Acrylic cement with gentamicin for surgical fixations.

DESCRIPTION:
The surgical use Cements with gentamicin, are acrylic compounds made of two components which polymerize at room temperature. They are available in standard and low viscosity.
The first component is a white fine powder polymer (Methyl Methacrylate), with Benzoyl Peroxide as polymerization initiator, Barium Sulphate as X-Ray opacifier, and Gentamicin Sulphate. The second component is a colorless, volatile and flammable liquid (Methyl Methacrylate Monomer), with Hydroquinone as stabilizer and NN dimethyl-p-toluidine as polymerization activator.
When both components are mixed, a polymerization process begins: At first, the mixture is fluid and its viscosity increases progressively to reach a plastic state similar to a putty or soft paste, before solidifying after a few minutes. As the polymerization is an exothermic reaction, the cement will become hot. The maximum temperature reached will depend on the volume, thickness and shape of the cement mass applied. The high thermal conductivity of the metal prostheses facilitates heat dissipation. The maximum temperature reached does not exceed 90°C, which is within the range specified by ISO 5833.

INDICATIONS:
These PMMA surgical cements with gentamicin are used for the fixation of joint endoprostheses into the bone, and also for the repair, filling or stabilization of bone defects. They are specially indicated in high risk patients, surgical revisions, or as adjuvants in the prevention of Infections by gentamicin sensitive germs.

PROPERTIES OF GENTAMICIN:
Gentamicin is a broad spectrum aminoglycoside antibiotic. It is effective on gram (-) aerobic bacteria, including enterobacteriaceae, Pseudomonas and Haemophilus. It is also effective on Gram positive germs such as staphylococci (Staphylococcus aureus and Staphylococcus epidermidis) including penicillinase producing strains, and has a very limited activity on streptococci. It has no activity on anaerobic bacteria.
Gentamicin is stable at the temperature reached during the polymerization process and-in the concentration used -does not modify the mechanical properties of the cement.

WARNING REGARDING GENTAMICIN:
Patients treated with aminoglycosides must be carefully controlled due to the possible toxicity on kidneys, hearing, and peripheral nervous system which could be associated to the use of this group of antibiotics. The concomitant use with other neurotoxic and/or nephrotoxic medicines such as cisplatin, cephaloridine, kanamycin, amikacin, vancomycin, streptomycin, neomycin, polimyxin B, colistin, paromomycin, tobramycin, viomycin, as well as diuretics like etacrynic acid or furosemide, could enhance its ototoxicity. Old age and dehydration can increase the risk of toxicity in the patient.

PREGNANCY:
Gentamicin falls into the D Category of FDA for medicines: There is positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience or studies in humans. As pregnant women may benefit from the use of this drug, it´s prescription should be evaluated by their treating physicians.

BREASTFEEDING:
Although Gentamicin is poorly excreted into breastmilk it´s use should be avoided during this period.

CONTRAINDICATIONS:
The use of PMMA cements with Gentamicin is contraindicated in patients with a medical history of allergy to any of its components.

USE IN GERIATRICS:
It is known that this drug is excreted in significant amounts by the kidneys and that there is an increase of side effects in patients suffering from kidney insufficiency.
As elderly persons have more possibilities of presenting some degree of kidney insufficiency that might not be manifest in routine laboratory tests, a Creatinine Clearance test can yield more specific information. It is very important to closely monitor the kidney function throughout the treatment.

USE IN PAEDIATRICS:
The use of PMMA cements with or without antibiotics in paediatric patients must be restricted to those exceptional cases in which no other alternative treatments are available.

PRESENTATION:

VISCOSITY	PRESENTATION	GENTAMICIN
STANDARD	20 g / 10	250 mg
STANDARD	40 g / 20	500 mg
LOW	40 g / 20	500 mg
LOW	60 g / 30	750 mg

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Both components are supplied in a cardboard package which contains the instructions for use and a molded PET-G blister sealed with Tyvek® containing: 1 plastic bag with powder (polymer) and one glass ampoule with liquid (monomer) protected by a PET-G thermoformed "cradle".
The blister contents are sterilized by ETO, while the liquid within the ampoule is sterilized by ultrafiltration.

