedure
Injection of CERAMENT G

96% of patients were infection-free after surgical management and CERAMENT G in a one-stage approach.

A reduction in hospital-related costs with CERAMENT® G has been shown in the largest analysis of hospital episode statistics for NHS England carried out for a bone graft substitute to date.[20]

The study was carried out at Oxford University Hospital, a world leader in osteomyelitis treatment and pioneer of the multi-disciplinary team (MDT) service (orthopaedics, plastics and microbiology).

In the analysis, 25,006 patients diagnosed with osteomyelitis in England between 2013 and 2017 were included and split between two groups: patient treated in a MDT service with CERAMENT® G as part of their treatment and patients treated in the rest of England.[20,27]

Oxford Protocol Results[20]

- 79% lower mortality rate
- 58% reduction in readmissions
- 39% reduction in length of stay
- 7% reduction in all hospital visits
- 48% reduction in Emergency Room visits over a 24 month post surgery period

CERAMENT® G in a Distal Tibial Osteomyelitis Case

Figure 2a
Pre-op X-ray of the tibia with haematogenous osteomyelitis present for more than ten years.

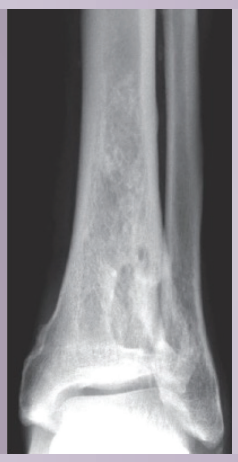
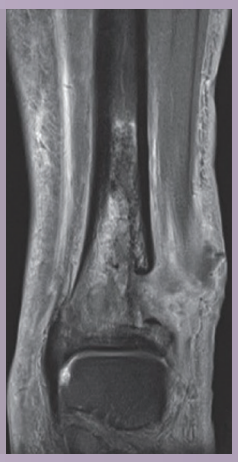


Figure 2b
MRI image demonstrates a cortical defect communicating with the skin sinus and central active infection, identified as Staph aureus.



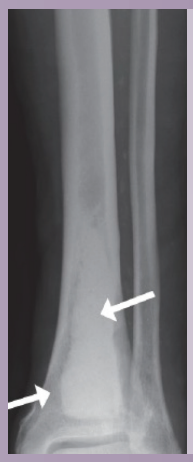


Figure 2c
3 days post-op, good contact between CERAMENT and bone surface can be seen.

Figure 2d
6 weeks post-op the margin is more diffused and a 'reactive zone' around CERAMENT G is visible in the cancellous bone and on the surface.

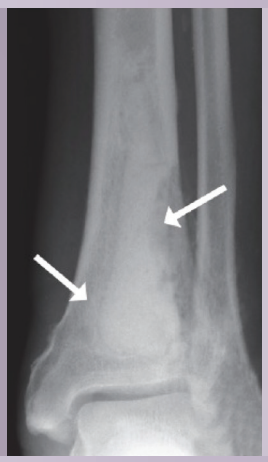
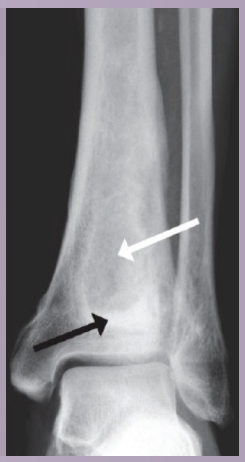


Figure 2e
At 6 months, residual CERAMENT is seen distally (black arrow) along with the reappearance of trabecular markings in the central zone (white arrow).



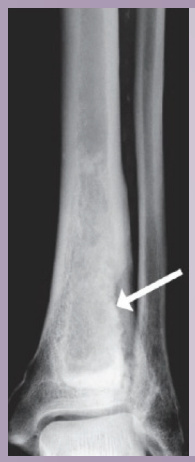
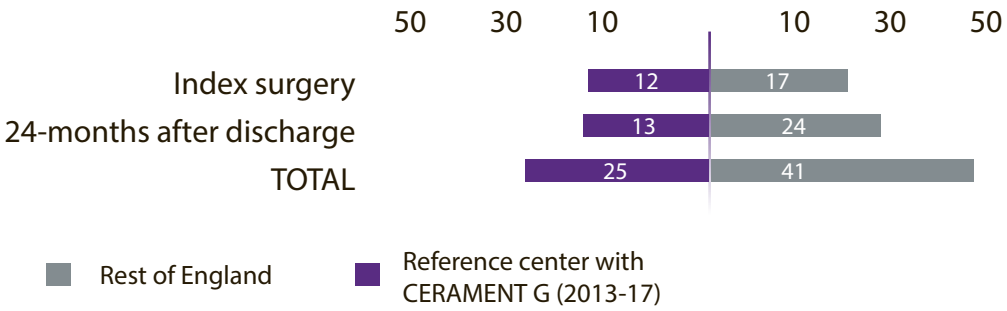


Figure 2f
At 18 months CERAMENT has undergone further remodeling, with increased density in the peripheral zone and the lateral cortext more defined.

