OsteoRemedies®
ADVANCED MEDICAL TECHNOLOGIES

SURGEON INFORMATION

UNITE® AB BONE CEMENT

1

Overview
UNITE® AB Bone Cement is a high-viscosity, radiopaque bone cement containing and releasing gentamicin sulphate for manual application. UNITE® AB Bone Cement is a single use, sterile medical device provided in doses of 40g.

The package contains a 40g packet of powder sterilized by gamma ray and a blister pack sterilized by ethylene oxide containing a 15.7ml vial of sterile liquid that is sterilized by filtration.

Component Formulation

Liquid component	**15.7 ml vial**
Methylmethacrylate	98.20% w/w
N-N Dimethyl-p-Toluidine	1.80% w/w
Hydroquinone	75 ppm

Powder component	**40g packet**
Polymethylmethacrylate	82.78% w/w
Barium Sulphate	10.00% w/w
Benzoyl Peroxide	3.00% w/w
Gentamicin sulphate	4.22% w/w*

**Equivalent to 1g (1.0 M.I.U.), 2,5% gentamicin base in 40g unit.*

For Internal Use Only

INDICATIONS FOR USE
UNITE® AB Bone Cement is indicated for the fixation of prostheses to living bone in the second stage of a two-stage revision for total joint arthroplasty after the initial infection has been cleared.

CONTRAINDICATIONS
UNITE® AB Bone Cement is contraindicated in primary orthopaedic musculoskeletal surgical procedures.

UNITE® AB Bone Cement is contraindicated in patients who are allergic or sensitive to any of its components, including gentamicin sulphate. If the patient has a history of hypersensitivity or

serious toxic reactions to aminoglycosides, the use of any other aminoglycosides may also be contraindicated due to the known cross-sensitivity of patients to drugs in this class.

UNITE® AB Bone Cement is contraindicated in the presence of active or incompletely treated infection, at the site where the bone cement is to be applied.

UNITE® AB Bone Cement is contraindicated where the loss of musculature or neuromuscular compromise in the affected limb would render the surgical procedure unjustifiable.

UNITE® AB Bone Cement must be considered carefully in the presence of myasthenia gravis. There may be increased risk of ototoxicity from gentamicin, if other ototoxic drugs such as cisplatin (an antineoplatic agent) and vancomycin (another antibiotic) are given at the same time. There also appears to be a synergistic effect of loop diuretics, such as furosemide or ethacrynic acid, and also loud noise, when combined with gentamicin.

CEMENT ACTIONS
UNITE® AB Bone Cement provides the fixation of a prosthesis to the anatomy/bone, and allows for even distribution of weight and stresses between bone and prosthesis. The presence of barium sulphate enables radiopacity.

ADVERSE EFFECTS
Negative reactions may arise when using bone cement but may not be directly attributable to the bone cement itself. Surgeons must be aware of these effects and be prepared to treat them accordingly. The blood pressure often drops temporarily immediately after implanting the bone cement and the prosthesis.

Serious reactions
- Sudden death
- Cardiac arrest
- Myocardial infarct
- Cerebrovascular incidents
- Pulmonary embolism

Miscellaneous reactions
- Dysuria
- Allergic pyrexia
- Hematuria
- Breakage of cement
- Local neuropathy
- Local vascular erosion and occlusion

- Delayed sciatic nerve entrapment from extrusion of the bone cement beyond the region of its intended application
- Intestinal obstruction because of adhesion and stricture of the ileum from the heat released during the exothermic polymerization
- Bladder fistula
- Trochanteric bursitis
- Pain and/or loss of function
- Heterotopic new bone formation
- Thrombophlebitis
- Hematoma-hemorrhage
- Infection of surface/deep surgical wound
- Loosening or displacement of prosthesis
- Elevated serum gamma-glutamyl-transpeptidase (GGTP) up to 10 days post surger
- Trochanteric separation
- Short-term cardiac irregularities

Recurring infections, though rare have been known to occur even with IV antibiotic use and do not ensure that recurrence or resistance is avoided.

Aminoglycosides (all) have the potential to produce reversible and irreversible vestibular, cochlear and renal toxicity.

Negative reactions to gentamicin sulphate are not expected at the levels contained within UNITE® AB Bone Cement.

