OSTEOREMEDIES®
ADVANCED MEDICAL TECHNOLOGIES

SURGEON INFORMATION

SPECTRUM® GV BONE CEMENT

Bone Cement with Gentamicin & Vancomycin

1

OVERVIEW

SPECTRUM® GV Bone Cement contains and releases Gentamicin and Vancomycin. SPECTRUM® GV Bone Cement is a sterile, single use medical device. The package consists of an aluminium sachet containing the powder and a Tyvek-sealed blister containing the liquid phial. The package contains one 40 g sachet of sterile powder and one 17.7 g phial of sterile liquid. The liquid is sterilized by filtration and the powder by gamma irradiation.

INDICATIONS FOR USE

SPECTRUM® GV Bone Cement is indicated for the fixation of a REMEDY SPECTRUM® GV Spacer, and for the fixation of prostheses to living bone in the second stage of a two-stage revision of a total hip arthroplasty after the initial infection has been cleared.

Formulation of the components	**SPECTRUM® GV Bone Cement (Ref. SPECTRUM 40)**
Powder component	**40 gr**
Polymethylmethacrylate	81.8%
Barium Sulphate	10%
Gentamicin Sulphate	4.2%*
Vancomycin Hydrochloryde	2.5%*
Benzoyl Peroxide	1.5%
Liquid component	**17.7 gr**
Monomethylmethacrylate	98.2%
N,N dimethyl-p-toluidine	1.8%
Hydroquinone	75 ppm

*equivalent to 2.5% Gentamicin and Vancomycin base: 1.0 g (1.0 M.I.U.) in 40 g unit.

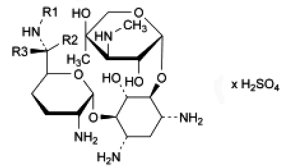
ANTIBIOTIC AND PMMA

Bacteria tend to adhere to surfaces where they can multiply and create a defensive barrier called a biofilm (complex structure mainly made by extracellular polysaccharides and proteins). Bacteria embedded in a biofilm are more resistant to most antibiotic therapy because the glycoprotein structure is difficult for antimicrobial agents to penetrate. PMMA, due to its surface characteristics, is one of the materials with the highest risk of bacterial colonization. It has been demonstrated in vitro that the presence of antibiotics in PMMA reduces bacterial adhesion.

GENTAMICIN SULPHATE

Chemistry/Structure

Gentamicin is an aminoglycoside antibiotic derived by the growth of an actinomycete, Micromonospora purpurea. Gentamicin is a complex of the gentamicins C1, C1a, C2 C2a and C2b as shown. The molecular weight is 449.55. The compound is supplied as sulphate.



Gentamicin	Mol. Formula	R1	R2	R3
C1	$C_{21}H_{43}N_5O_7$	CH_3	CH_3	H
C1a	$C_{19}H_{39}N_5O_7$	H	H	H
C2	$C_{20}H_{41}N_5O_7$	H	CH_3	H
C2a	$C_{20}H_{41}N_5O_7$	H	H	CH_3
C2b	$C_{20}H_{41}N_5O_7$	CH_3	H	H

Mechanism of action

Gentamicin is rapidly bactericidal. It binds to the prokaryotic ribosome and interferes with protein synthesis by causing misreading and premature termination of mRNA translation, 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. *In vitro* it is bactericidal against Gram-positive and Gram-negative bacteria. Gentamicin is active against susceptible strains of enterococci and streptococci at concentrations that can be achieved clinically only when combined with a penicillin or vancomycin. Gentamicin has been shown to be active against most strains of the following organisms both in vitro and in clinical infections.

Common susceptible pathogens (*)

Gram positive bacteria	Gram negative bacteria
Staphylococcus aureus *Streptococcus pyogenes* *Streptococcus pneumoniae* *Streptococcus faecalis* *Listeria monocytogenes*	*Citrobacter* *Enterobacter* *Escherichia coli* *Klebsiella* spp. *Proteus mirabilis* *Proteus vulgaris* *Morganella morganii* *Providencia* spp. *Salmonella* spp. *Serratia* *Shigella* spp. *Pseudomonas aeruginosa*

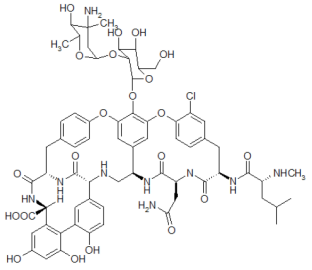
**Kucers A, Bennett N. The use of antibiotics 4th Ed. 1987, Butterworth-Heinemann Ltd*

Bibliography
• Goodman & Gilman's The Pharmacological Basis of Therapeutics - 2011, XII Ed., Chapter 54 (Henry F. Chambers); McGraw Hill, New York.