CERAMENT® G can help reduce hospital admissions, length of stay and costs

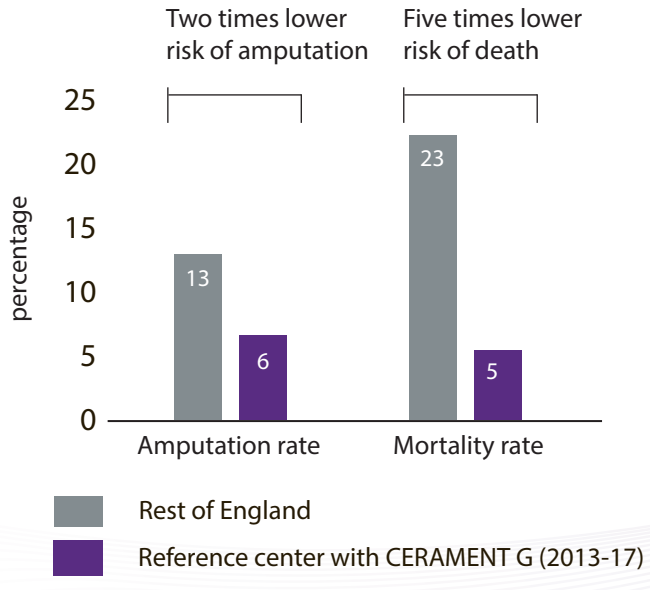
16 fewer bed days during index surgery and 24-months after discharge generates large cost savings per patient[20]



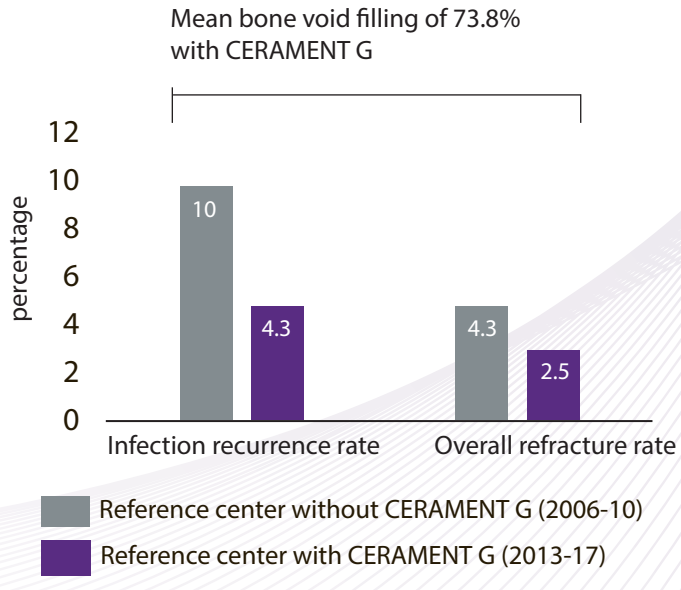
$10,266 Direct cost savings per patient from reduced length of stay*

*Average cost per bed day of £500; the average annual exchange rate between pound sterling and US dollars for 2020 was used (£1 = $1.2832); data sourced from the Office for National Statistics (ons.gov.uk)

Improved patient outcomes at the reference center relative to the rest of England[20]



Use of CERAMENT G contributes to improved clinical outcomes at the reference center[4,7]



CERAMENT® G Difference

Improve Osteomyelitis Outcomes & Reduce Costs

Value is about achieving the best outcomes per dollar spent. When bone healing fails, and infection occurs or reoccurs after surgery, more resource-intensive procedures are required. The quality of life for patients also worsens as a result.

Calculating the Value of CERAMENT® G

CERAMENT® G is uniquely positioned to decrease healthcare costs while improving patient's lives. To support CERAMENT® G's value and ease the decision between cost and care, BONESUPPORT is developing tools and pursuing product focused reimbursement pathways.