High serum peaks of aminoglycoside created by once-daily drug administration are well tolerated; the once-daily regimens are just as safe as or safer than multiple-dose regimens.

The following adverse reactions have been connected with doses typical of prescribed dosages of gentamicin sulphate for systemic parenteral administration.

Nephrotoxicity
- Patients with normal renal function to whom aminoglycosides are administered for longer periods or in higher doses than suggested
- Patients with pre-existing renal damage
- Symptoms of nephrotoxicity may manifest after the conclusion of therapy

Renal function changes, as shown by increasing NPN, BUN, and serum creatinine and by oliguria, cylindruria, and increased proteinuria, have been noted, primarily in patients with a history of renal impairment who are treated for prolonged periods or with higher doses than those suggested. Negative renal effects may occur in patients with initial normal renal function.

Clinical and animal studies have been conducted to compare the nephrotoxic potential of tobramycin and gentamicin. In some of these studies, tobramycin caused nephrotoxicity significantly less frequently than gentamicin. In other studies, no significant difference in the incidence of nephrotoxicity between tobramycin and gentamicin was discovered.

Neuromuscular blockage or respiratory paralysis can occur, more commonly in patients with Parkinson's disease or myasthenia gravis. Aminoglycosides have limited allergenic potential; both anaphylaxis and rash are uncommon. Rare hypersensitivity reactions, which include fever, skin-rashes, eosinophilia, etc., have been noted.

Additional reported negative effects possibly related to gentamicin include: rash, thrombocytopenia, fever, exfoliative dermatitis, itching, urticaria, vomiting, diarrhea, nausea, headache, anemia/granulocytopenia, lethargy, confusion and disorientation. Lab abnormalities related to gentamicin include: increased serum LDH and bilirubin, serum transaminases including AST and ALT; decreased magnesium, sodium and potassium, serum calcium; leukopenia, leukocytosis, and eosinophilia.

Neurotoxicity
- Twitching muscles
- Convulsions
- Vestibular and auditory ototoxicity – includes irreversible hearing loss
- Numbness
- Skin tingling

Adverse effects on auditory and vestibular branches of the eighth nerve have been found, primarily in patients receiving prolonged therapy or high doses, in those given previous courses of therapy with an ototoxic drug, and those suffering from dehydration. Symptoms may include, tinnitus, vertigo, dizziness, roaring in the ears and hearing loss. Hearing loss is typically irreversible and is brought on initially by diminution of high-tone acuity. Gentamicin and tobramycin sulfate share similar ototoxic potential.

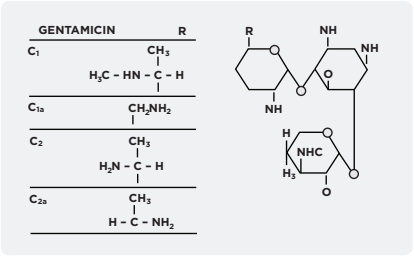
PRECAUTIONS DURING PREGNANCY, BREAST-FEEDING AND IN CHILDREN
Tests which demonstrate the utilization safety of bone cement during pregnancy or breast-feeding, and in children are not available. It is advised that bone cement should not be implanted during the first three months of pregnancy and for the balance of the gestation

period, bone cement should only be used in critical, life endangering situations. Animal teratology study results using standard nonantibiotic bone cement were shown to be negative. Systemic administration of aminoglycosides may cause fetal harm when administered to a pregnant woman. Aminoglycosides antibiotics cross the placenta. Several reports of total irreversible bilateral congenital deafness in children whose mother received streptomycin during pregnancy have been noted. Issues to mother, fetus, or newborn in the treatment of pregnant women with other aminoglycosides have not been reported.

In the event gentamicin bone cement is used during pregnancy or if the patient becomes pregnant while gentamicin bone cement is in use, she should be notified of the possible dangers to the fetus. Women of childbearing potential should consider the benefits and dangers associated with the use of the product. Gentamicin bone cement is indicated for use in skeletally young patients only when it is assumed that saving the joint through other forms of intervention is not possible.

MICROBIOLOGY OVERVIEW

Gentamicin sulphate is an aminoglycoside antibiotic derived from the actinomycete micromonospora purpurea. The molecular weight is 449.55. The product contains no preservative or sodium bisulfite. Gentamicin sulphate is a complex of the gentamicins C1, C1a, C2, and C2a illustrated below:



PHARMACOLOGY

Mechanism of action

Gentamicin is rapidly bactericidal. It acts primarily by inhibiting protein synthesis and leading to misreading of mRNA leading to altered cell membrane permeability, progressive disruption of the cell envelope as well as other vital processes and cell death.