VANCOMYCIN HYDROCHLORIDE

Chemistry/Structure

Vancomycin hydrochloride is a tricyclic glycopeptide antibiotic derived from Streptococcus orientalis. The molecular weight is 1449.22. The compound is supplied as hydrochloride.



Mechanism of action

Vancomycin is bactericidal. It inhibits the synthesis of the cell wall in sensitive bacteria by binding with high affinity to the cell wall precursor units. This binding occurs at a different site of action from that of penicillin. The result is an alteration of bacterial cell wall permeability. In addition, RNA synthesis is inhibited.

Antibacterial activity

Vancomycin is primarily active against gram-positive bacteria. Strains are considered susceptible at MICs of ≤2 µg/ml for Staphylococcus aureus, ≤4 µg/ml for S. epidermidis and ≤1 µg/ml for streptococci. Vancomycin is particularly useful against penicillin- and methicillin-resistant staphylococcal infections and for treating gram-positive infections in penicillin-allergic patients. All species of gram-negative bacilli and mycobacteria are resistant to vancomycin. The combination of an aminoglycoside with a cell-wall synthesis inhibitor is the only reliably bactericidal regimen for treatment of enterococcal infections.

Most common susceptible pathogens (*)

Gram positive bacteria	Gram negative bacteria
Actinomyces sp. *Bacillus cereus* *Bacillus sp.* *Bacillus subtilis* *Clostridium difficile* *Clostridium sp.* *Corynebacterium jeikeium* *Corynebacterium sp.* *Enterococcus faecalis* *Enterococcus faecium* *Enterococcus sp.* *Lactobacillus sp.* *Listeria monocytogenes* *Staphylococcus aureus* *Staphylococcus epidermidis* *Streptococcus agalactiae* *Streptococcus bovis* *Streptococcus pneumoniae* *Streptococcus pyogenes* *Viridans streptococci*	Not effective
*Kucers A, Bennett N. The use of antibiotics - 4th Ed. 1987, Butterworth-Heinemann Ltd	

Bibliography

• Goodman & Gilman's The Pharmacological Basis of Therapeutics - 2011, XII Ed., Chapter 55 (Henry F. Chambers); McGraw Hill, New York.

ANTIBIOTIC RELEASE FROM PMMA

Pharmacological warnings

In vitro elution studies (microbiological method) has shown that the daily combined release of gentamicin and vancomycin never exceeds the recommended systemic adult dose for gentamicin (5-7 mg/kg/day) – and vancomycin (30 mg/Kg/day) according to the Goodman and Gilman's recommendations (adults with normal renal function). It is therefore unlikely that the amount of gentamicin and vancomycin absorbed locally from SPECTRUM® GV Bone Cement will result in serum levels in the toxic range.

Systemic administration of gentamicin and vancomycin

When administered systemically, plasma trough concentrations of gentamicin which exceed 2mg/ml for longer than 10 days have been associated with toxicity. Auditory impairment, which is frequent, although not permanent, may follow the use of vancomycin. Ototoxicity is associated with excessively high concentration of the drug in plasma (60 to 100 µg/ml). Nephrotoxicity due to vancomycin is unusual when appropriate doses are used, as judged by renal function and determinations of the antibiotic concentration in blood.

Special caution must be exercised if the patient:

has kidney problems, is elderly, has hearing difficulties, will have a general anaesthetic, is taking medicines such as other antibiotics that can affect the kidneys (streptomycin, neomycin, gentamicin, kanamycin, amikacin, tobramycin, polymixin B and colistin; water tablets, e.g. ethacrynic acid and furosemide; cholestyramine).

Local administration of gentamicin and vancomycin
The local release of both antibiotics produces low serum concentration. Nonetheless, the SPECTRUM® GV Bone Cement should be used with caution (mainly in the first days of implantation of a spacer) when used in conjunction with other nephrotoxic or ototoxic drugs administered systemically. The device should be used with caution in patients who are predisposed to or who have preexisting clinical conditions that would put them at risk for gentamicin and vancomycin toxicity (e.g. renal dysfunction, dehydration, advanced age etc.).