WARNING BEFORE USE:

Both the cement and the preparation and application elements must be stored at a temperature below 23 °C for (at least) 5 hours in order to comply with the parameters specified in these instructions for use.
Make sure that the temperature in the OR does not exceed 23°.
Note : It is not advisable to cool PMMA cements before use, with the purpose of delaying their polymerization, because the low temperature might lead to an inadequate monomer/polymer combination.
The approximate times shown in the chart correspond to the different polymerization stages of the product according to room temperature. The count starts at the moment the powder and the liquid components are incorporated into the mixing bowl.
The higher the temperature, the shorter the working, placing and hardening times of the cement will be. The opposite occurs when the temperature is lower.

WARNING:
The product's physical and chemical properties and the quality of the cementation can be seriously altered in the following cases:
The incorporation of air within the cement during its preparation, handling, and transfer.
The incorporation of air, blood, fat or flushing liquid during the application of the product.
The addition of water solutions (i.e.: injectable antibiotics) as they are incompatible with the cement.
Partial or incomplete mixing of the components: All the liquid must always be mixed with all the powder.

PREPARATION:
For a safe and adequate use of the product, the surgeon must have a previous experience in the use of PMMA Cements with Gentamicin, and be familiar with their characteristics, handling and application.

STANDARD VISCOSITY CEMENT:
(MANUAL APPLICATION)
Open the blister and slide its contents onto a sterile surface.
Remove the glass ampoule from its protective "cradle", open it carefully and pour all its contents into a mixing device or sterile container (stainless steel, polyethylene or glass) with a 160 ml minimum capacity. It is important that these elements be dry and at room temperature.
Open the plastic pouch which contains the powder and pour its contents upon the liquid.
Mix the two components for approximately 30 seconds until the cement reaches a doughy consistency. After two more minutes, it will be possible to take this dough with your gloved hands. If it should still stick to the gloves, knead it for a few more seconds until it is no longer sticky. The surgeon will determine the optimal time for the application of the cement.
The time for inserting the prosthesis can be affected by room temperature (see chart). Once it has been inserted, the prosthesis must be kept immobilized in place, until the cement has completely hardened/cured. Remove all excess of cement while it is still soft.

LOW VISCOSITY CEMENT:
(SYRINGE APPLICATION)
A cement application device in good working conditions must be available.
Open the blister and transfer its contents onto a sterile surface.
Remove the glass ampoule from its protective cradle, open it carefully and pour all its contents into a mixing device or sterile container (stainless steel, polyethylene or glass) with a 160 ml minimum capacity. It is important that these elements be dry and at room temperature.
Open the plastic bag which contains the powder and pour its contents upon the liquid.
Mix the two components for approximately 15 seconds and transfer the cement into the application device. When this process is over (30 seconds maximum), the product will be ready for use.
Apply evenly according to the specified technique. When this step is completed, wait until the mass reaches the appropriate plastic state. The surgeon will determine the right time to insert the prosthesis.
The time for inserting the prosthesis can be affected by room temperature. Once it has been inserted, the prosthesis must be kept in place, without moving it until the cement has completely hardened/cured. Remove all excess of cement while it is still soft.
ADVERSE REACTIONS:
Severe adverse reactions, attributed to the use of PMMA cements, have been reported, including some with a fatal outcome: Cardiac arrest, Pulmonary Thromboembolism, Myocardial Infarction, CVA (stroke), and also the above mentioned reactions apparently related to the use of aminoglycoside antibiotics.
The Anesthesiologist must be warned about a possible temporary fall of the blood pressure in the patient, which might occur during or immediately after the cementation procedure. If the patient is hemodynamically compensated, and the surgical aggression has not been severe, this reaction is usually temporary and does not entail any ulterior clinical consequences.