Antibacterial activity
Gentamicin activity is primarily directed against aerobic, gram negative bacilli. The action against most gram positive bacteria is limited. Gentamicin is active against sensitive strains of enterococci and streptococci at concentrations which can be achieved clinically only when combined with a penicillin. Gentamicin is active *in vitro* against more than 90% of strains of *S. aureus* and 75% of *S. epidermidis*. Gentamicin has been shown to be active against most strains of the following organisms both *in vitro* and in clinical infections.

Most common susceptible pathogens
Gram positive bacteria
Staphylococcus aureus; Streptococcus pyogenes; Streptococcus pneumoniae; Streptococcus faecalis; Listeria monocytogenes

Gram negative bacteria
Citrobacter; Enterobacter; Escherichia coli Klebsiella spp.; Proteus mirabilis; Proteus vulgaris; Morganella morganii; Providencia spp.; Salmonella spp.; Serratia; Shigella spp.; Pseudomonas aeruginosa

The drug claims for gentamicin, including its mechanism of actions and antibacterial activities for the gentamicin containing bone cements have not been clinically proven. Gentamicin containing bone cements have not been shown clinically to be active against strains of the organisms indicated above.

Aminoglycosides
The aminoglycosides are a clinically important group of antibiotics that have a broad antibacterial spectrum and their action is bactericidal. The family includes streptomycin, gentamicin, tobramycin, kanamycin, amikacin and netilmicin. The aminocyclitols such as spectinomycin are closely related and have a similar mode of action. Aminoglycosides have a variety of effects within the bacterial cell but principally they inhibit protein synthesis. Another important function of the aminoglycosides is that they increase membrane leakage. Aminoglycosides have a little activity against most gram-positive bacteria, including Streptococcus pyogenes, S. pneumoniae, and enterococci. Although most strains of enterococci demonstrate *in vitro* resistance, some strains in this group are susceptible (*E. faecalis*). *In vitro* studies have shown that an aminoglycoside combined with an antibiotic interfering with cell-wall synthesis (e.g. penicillin, vancomycin) affects some enterococcal strains synergistically, resulting in more bactericidal effect. The ®-lactam antibiotic favors the intracellular penetration of aminoglycoside. The combination of penicillin G and gentamicin results in a synergistic bactericidal effect *in vitro* against certain strains of Enterococcus faecalis. However this combination is not synergistic against other closely related organisms (e.g. *E. faecium*). Susceptibility testing and tests for antibiotic synergisms are emphasized.

Microbial resistance
Bacteria may be resistant to the antimicrobial activity of the aminoglycosides because of failure of permeation of the antibiotic, low affinity of the drug for the bacterial ribosome, or inactivation of the drug by microbial enzymes. Drug inactivation is by far the most important explanation for the acquired microbial resistance to aminoglycosides that is encountered in clinical practice. Cross-resistance between aminoglycosides may occur.

Absorption
All of the aminoglycosides are absorbed rapidly from intramuscular sites of injection. Peak concentrations in plasma occur after 30 to 90 minutes and are similar to those observed 30 minutes after completion of an intravenous infusion of an equal dose over a 30-minute period. In critically ill patients, especially those in shock, absorption of drug may be reduced from intramuscular sites because of poor perfusion. The aminoglycosides are highly polarcations and therefore are very poorly absorbed from the gastrointestinal tract.

Distribution
Because of their polar nature, the aminoglycosides largely are excluded from most cells, from the central nervous system, and from the eye. The apparent volume of distribution of these drugs is 25% of lean body weight and approximates the volume of extracellular fluid. Concentrations of aminoglycosides in secretions and tissues are low. High concentrations are found only in the renal cortex and in the endolymph and perilymph of the inner ear; this may contribute to the nephrotoxicity and ototoxicity caused by these drugs. Concentrations in bile approach 30% of those found in plasma as a result of active hepatic secretion, but this represents a very minor excretory route for the aminoglycosides. Penetration into respiratory secretions is poor. Diffusion into pleural and synovial fluid is relatively slow, but concentrations that approximate those in the plasma may be achieved after repeated administration. Inflammation increases the penetration of aminoglycosides into peritoneal and pericardial cavities. Concentrations of aminoglycosides in cerebrospinal fluid (CSF) that are achievable with parenteral administration of drug usually are subtherapeutic. Penetration of amino glycosides into ocular fluids is so poor that effective therapy of bacterial endophthalmitis requires periocular and intraocular injections of the drugs.

