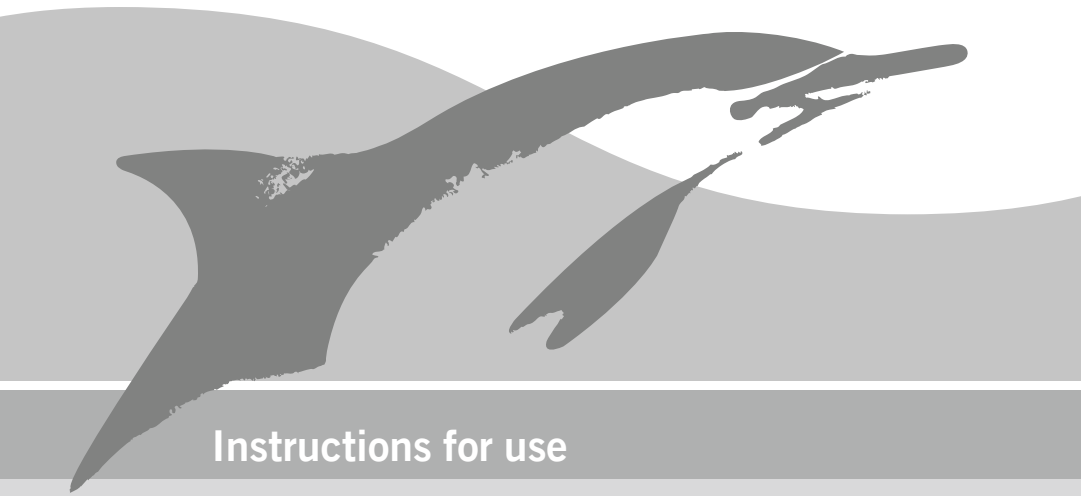
Heraeus

PALACOS® MV+G

Medium-viscosity, radiopaque bone cement containing gentamicin



Instructions for use

PALACOS® MV+G

General information
Device description

PALACOS® MV+G is a standard-setting, medium-viscosity, radiopaque, poly(methyl methacrylate)-based (PMMA) bone cement.
It contains the aminoglycoside antibiotic gentamicin to protect the cured bone cement and contiguous tissue against colonization by bacteria that are sensitive to gentamicin. It contains the X-ray contrast medium zirconium dioxide. To improve visibility in the surgical field, it has been colored with chlorophyll-copper-complex (E141).
The bone cement consists of two components and is prepared immediately before use by mixing the polymer powder (= powder) with the monomer liquid (= liquid). A ductile dough forms that sets within a few minutes.

Device sizes and packaging
Device sizes
PALACOS® MV+G is available in the size 40.

Package content
– 1 pouch filled with gentamicin-containing powder
– 1 brown glass ampoule filled with liquid
– 1 set of patient stickers for documentation
– 1 instructions for use

Packaging design
The powder is triple packaged and sterilized using ethylene oxide. The protective, non-sterile aluminum pouch contains an outer polyethylene (PE) paper pouch (peel-off), which is non-sterile on the outside and sterile on the inside. The outer PE-paper pouch contains the sterile inner PE-paper pouch with the powder.
The liquid is single packaged. The ampoule blister is sterilized using ethylene oxide and contains a brown glass ampoule with sterile-filtered liquid.

Composition

Powder	
PMMA copolymer	85 %
Zirconium dioxide	12 %
Benzoyl peroxide	1 %
Gentamicin sulfate	2 %
Liquid	
Methyl methacrylate	98 %
N, N-dimethyl-p-toluidine	2 %

The percentages are rounded off

Other constituents:
– Powder: Chlorophyll-copper-complex (E141)
– Liquid: Chlorophyll-copper-complex (E141), hydroquinone
It cannot be excluded that **PALACOS® MV+G** contains traces of histamine. **PALACOS® MV+G** does not contain a radiation source.

Device size	40
Powder	45.2 g
including gentamicin	0.6 g
Liquid	20 ml

The data is rounded to one decimal place

The mass ratio is about 30 % liquid to 70 % powder.

Supporting equipment
Mixing equipment is required to mix the two components of **PALACOS® MV+G**. All mixing and application systems from Heraeus Medical GmbH are suitable. An overview can be found in the product brochures: www.heraeus-medical.com.
The instructions for use of the supporting equipment must be followed.

MRI safety information
PALACOS® MV+G is MR safe.

Directions for use
Intended use
PALACOS® MV+G is a PMMA bone cement intended for use in arthroplastic procedures of the hip, knee, and other joints for the fixation of polymer or metallic prosthetic implants to living bone.

Intended patient population
Adult population.