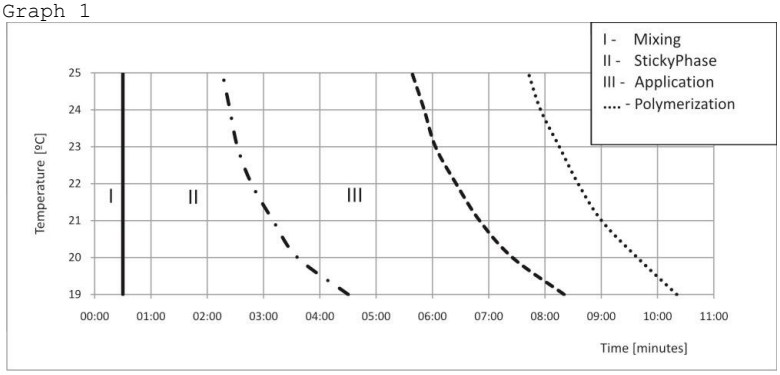
PRECAUTIONS:
The monomer is a volatile liquid which must be handled with special care: avoid contact with eyes, skin, and mucous membranes. While handling it, use latex gloves and avoid unnecessary exposure to its fumes.
Open the ampoule with care so as to avoid breaking it and spilling its contents.
The OR where the surgery is to take place must be equipped with an adequate air renovation system.
Do not use this product after the expiry date.
Single use Product. DO NOT RE-USE. This single use product is destined to a single patient. Re-using it may entail mechanical, physical and chemical risks, as well as biological contamination risks.
After using this product, discard the remaining cement and dispose of it according to the laws and regulations in force.
Do not re-sterilize any of its components: re-sterilization implies a high biological risk.
Discard if the blister that ensures sterility is found damaged or open. .
Handle with care and store in a cool (below 25°C) and dry place, away from the light.
SOLD EXCLUSIVELY TO PROFESSIONALS AND SANITARY INSTITUTIONS.

WARNING:

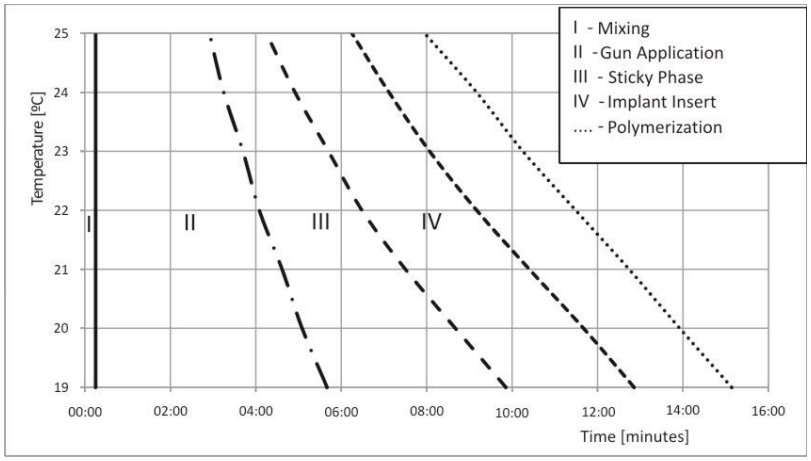
The use of this product for purposes other than those described in these instructions for use will be under the exclusive responsibility of the medical professional, as he may endanger the physical integrity and/or the life of the patient.

RELATIONSHIP BETWEEN WORKING TIMES AND ROOM TEMPERATURE.
Effect of the temperature on the duration of the different application stages of the bone cement.
Standard viscosity Cement: Graph 1
Low viscosity Cement: Graph 2

Graph 1



Graph 2



NOTE:
The Sticky, Insertion and Polymerization phases correspond to average values.
A deviation of ± 30 seconds is possible in the sticky and implant insertion phases.
A deviation of ± 90 seconds is possible in the Polymerization phase.

PLASTIC POUCH CONTENTS			
POWDER WITH GENTAMICIN FORMULA	**20 g**	**40 g**	**60 g**
POLY-METHYL METHACRYLATE	17.27 g	34.54 g	51.81 g
BENZOYL PEROXIDE	0.48 g	0.96 g	1.44 g
BARIUM SULPHATE EUR. PH.	2.00 g	4.00 g	6.00 g
GENTAMICIN BASE (AS SULPHATE)	0.25 g	0.50 g	0.75 g

AMPOULE CONTENTS			
LIQUID FORMULA:	**10 ml**	**20 ml**	**30 ml**

METHYL METHACRYLATE	9.88 ml	19.76 ml	29.64 ml
N,N, DIMETHYL- P-TOLUIDINE	0.12 ml	0.24 ml	0.36 ml
HYDROQUINONE	18 - 20 ppm		

Components relative ratio (in weight): Powder: 67.8 % / Liquid: 32.2 %