Systemic Dosing
Traditionally, the total daily dose of aminoglycosides is administered as two or three equally divided doses. Administration of the total dose once daily, however, appears to be less toxic and just as effective. Toxicity results from accumulation of drug in the inner ear and kidney. The amount of drug that accumulates increases with higher plasma concentrations and longer periods of exposure. Elimination (or washout) of aminoglycoside from these organs occurs more slowly than from plasma and is retarded by high plasma concentrations

accounting for the association between toxicity and high plasma trough concentrations. Toxicity, then, can be considered as a threshold phenomenon, more likely to occur the longer the plasma concentration exceeds a relatively safe upper limit (e.g., above a recommended trough concentration). A once daily dosing regimen, despite the higher peak concentration, provides a longer period when concentrations are below the threshold for toxicity than does a multiple-dosing regimen (12 hours versus less than 3 hours total in the example shown in the figure), accounting for its lower toxicity. Aminoglycoside bactericidal activity, on the other hand, is directly related to the concentration achieved, because aminoglycosides have concentration-dependent killing and a concentration-dependent postantibiotic effect. This enhanced activity at higher concentrations probably accounts for the equivalent efficacy of a once-daily regimen compared to a multiple-dosing regimen despite the relatively prolonged periods of time that plasma concentrations are "subtherapeutic," i.e.,below the minimum inhibitory concentration (MIC).

Elimination

The aminoglycosides are excreted almost entirely by glomerular filtration, and concentrations in the urine of 50 to 200 mg/ml are achieved. A large fraction of a parenterally administered dose is excreted unchanged during the first 24 hours, with most of this appearing in the first 12 hours. The half-lives of the aminoglycosides in plasma are similar and vary between 2 and 3 hours in patients with normal renal function. Renal clearance of aminoglycosides is approximately two-thirds of the simultaneous creatinine clearance; this observation suggests some tubular reabsorption of these drugs. The concentration of aminoglycoside in plasma produced by the initial dose is dependent only on the volume of distribution of the drug. Since the elimination of aminoglycosides is almost entirely dependent on the kidney, a linear relationship exists between the concentration of creatinine in plasma and the half-life of all aminoglycosides in patients with moderately compromised renal function. In anephric patients, the half-life varies from 20 to 40 times that determined in normal individuals. Because the incidence of nephrotoxicity and ototoxicity is related to the concentration to which an aminoglycoside accumulates, it is critical to reduce the maintenance dosage of these drugs in patients with impaired renal function. Aminoglycosides are removed from the body by either hemodialysis orperitoneal dialysis.

Bibliography

Godman & Gilman's The Pharmacological Basis of Therapeutics 2005, XI Ed., Chapter 45 (Henry F. Chambers) pp.1155-1170; McGraw Hill, New York.

GENERAL PRECAUTIONS

- Prosthesis to be implanted must be compatible with the use of bone cement.
- Store in a dry place away from all sources of light at a temperature below 25°C.
- Read instruction booklet carefully.

CEMENT PREPARATION PRECAUTIONS

- Do not resterilize any of the components.
- Sterility is assured only if the unit containers are not damaged or opened.
- If the powder has a yellowish or brownish color or if the liquid is syrupy, do not use product. This indicates the product has not been stored properly.
- Do not use after the expiration date since the effectiveness of the device may be compromised.
- Ensure the inner packages and components are undamaged. Powder should be consistent (no agglomerations) and not yellow or brown in color. The contents within the vial should appear as a low viscosity liquid.
- Preparation characteristics of bone cement may be affected by temperature. Temperatures of more than 23°C for the product, the preparation accessories and the environment accelerate the various stages in the preparation procedure. Lower temperatures retard the preparation stages. Prior to using UNITE® AB Bone Cement it is strongly advised to make sure that the product has been stored at a temperature of 23°C ± 1°C for 24 hours before surgery.