Intended user
Healthcare professionals in a clinical context and experienced in the handling of the product.
The surgeon must be thoroughly familiar with the properties and handling characteristics of **PALACOS® MV+G**. As the handling of **PALACOS® MV+G** varies with temperature, humidity, and mixing technique, a test mix should be performed to ensure familiarity with its characteristics.

Indications
PALACOS® MV+G is indicated for use in the second stage of a two-stage revision for total joint arthroplasty after the initial infection has been cleared.

Contraindications
PALACOS® MV+G must not be used in the following cases:
– suspected or proven hypersensitivity to components of the bone cement including gentamicin
– patients with a history of hypersensitivity or serious toxic reactions to other aminoglycosides
– patients with renal impairment

– for permanent fixation purposes in the presence of an active or incompletely treated infection at the bone site caused by gentamicin non-sensitive strains
– during pregnancy or breast-feeding
– children
– spinal surgery

The safety of the bone cement in pregnant women or in children has not been established. Bone cement may adversely affect bone growth and fetal health.

Adverse events

General

Serious adverse events, some with fatal outcome, that are associated with the use of acrylic bone cements include bone cement implantation syndrome (BCIS): hypotension, hypoxia, embolism; resuscitation may be required. Rarely there is a temporary drop in blood pressure after preparation of the prosthesis bed or immediately after the implantation of bone cements and the endoprosthesis. To avoid pulmonary or cardiovascular complications such as pulmonary embolism and cardiac arrest, it is recommended that the implantation site be irrigated thoroughly with an isotonic solution (pulse lavage application) before the bone cement is introduced. In the event of pulmonary or cardiovascular events, it is necessary to monitor blood volume and possibly increase it.
In the case of acute respiratory failure, anesthesiologic measures should be taken.
The following adverse events have been observed when using PMMA bone cements: thrombophlebitis, hemorrhage, trochanteric bursitis, trochanteric separation, osteolysis due to bone cement fragments, heterotopic bone formation.
In individual cases severe complications can occur such as severe allergic reactions that are associated with pyrexia, anaphylactic shock, or even sudden death.
Other reported adverse events are myocardial infarction, brief cardiac arrhythmia, short-term cardiac conduction irregularities, cerebrovascular accident, hemorrhagic encephalitis, pain and/or loss of function, infection, superficial or deep wound infection, hematoma, hematuria, dysuria, bladder fistula, delayed sciatic nerve entrapment, adhesions and strictures of the ileum, numbness, skin tingling, muscle twitching, convulsions.

Adverse effects of gentamicin

PALACOS® MV+G contains gentamicin and the adverse effects of this antibiotic are in particular:
– impairment of auditory and vestibular nerves
– renal toxicity: adverse renal effects have been reported, as demonstrated by the presence of cells or protein in the urine or by increases in serum creatinine or oliguria. They occur more frequently in patients with a history of renal impairment. Application of clinical doses of gentamicin has led to the occasional appearance of Fanconi's syndrome or a Bartter's-like syndrome
– neuromuscular blockade/neurotoxicity: serious adverse effects on both vestibular and auditory branches of the 8th cranial nerves have been reported, primarily in patients with renal impairment. Symptoms include dizziness, vertigo, tinnitus, roaring in the ears, and hearing loss, which may be irreversible.

Other factors that may increase the risk of toxicity include dehydration and previous exposure to other ototoxic drugs:
– rare cases of paresthesia, tetany, and myasthenia
– rare cases of allergic reactions (exanthema, urticaria, anaphylactic reactions)

Like all aminoglycosides, gentamicin is also potentially nephrotoxic and/or ototoxic. In most cases, damage to hearing caused by gentamicin is irreversible, whereas renal damage is reversible.

Other reported adverse effects possibly related to gentamicin include:
– respiratory depression, lethargy, confusion, depression, visual disturbances, decreased appetite, weight loss, and hypotension or hypertension
– rash, itching, urticaria, generalized burning, laryngeal edema, anaphylactoid reactions, fever, and headache, nausea, vomiting, increased salivation, and stomatitis purpura, pseudotumor cerebri, acute organic brain syndrome, pulmonary fibrosis, alopecia, joint pain, transient hepatomegaly, and splenomegaly

The use of **PALACOS® MV+G** results in a desired high bactericidal but locally limited concentration of gentamicin. Therefore, the occurrence of the afore mentioned adverse effects is highly unlikely. Care should be taken, and the level of gentamicin should be monitored in patients with impaired renal function, especially if treated with parenteral aminoglycosides or muscle relaxants simultaneously. The same applies to patients with previous neuromuscular disorders (e.g., myasthenia gravis, Parkinson's disease).

Allergic reactions can occur independent of dosage.

Interactions

Gentamicin

Owing to the administration of muscle relaxants and ether, the neuromuscular blocking properties of gentamicin may be intensified. However, in view of the very low serum levels, this is relatively unlikely in patients with healthy kidneys. The probability of interactions occurring increases in proportion to the serum levels of gentamicin, e.g., in patients with impaired renal function.