1. A cost-effectiveness analysis to demonstrate how the use of CERAMENT® G in a single-stage approach can reduce healthcare-related expenses (vs. multi-stage approaches) while improving patient quality of life.
2. An interactive companion to the VAC Guide showcasing different ways that adopting CERAMENT® G can help hospitals make managing bone infections more effective.
3. CMS has proposed to approve new technology add-on payments (NTAP) for CERAMENT G. This will be a cost off-setting resource to help adoption and support health systems to gain access to new technology and provide the most advance care for their patients.

Reimbursement

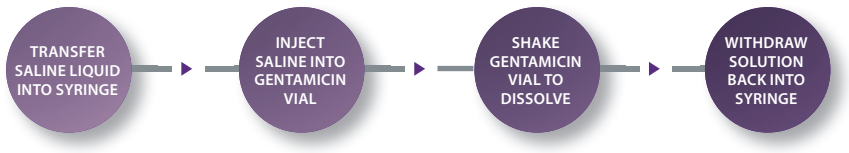
Currently all bone void fillers get allocated under the primary DRG in a bundled payment. BONESUPPORT, through it's FDA Breakthrough Designation, was awarded a unique ICD-10 Procedure Code and NTAP is expected to go into effect October 1st 2022. NTAP will provide inpatient hospital stays with additional payment for the use of CERAMENT G when the hospital costs exceeds the payment threshold.

ICD-10-PCS	DESCRIPTION
XWOV0P7	Introduction of Antibiotic eluting Bone Void Filler into Bones, Open Approach, New Technology Group 7

EASY MIXING

Pre-measured, Self-contained, Predictable

Step 1: Prepare the Gentamicin Solution



Step 2: CERAMENT G Mixing and Setting Time

CERAMENT: Summary of Unique Features and Clinical Benefits

FORMULA	DETAILS	CLINICAL VALUE
Proprietary Formula	• 60% calcium sulfate (CaS) • 40% hydroxyapatite (HA) • Gentamicin (17.5 mg of gentamicin/mL of CERAMENT paste)	• CaS enhances injectability[1] and acts as a carrier for HA and gentamicin • HA is highly osteoconductive and provides a longterm scaffold for bone remodeling[1] • Inhibits gentamicin-sensitive microorganisms from colonizing the bone void filler to protect bone healing[2]
Bone remodeling	• Proven bone remodeling[3-5]	• Reduces the risk of re-fracture, non-union and (re)infection[4,5] and the costs associated with additional treatment • Improves patient outcomes[4]
Antibiotic elution	• Reliable, consistent elution at a concentration and for a time period that is clinically relevant[8] • Far higher local concentrations at site than achievable with systemic antibiotics[8] • No reported risk of systemic toxicity[8,29]	• Gentamicin elution stays above Minimum Inhibitory Concentration (MIC) for at least 28+ days[8] to reduce the risk of (re)infection[4,5,9] • Reduce readmission rates, length of stay and cost of care[20] • Protects bone healing[6] and improves patient outcomes[4] • Reduces overall antibiotic use due to reduction in surgical stages and reinfection rates
Preparation	• Self-contained, sterile mixing device • 30-second mixing	• Easy to mix and use • Consistent and reliable antibiotic concentration
Handling & Timing	• Injectable between 4- 7 minutes • Drillable after 15 minutes • Not temperature sensitive	• Intra-operative flexibility to inject, mold and drill, reducing need for multiple products • Injectability ensures complete filling of voids to reduce risk of (re)infection
Temperature	• Not temperature sensitive • Product is stored at room temperature (15-25°C / 59-86°F) • Isothermic setting process	• Product can be used straight off the shelf • Setting time is not affected by room or body temperature • Isothermic - no heat or cold is given off during setting, so there is no damage to surrounding cells and tissues
Clinical data / FDA / Adoption	• Over 240 publications and 70,000 patients treated worldwide with the CERAMENT portfolio • Received FDA authorization in 2022 • Received CE-mark in 2013	• 58% reduction in readmissions[20] • 46% reduction in length of stay[20] • 7% reduction in all hospital visits[20] • 48% reduction in Emergency Room visits over a 24 month post surgery period[20] • Level I study against the gold standard autograft[24], CERAMENT BVF demonstrated equivalence to autograft with: - proven bone remodeling - less post-op pain - less blood loss - trend towards shorter duration of surgery

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