CEMENT APPLICATION PRECAUTIONS

Clinical studies show the need to maintain strictly aseptic surgical procedures. Any deep infection of a surgical wound is a serious risk and will affect the successful outcome of the technique. Some infections may appear later without clinical signs years after surgery.

In order to reduce the risk of inclusion of blood and debris within the cement, and of marrow content in the vascular system, the bone cavity must be properly irrigated with Ringer or saline solutions and dried prior to the application of bone cement. It is critical to maintain the position of the prosthesis with manual pressure until the end of the polymerization process while the cement hardens; this is important to ensure ideal implantation.

SPECIAL PRECAUTIONS

Properly cemented implants are stable and last. The cement or the prosthesis (or both) may loosen or fracture due to incorrect cement insertion, trauma, or dormant infection. Follow-up on all patients regularly and in the long-term after procedure.

Extrusion of the cement beyond the area of its intended application may occur resulting in the following complications: local neuropathy; bladder fistula; hematuria; dysuria; delayed sciatic nerve entrapment from extrusion of the bone cement beyond the region of its intended application local vascular erosion and occlusion; intestinal obstruction because of the adhesion and stricture of the ileum due to heat released during the exothermic polymerization.

If any form of infection should arise following surgery, patients are instructed to inform their doctors to reduce the risk of infection immediately.

Caution: NEVER add other substances or foreign bodies to UNITE® AB Bone Cement.

Caution: Bone cements reach temperatures higher than physiological temperatures during the polymerization reaction. Polymerization of the bone cement is an exothermic reaction that occurs while the bone cement is hardening in situ. The released heat may damage bone or tissue adjacent to the implant.

USER PRECAUTIONS

Contact with monomer to skin and mucous membranes should be avoided as instances of contact dermatitis have been noted in susceptible subjects. It is advised to wear a second pair of surgical gloves and carefully observe the instructions for mixing cement in order to reduce the possibility of negative reactions.

UNITE® AB Bone Cement liquid is a powerful lipid solvent. Do not come into contact with latex or rubber gloves. UNITE® AB Bone Cement should not come into contact with the gloved hand until the cement has formed into the consistency of dough (roughly 1-2 minutes after mixing). Due to the volatility and flammability of liquid monomer, it should be evaporated in a properly ventilated hood or absorbed by an inert material and transferred into a suitable container for disposal in a landfill.

The consistency of the bone cement changes in just a few minutes once the two components are mixed. Viscosity increases rapidly to form a mass which securely adheres the prosthesis to the host site.

Achievement of this state is determined by the increase in temperature of the cement. The cement cools spontaneously after a few minutes, which is the end of the reaction and time when the surgeon can release the prosthesis.

PHARMACOLOGICAL PRECAUTIONS

If gentamicin, tobramycin, or other aminoglycosides have been administered to the patient prior to surgery, monitoring of trough serum concentrations should be performed on the day before the operation. If serum concentrations exceed 1µg/ml gentamicin, tobramycin, or other aminoglycosides (amikacin, streptomicin) UNITE® AB bone cement should not be used. Simultaneous or sequential use of aminoglycosides (i.e. IV antibiotics, antibiotic beads impregnated bone cement) in patients with renal or vestibular/auditory compromise should

be avoided. Gentamicin bone cement should not be used in patients with impaired renal function (creatinine clearance less than or equal to 20 ml/min).

Monitoring
Patients receiving gentamicin bone cement should be periodically monitored with peak and trough levels of the antibiotic, serum electrolytes, serum renal function, urinalysis, and audiograms (in the elderly and/or dehydrated patient in whom there is a higher risk of adverse events associated with gentamicin use). Elderly patients may have reduced renal function that may not be evident in the results of routine screening tests, such as BUN or serum creatinine. A creatinine clearance determination may be more useful. Monitoring of renal function during treatment with aminoglycosides is particularly important in such patients. The inactivation of gentamicin and other aminoglycosides by ß-lactam type antibiotics (penicillins, cephalosporins) has been demonstrated in vitro and in patients with severe renal impairment. Such inactivation has not been found in patients with normal renal function who have been given the drugs by separate routes of administration. Therapy with gentamicin bone cement may result in overgrowth of nonsusceptible organisms. If overgrowth of nonsusceptible organism occurs, appropriate therapy should be initiated.