Interactions have been reported to occur between gentamicin and the following groups of drugs:
– concurrent or sequential use of neurotoxic and/or nephrotoxic pharmaceuticals, including other aminoglycosides, polymyxin B, colistin, cisplatin, ciclosporin, foscarnet, vancomycin, amphotericin B, clindamycin, and cephalosporins
– potent diuretics: ethacrynic acid, furosemide, or other potent diuretics that may themselves cause ototoxicity or enhance aminoglycoside toxicity by altering antibiotic concentrations in serum and tissue
– muscle relaxants: in particular, succinyl choline and tubocurarine, decamethonium, halogenated hydro carbon inhalation anesthetics, or opioid analgesics

Gentamicin may interact with these medications and result in skeletal muscle weakness and respiratory depression (apnea). Concurrent application of these medications and gentamicin during surgery or in the post-operative period should be monitored with caution, especially if there is a possibility of incomplete reversal of neuromuscular blockade post-operatively. Moreover, complications that may occur during any surgical procedure are also possible.

Warnings

Regarding intended users

Caution should be exercised during the mixing of the two components of **PALACOS® MV+G** to prevent excessive exposure to the concentrated monomer vapors, which may produce irritation of the respiratory tract, eyes, and possibly the liver. Personnel wearing

contact lenses should not be near or involved in mixing this bone cement. Manufacturers of soft contact lenses recommend removing the lenses in the presence of damaging or irritant vapors. Since soft contact lenses are permeable to liquids and gases, they should not be worn in the operating room if methyl methacrylate is being used.
The monomer is a powerful lipid solvent and should not come into direct contact with the body. When handling **PALACOS® MV+G** it is essential to wear gloves that provide the necessary protection against penetration of the monomer into the skin. Three-layered PVP gloves (polyethylene, ethylene vinyl alcohol copolymer, and polyethylene) and Viton®/butyl gloves have proved to provide good protection over an extended period. It is recommended that two pairs of gloves be worn over one another, e.g., a polyethylene surgical glove over an inner pair of standard latex surgical gloves. Do not allow the monomer to contact latex or polystyrene-butadiene gloves. Request confirmation from your glove supplier that the respective gloves are suitable for use with this bone cement.
Polymerization of the bone cement is an exothermic reaction, which occurs while the bone cement is hardening in situ. The released heat may damage bone or other tissues surrounding the implant.
Avoid over-pressurizing the bone cement because this may lead to extrusion of the bone cement beyond the site of its intended application and damage to the surrounding tissue.
Inadequate fixation or unanticipated postoperative events may affect the cement-bone interface and lead to micro motion of bone cement against bone surface. A fibrous tissue layer may develop between the bone cement and the bone and loosening of the prosthesis may occur leading to implant failure. Long-term follow-up is advised for all patients on a regularly scheduled basis.

Note: PALACOS® MV+G is a single-use device and must never be re-used! Re-use may result in diminished safety, performance, and compliance with relevant specifications.

Regarding the intended patient population
PALACOS® MV+G is considered most unlikely to cause gentamicin overdosage, because high local gentamicin concentrations only led to low (≤ 1 µg/ml) and short-lived systemic concentrations (Wahlig et al. 1984).
Monitor patients carefully for any change in blood pressure during and immediately after the application of bone cement. Adverse patient reactions involving the cardiovascular system have been associated with the use of bone cements. Hypotensive reactions have occurred between 10 and 165 seconds of application of bone cement. They have lasted from 30 seconds to 5 or more minutes. Some have progressed to cardiac arrest.

Precautions
Regarding intended users
Do not use **PALACOS® MV+G** after the expiration date printed on the package. This device may not be safe or effective beyond its expiration date.
Follow the handling and mixing instructions to avoid contact dermatitis. Strict adherence to the instructions for mixing the powder and liquid components may reduce the incidence of this complication.
Adequately ventilate the operating room to eliminate as much monomer vapor as possible.
The liquid is highly volatile and flammable. Ignition of monomer fumes caused by use of electrocautery devices in surgical sites near freshly implanted bone cements has been reported.

Regarding the intended patient population
Intended patients receiving gentamicin should be periodically monitored with peak and trough levels of the antibiotic, serum electrolytes, serum renal function, urine analysis, and audiograms (in the elderly and/or dehydrated in whom there is a higher risk of adverse events associated with gentamicin use).
Blood pressure, pulse, and breathing must be monitored carefully during and immediately after introduction of the bone cement. Any significant change in these vital signs must be resolved without delay by taking appropriate action. When using **PALACOS® MV+G**, the prepared bone should be carefully cleaned, aspirated, and dried just before the bone cement is placed.