Monitoring
Patients receiving SPECTRUM® GV Bone Cement should be periodically monitored (first 7 days) with peak and trough levels of the antibiotics, 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, Aminoglycodes, Vancomycin, Glycopeptides 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 and glycopeptides 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.

The use of SPECTRUM® GV Bone Cement may result in overgrowth of non-susceptible organisms.
If overgrowth of non-susceptible organism occurs, appropriate therapy should be initiated.

There may be increased risk of ototoxicity from gentamicin, if other ototoxic drugs such as cisplatin (an antineoplastic 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.

POTENTIAL ADVERSE EVENTS
The following serious and negative reactions may arise when using bone cement. However, they are not directly attributable to the bone cement as such. Surgeons must be aware of these complications and be ready to treat them if they occur.

Serious	Other referred adverse event
Myocardial infarct	Temporary drop in blood pressure
Cerebrovascular incidents	Thrombophlebitis
Cardiac arrest	Haematoma-haemorrhage
Sudden death	Infection of surface/deep surgical wound
Pulmonary embolism	Trochanteric separation or bursitis
	Short-term cardiac irregularities
	Pain and/or loss of function
	Loosening or displacement of spacer or prosthesis fixed with the cement
	Elevated serum gamma-glutamyl-transpeptidase (GGTP) up to 10 days post operation
	Breakage of the bone cement
	Allergic pyrexia
	Hematuria
	Dysuria
	Bladder fistula
	Local neuropathy
	Delayed sciatic nerve entrapment from extrusion of bone cement outside the region of its intended application
	Local vascular erosion and occlusion
	Intestinal obstruction because of adhesion and stricture of the ileum from the heat release during the exothermic polymerization

Application of gentamicin and vancomycin may, in principle, trigger the typical adverse reactions of these antibiotics following systemic use, which are in particular:

GENTAMICIN (and Aminoglycosides) Risks
All aminoglycosides have the potential to produce reversible and irreversible vestibular, cochlear and renal toxicity.

Ototoxicity: Vestibular and auditory dysfunction can follow the administration of any of the aminoglycosides. It is more likely to occur in patients with persistently elevated concentrations of drug in plasma. Ototoxicity is largely irreversible and results from progressive destruction of vestibular or cochlear sensory cells, which are highly sensitive to damage by aminoglycosides. Repeated courses of aminoglycosides can lead to deafness. Older patients may be more susceptible to ototoxicity. Drugs such as ethacrynic acid and furosemide potentiate the ototoxic effects of the aminoglycosides in animals, but data from humans implicating furosemide are less convincing. Hearing loss is more likely to develop in patients with pre-existing auditory impairment following exposures to these agents. It is recommended that patients receiving high doses and / or prolonged courses of aminoglycosides be monitored carefully for ototoxicity, since initial symptoms may be reversible. However, deafness may occur several weeks after therapy is discontinued.

Nephrotoxicity: Approximately 8-26% of patient receiving an aminoglycoside for several days will develop mild renal impairment that is almost always reversible. Toxicity is correlated with the total amount of drug administered. Other drugs, such as amphotericin B, vancomycin, angiotensin-converting enzyme inhibitors, cisplatin and cyclosporine may potentiate aminoglycoside-induced nephrotoxicity. Monitoring drug concentrations in plasma is useful, particularly during prolonged and/or high dose therapy.

Neuromuscular blockade: Neuromuscular blockade generally has occurred after intrapleural or intraperitoneal instillation of large doses of an aminoglycoside; however, the reaction can follow intravenous, intramuscular and even oral administration of these agents. Most episodes have occurred in association with anesthesia or administration of other neuromuscular blocking agents. Patients with myasthenia gravis are particularly susceptible to neuromuscular blockade by aminoglycoside.

Other untoward effects: Aminoglycosides have little allergenic potential; anaphylaxis and rash are unusual. Rare hypersensitivity reactions, - including skin rashes, eosinophilia, fever, blood dyscrasia, angioedema, exfoliative dermatitis and anaphylactic shock - have been reported as cross-hypersensitivity among drugs in this class.

Note: Allergic reaction may appear independent to dosage.