Use of gentamicin bone cement should be avoided in the following situations:
• Concurrent/sequential use of other neurotoxic/ nephrotoxic antibiotics

Other antibiotics
• Cephaloridine (1st gen.b-lactams)
• Viomycin (cyclic peptides)
• Polymixins, Colistin (polypeptides)
• Cisplatin (antineoplastic agent)
• Vancomycin and Teicoplanin (glycopeptides)
• Cyclosporins (immunosuppressant)
• Amphotericin B (antifungal)

Other drugs
• Furosemide, ethacrynic acid (loop diuretics)

WARNINGS
Before, during or immediately after the use of gentamicin bone cement, consideration should be given to the administration of ototoxic or nephrotoxic drugs. This is most important in regards to elderly patients with impaired creatinine clearance and renal impairment. The use of bone cement requires a high level of coordination between the anesthetist and the surgeon. The surgeon must communicate to the anesthetist that the cement is about to be introduced during the procedure.

In some cases events defined as “bone implantation syndrome” (BCIS) may occur which are characterized by a number of clinical features that include hypoxia, hypotension, cardiac arrhythmias, increased pulmonary vascular resistance (PVR), and cardiac arrest, which must be controlled with the methods in use in modern anaesthesiology. These phenomena are commonly associated with, but is not restricted to, cemented hip arthroplasty which usually occurs at one of the five stages in the surgical procedure: femoral reaming, acetabular or femoral cement implantation, insertion of the prosthesis or joint reduction (Donaldson et al., 2009, Br J Anaesth).

Patient blood pressure should be watched during and immediately after application of bone cement. Overpressurization of the bone cement should be avoided while inserting the prostheses to minimize the possibility of pulmonary embolism.

Surgeons should be prepared and familiar with the application, properties, and handling characteristics of UNITE® AB Bone Cement to ensure a successful procedure. Curing characteristics of UNITE® AB Bone Cement may differ with their mixing technique preference and temperature, and are best determined by the surgeon. It is recommended that the surgical team perform trials prior to use in patients under the same environmental and instrumental conditions.

The operative area must be correctly ventilated as the liquid component is both flammable and volatile. The liquid monomer and vapors must never directly be exposed to flames or heated items. It has been reported that monomer vapors have ignited by use of electrocautery devices in surgical sites near newly implanted bone cement. Exercise caution while mixing the liquid and powder components of the bone cement to prevent prolonged exposure to the concentrated vapors of liquid monomer. This exposure may cause irritation of the respiratory tract, eyes, and in some cases the liver. Those with contact lenses should not prepare bone cement or be near the mixing process.

SPECIAL WARNINGS
It is not recommended to treat active infections with UNITE® AB Bone Cement.

If used under conditions not suggested it is unlikely to provide benefits to the patient and therefore may increase the risk of the development of drug-resistant bacteria.

Do not add foreign bodies or other substances (including other antibiotics) to the bone cement.

Diuretics are rarely a source of vestibulotoxicity and may be a source of hearing impairment. Diuretics may be synergistic with other aminoglycoside ototoxins such as streptomycin,

gentamicin, kanamycin, and neomycin. Avoid exposure to these agents in the event hearing is impaired.

The dual use of gentamicin and neuromuscular blocking agents can cause respiratory paralysis/neuromuscular blockage and may be reversed by calcium salts.

DOSAGE AND ADMINISTRATION
UNITE® AB Bone Cement (single dose) is prepared by mixing the entire contents of one packet of powder with one vial of liquid per the instructions below. Should the need arise more doses may be mixed if required.

Different lot numbers of UNITE® AB Bone Cement may be used in tandem when mixed properly.

APPLICATION INSTRUCTIONS
To improve the use of UNITE® AB Bone Cement:

- Cement should be used at a temperature of 23°C ± 1°C and relative humidity of 60%.
- Remove detritus and irrigate the bone site carefully with saline solution.
- The presence of liquid between the bone tissue and the cement should be avoided. The bone surface must be dried with gauze and/or suction catheters before and during the cementation process.
- It is important to apply an optimal thickness of bone cement. The entire stem of the prosthesis should be covered by a uniform coating of bone cement.

PREPARATION
Temperatures affect bone cement: an increase of the local environment over 23°C reduces the times, while lower temperatures increase the times shown in the table below.

Step 1
Open the package and remove internal items. Place the powder packet and vial of liquid onto a sterile working surface within the operative area.

Step 2
Break open vial and pour the liquid into a proper container for mixing. Open powder and pour over liquid. Mix the cement with a spatula from the outside of the container towards the center to minimize the presence of air bubbles. All powder must be moistened by the liquid, therefore use the spatula delicately to remove any lumps of unmoistened powder into the overall grouping of moist cement. The surgeon will determine the amount of cement needed based on the clinical application and needs.

WARNING: Never change the ratio between liquid and solid components.

Do not resterilize and/or reuse the device as it is designed for single-use on a single patient. Never divide the product into two or more portions, in order to use it for other clinical applications or at different times. This reutilization may lead to an error in the correct proportion of powder-to-liquid mix. It could also cause a sterility loss. Avoid resterilization as it may cause infection risks for the patient. Resterilization may change and affect negatively the product and its performances, including the effectiveness of the antibiotic, causing a malfunction of the same with serious risks for the patient's well-being. Residues (all) must be viewed as surgical material waste and therefore be removed at the conclusion of the procedure.

Step 3
RESTING TIME
The mixture must be left to rest once the powder has been mixed with the liquid. The mixture must rest until its viscosity increases and it no longer runs when the container is tipped.

Step 4
HANDLING
Collect the cement from the container and roll it with your fingers until the cement stops sticking to the gloves after the resting time.

Step 5
APPLICATION
The cement must be inserted into the bone cavity at this time and be well compressed within. The cement flow must be kept as consistent as possible as this avoids the inclusion of possible air bubbles.

Step 6
PROSTHESIS INSERTION
The prosthesis can be positioned once the cement has been placed within the cavity. Hold the implant firmly in place until the cement has hardened. Excess cement should be removed prior to hardening. Hardening time of the cement depends on the temperature, type of cement, humidity and the amount of manipulation.

Caution! Application of the prosthesis should be completed as quickly as possible as the temperature of the host bone cavity accelerates cement polymerization.

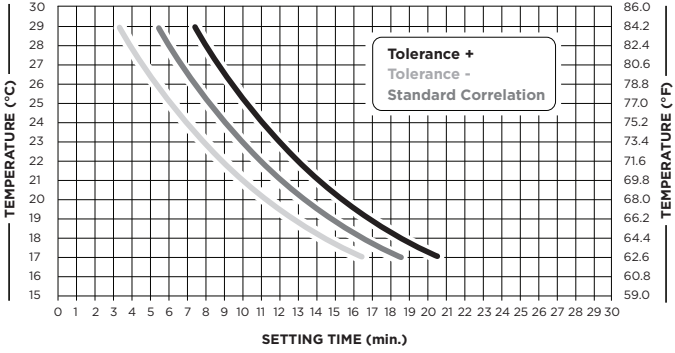
TEMPERATURE EFFECTS ON PREPARATION AND APPLICATION TIMING OF UNITE® AB Bone Cement

The temperature of the storage and of the operative area influences the preparation and application of the cement. The temperature's effect on cement setting time was evaluated with a laboratory test. A graph on setting time according to temperature is shown below for ease of reference. The data provided was obtained in controlled environmental and storage conditions subjected to standard deviation.

In addition to temperature and humidity, different factors can alter the cement's setting time. These include the mixing process (speed, use of mixer), the thoroughness of mixing, the usage of the entire liquids and solids, the addition of external substances inside the cement (such as, saline solution, blood etc.), and the pre-heating of the prosthesis component itself.

Manual application is the most effective and recommended for the application of UNITE® AB Bone Cement.

UNITE® AB Bone Cement
Setting Time - Temperature Chart



CAUTION

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

INFORMATION

For further product information, please contact Customer Service.

Symbols

Catalog Number

Batch Number

Use By

Do Not Reuse

Consult Instruction For Use

Keep Away From Sunlight

Store at a temperature Below 25°C

Caution

Flammable Liquid

Do Not Resterilize

Do Not Use If Package Is Damaged Or Opened

Sterile

Sterile Using Aseptic Processing Techniques

Sterilized By Ethylene Oxide

Sterilized Using Irradiation

6800 Poplar Avenue | Suite 120 | Memphis, TN 38138

901.453.3141 | info@OsteoRemedies.com | OsteoRemedies.com