VANCOMYCIN Risks

Nephrotoxicity: Nephrotoxicity, formerly very problematic due to the impurities in earlier formulations of vancomycin, has become less common with modern formulations at standard dosages. However, the more aggressive dosing regimens recently advocated have been demonstrated to increase nephrotoxicity risk. In a recent observational study, nephrotoxicity occurred in 33% of patients with initial vancomycin trough concentrations of >20 µg/mL, compared to 5% among patients with trough concentrations of <10 µg/mL.

Ototoxicity: Auditory impairment, sometimes permanent, may follow the use of vancomycin. Ototoxicity is associated with excessive high concentrations of the drug in plasma (60 – 100 µg/ml of vancomycin).

Hematologic: Anemia, reversible neutropenia, thrombocytopenia, reversible agranulocytosis, leukopenia are frequency not reported.

Miscellaneous: Among the hypersensitivity reactions produced by vancomycin and teicoplanin are macular skin rashes and anaphylaxis. Phlebitis and pain at the site of intravenous injection are relatively uncommon. Chills, rash, and fever may occur. Rapid intravenous infusion of vancomycin may cause erythematous or urticarial reactions, flushing, tachycardia, and hypotension. The extreme flushing that can occur called red-neck or red-man syndrome. This is not an allergic reaction but a direct toxic effect of vancomycin on mast cells, causing them to release histamine.

Note: Allergic reaction may appear independent to dosage.

CONTRAINDICATIONS

SPECTRUM® GV Bone Cement is contraindicated:

- in primary orthopaedic musculoskeletal surgical procedures.
- in the presence of serious myasthenia.
- in the presence of hypersensitivity to Gentamicin, Aminoglycosides, Vancomycin, Glycopeptides or any of the other components in the bone cement.
- in patients with impaired renal function (creatinine clearance less than or equal to 20 ml/min).
- where the loss of musculature or neuromuscular compromise in the affected limb would render the surgical procedure unjustifiable.
- in presence of an infection caused by pathogens resistant contemporaneously to gentamicin and vancomycin
- in presence of an infection caused by pathogens not susceptible to both gentamicin and vancomycin.

GENERAL PRECAUTIONS

The revision hip prosthesis that the surgeon chooses for the implantation must be compatible with the use of bone cement.

Read this instruction booklet very carefully.

Store in a dry place away from all sources of light at a temperature below 25°C and relative humidity not higher than 70% since high humidity influence viscosity and cement preparation and application times.

CEMENT PREPARATION PRECAUTIONS

- Sterility is assured only if the unit container is not damaged or opened.
- Do not re-sterilize any of the components.
- Do not use the product if the powder has a yellowish or brownish color or if the liquid is syrupy. These conditions indicate that the product has not been stored correctly.
- Do not use the product after the expiration date because the effectiveness of the device may be compromised.
- Make sure that the inner package is undamaged and that the components are undamaged. The powder should be uniform (no agglomerations) and should not present yellow or brown discoloring and the liquid in the vial should appear as a low viscosity liquid.
- Temperature has a major effect on the preparation characteristics of any bone cement. 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. Before using SPECTRUM® GV Bone Cement is strongly advised to make sure that the package was stored at a temperature of 23°C ± 1°C for the previous 24 hours.

CEMENT APPLICATION PRECAUTIONS

Clinical study data demonstrate the need to maintain strictly aseptic surgical techniques. To minimize the risk of inclusion of blood and debris in the cement, and of marrow content in the vascular system, the bone cavity should be thoroughly irrigated with Ringer or saline solutions and dried prior to the application of bone cement. While the cement hardens, it is very important to maintain the position of the spacer or the prosthesis by means of manual pressure until the end of the polymerization process; this is essential to ensure optimal implantation results.

Inadequate fixation or unanticipated postoperative events may affect the cement-bone interface and lead to micromotion of cement against bone surface. A fibrous tissue layer may develop between the cement and bone, and loosening of the spacer or prosthesis may occur.

USER PRECAUTIONS

Avoid monomer contact with the skin and mucous membranes. Cases of contact dermatitis have been observed in susceptible subjects. It is therefore advisable to wear a second pair of surgical gloves and scrupulously observe the instructions for mixing the components in order to reduce the possibility of reactions caused by hypersensitivity.

The liquid component of SPECTRUM® GV Bone Cement is a powerful lipid solvent. It should not contact rubber or latex gloves. The bone cement should not contact the gloved hand until the cement has acquired the consistency of dough, about 1-2 minutes after mixing.

Because of the volatility and flammability of the liquid monomer of the bone cement, the liquid monomer should be evaporated in a well ventilated hood or absorbed by an inert material and transferred into a suitable container for disposal. The polymer component may be disposed in an authorized waste facility. Once the two components are mixed, the consistency of the bone cement changes in just a few minutes: viscosity increases rapidly to form a marble-like mass which securely anchors the spacer or the prosthesis to the host site. The increase of the temperature of the cement indicates the achievement of this state. After a few minutes, the cement cools spontaneously, indicating the end of the reaction and time when the spacer or the prosthesis can be released.

SPECIAL PRECAUTIONS
SPECTRUM® GV Bone Cement which is used to fix the REMEDY SPECTRUM® GV Spacer devices or a hip prosthesis may become loose or fracture following trauma, incorrect cement insertion technique or infection recurrence: it is therefore advisable to follow-up all patients regularly. NEVER add other substances or foreign bodies to the bone cement. 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. The use of SPECTRUM® GV Bone Cement should be carefully considered in patients with coagulation disorders and in patients with severe cardiopulmonary insufficiency.

Pregnancy and Breast-feeding
There are no existing data that illustrates the usage safety of the SPECTRUM® GV Bone Cement during pregnancy and breast-feeding. It is recommended that hip revision surgery be avoided during the first three months of pregnancy. The SPECTRUM® GV Bone Cement can be used in the remaining gestation time only when it is determined that it is impossible to save the joint or preserve the patient's life by other means of intervention.

Use in Children
No data or tests support that the SPECTRUM® GV Bone Cement is safe to use in children.
The SPECTRUM® GV Bone Cement should only be used in mature adults.

WARNINGS
Prior to, concurrently or immediately following the use of SPECTRUM® GV Bone Cement, consideration should be given to the administration or ototoxic or nephrotoxic drugs. This applies particularly to elderly patients with impaired creatinine clearance and renal impairment.

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 are 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, and insertion of the prosthesis or joint reduction *(Donaldson et al., 2009, Br J Anaesth)*.

Patient blood pressure should be monitored during and immediately after application of bone cement. During the prostheses insertion step, the surgeon must avoid over pressurizing the bone cement in order to minimize the possibility of pulmonary embolism.

The use of bone cement demands a high level of cooperation between the surgeon and the anaesthetist. During the operation, the surgeon must inform the anesthetist that the cement is about to be introduced. The surgeon should be thoroughly familiar with the properties, handling characteristics and application of the SPECTRUM® GV Bone Cement. Because the curing characteristics of this cement vary with temperature and mixing technique, they are best determined by the surgeon's actual experience. It is strongly recommended that the surgical team carry out practical trials prior to use in patients under the same instrumental and environmental conditions.

The liquid component is flammable and volatile and for this reason the operating theatre must be correctly ventilated. The liquid component and/or its vapors must never be directly exposed to naked flames or heated materials. Ignition of monomer vapours caused by the use of electrocautery devices in surgical sites near freshly implanted bone cement has been reported.

Caution should be exercised during the mixing of the liquid and powder components of the bone cement to prevent excessive exposure to the concentrated vapours of liquid monomer, which may produce irritation of the respiratory tract, eyes, and possibly the liver. Personnel wearing contact lenses should not mix bone cement or be near its mixing.

SPECIAL WARNINGS
Using SPECTRUM® GV Bone Cement under conditions other than the indicated use is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria. Do not add other substances (including other antibiotics) or foreign bodies to the bone cement.

DOSAGE AND ADMINISTRATION
A dose of SPECTRUM® GV Bone Cement is prepared by mixing the entire contents of one packet of powder mixed with the one vial of the liquid according to the instructions in the following section. Depending upon the surgical procedure and technique more doses may be mixed as required. Differing lot numbers of SPECTRUM® GV Bone Cement may be used together when mixed in accordance with the recommended instructions.

APPLICATION INSTRUCTIONS
PREPARATION
Remove debris and irrigate the bone site carefully with saline solution. It is important to avoid the presence of liquid between the bone tissue and the cement. The bone surface must be dried with gauze and/or suction catheters before and during the cementation process. The surface of the spacer or the prosthesis that it is intended to be cemented should be covered by a uniform coating of bone cement. It is important to apply an optimal thickness of bone cement. Open the unit container/s and transfer the powder sachet and the liquid phial on a sterile working surface in the operating theatre. Break open the phial and pour the liquid into a mixing bowl. Open the powder sachet and pour the powder over the liquid. To minimise the inclusion of air bubbles, it is advisable to mix the cement with a spatula from the outside of the container towards the centre. All the powder must be moistened by the liquid; inasmuch, use the spatula delicately to work any lumps of unmoistened powder into the overall mass of moist dough. The necessary amount of cement for the particular clinical application is defined by the surgeon once the components have been mixed.

Caution: Never arbitrarily modify the ratio between the liquid and solid components.

DO NOT re-sterilize and/or re-use. The device is single-use and intended for a single-patient. Avoid the partition of the product in two or more portions to be used in different moments. This would be a re-use which could lead to a ratio error between powder and liquid components and loss of sterility. Re-sterilization can also alter the device morphology, the efficiency of the antibiotics and the mechanical features of the device, causing a malfunction of the same with serious risks for the patient's health.

The residual material must be considered surgical waste and therefore it must be eliminated at the end of the surgical procedure.

Mixing time is between 1-1.5 minutes, but the actual time is affected by the room temperature and humidity, by the mixing technique and it has to be determined by the experience of the surgeon. At the end of the mixing phase, keep moving the mass till the cement does not stick the gloves. At this stage the mass is ready for application. The temperature and humidity of the operating and storage room, of the mixing accessories and other environmental conditions may determine differences in the timing for preparation and application, which has to be determined by the experience of the surgeon.

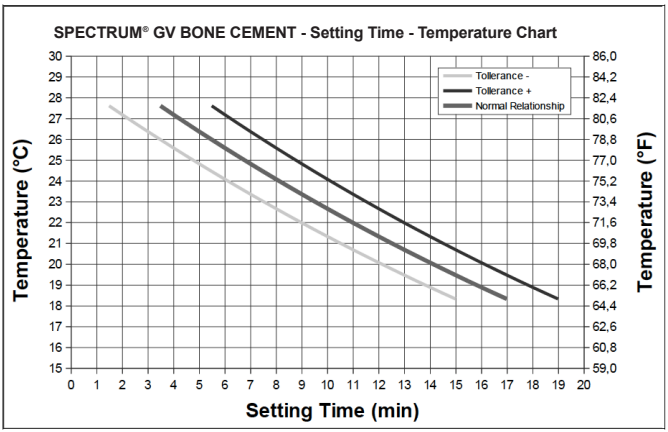
APPLICATION
When the cement is ready to be handled, it will be used to fix REMEDY SPECTRUM® GV Spacers or a revision hip prosthesis. Remove excess cement before it hardens. The final hardening time of the cement depends on temperature, humidity and the degree of manipulation.

Caution! The temperature of the host bone cavity accelerates cement polymerisation therefore the application of the spacer or the prosthesis should be completed as quickly as possible.

THE EFFECT OF TEMPERATURE ON PREPARATION AND APPLICATION TIMING OF SPECTRUM® GV BONE CEMENTS
Bone cements are sensitive to temperature.

The timing for preparation and application of bone cement is strongly affected by the temperature of the storage and of the operating room. Any increase in temperature of the working environment, the cement components or the mixing instrumentation over 23°C reduces preparation times. Equally, lower temperatures increase such times.

The effect of temperature on cement setting time has been evaluated with a laboratory testing. As a reference it is reported a setting time-temperature chart (data obtained in controlled laboratory environment and storage conditions, subjected to standard deviation). Beside temperature and humidity, other factors can affect setting time: mixing technique (speed, use of mixer), thoroughness of mixing, utilisation of the entire powder and liquid components, inclusion of external substances in the cement (such as saline solution, blood, etc), and the pre-heating of the prosthesis component itself.



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 Code

Use By Date

Do Not Reuse

Consult Instruction For Use

Keep Away From Sunlight

Store at a temperature Below 25°C

Caution

Flammable

Do Not Resterilize

Do Not Use If Package Is Damaged

Sterile

Sterile Using Aseptic Processing Techniques

Sterilized Using Ethylene Oxide

Sterilized Using Irradiation

Manufactured By:

For Internal Use

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