Handling
Perform mixing and application of **PALACOS® MV+G** under sterile conditions. **PALACOS® MV+G** is mixed in a mixing system with or without vacuum (see Supporting equipment). Prior to using **PALACOS® MV+G**, consult the instructions for use of the selected supporting equipment. Make sure that the handling steps of the supporting equipment are followed adequately (see Supporting equipment).

If **PALACOS® MV+G** is used pre-chilled, it is recommended that the bone cement components be pre-chilled at 4 °C – 7 °C for at least 24 hours. It should be removed from cooling and filled into the mixing system just before mixing.

The mixing, waiting, application, and setting times of **PALACOS® MV+G** are shown in the diagrams at the end of the instructions for use (see Working times).

Note: These are stated for guidance only because the application and setting times depend not only on temperature but also on mixing method used and the humidity in the operating room. The storage temperature also influences the application time. In general, higher temperatures during storage and in the operating room, higher humidity, and vigorous mixing of the bone cement lead to shorter application times and vice versa.
Apart from the handling procedure described below, **PALACOS® MV+G** must not be modified in any way. Any admixing of substances, especially aqueous (e.g., antibiotic containing) solutions, has a considerable detrimental effect on the mechanical properties of the bone cement (Frommelt L., 2007).

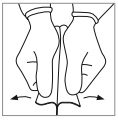
PALACOS® MV+G contains the following non sterile/sterile packaging components:

Packaging component	Condition
Powder	
Aluminum pouch:	Non-sterile
Outer PE-paper pouch	Outside: non-sterile Inside: sterile
Inner PE-paper pouch	Sterile
Liquid	
Ampoule blister	Outside: non-sterile Inside: sterile
Ampoule	Sterile

Amount required
The amount of bone cement dough required depends on the specific surgical intervention and on the technique being used. At least one additional pack of **PALACOS® MV+G** should be available before commencing the operation.

Non-sterile preparation steps
Non-sterile user
- Open the folding box, take out the aluminum pouch, the ampoule blister, the instructions for use and the set of patient stickers
- Before opening the aluminum pouch, move the content down by shaking or tapping to ensure that when the aluminum pouch is cut open at the top, the content is not damaged
- Open the aluminum pouch and take out the outer PE-paper pouch
- First break the orange sterility seal, then open the outer PE-paper pouch as shown in Figure 1, and present the sterile inner PE-paper pouch to the sterile user for sterile removal
- Open the ampoule blister using its flap and present the sterile ampoule to the sterile user for sterile removal

Open the outer PE-paper pouch



The opening flaps of the pouch top help to detach the foil from the paper. To maximize the area of the opening flaps that can be grasped, the side of the paper/foil should be kept between thumb, index, and middle finger. Use the whole thumb surface to grasp the foil and paper side and peel off each side evenly.

Sterile preparation steps
It is advisable to first add the liquid and then the powder. If this order is reversed, nests of unpolymerized powder are more likely to form due to polymerization commencing immediately at the surface.

Sterile user
- Remove the ampoule and open it under sterile conditions: the liquid is ready to fill into the mixing system
- Remove the inner PE-paper pouch and open it under sterile conditions: the powder is ready to fill into the mixing system

Note: Do not open the ampoule over the mixing device to prevent contamination of the bone cement with glass fragments. To make it easier to open the ampoule, it is provided with a predetermined breaking point at the transition to the head of the ampoule.
The 20 ml ampoule is provided with a snap off device (tube) to facilitate the opening procedure. To do so, grasp the fitted snap-off device instead of the ampoule head and break off the ampoule head using the device. When the ampoule head has snapped off, it remains inside the tube.

Mixing and application
For mixing and application of **PALACOS® MV+G**, the instructions for use of the suitable systems must be followed (see Supporting equipment).
Mixing the powder and liquid together produces a paste that is used to anchor the prosthesis to the bone. The hardened bone cement allows stable fixation of the prosthesis and transfers all stresses generated in a movement to the bone via the large interface. Powder and liquid should only be added to the mixing system just before mixing. During the mixing time of 30 seconds, the two components are mixed with one another while stirring evenly.
Always mix the entire contents of a pouch with the entire contents of an ampoule of liquid. If powder or liquid is spilled, a new package must be used.
The bone cement can be applied as soon as the doughy bone cement no longer adheres to the gloves (doctor finger test). The application time depends on the temperature of the material and the room temperature. To ensure adequate fixation, the prosthesis should be introduced and held in position within the time window allowed for application until the bone cement has set completely. Remove any surplus bone cement while it is still soft.

Storage, transport, shelf life, sterilization
Storage
Do not store above 25 °C (77 °F).
PALACOS® MV+G must be stored in dry conditions and must not be exposed to direct sunlight, ionizing radiation, extremes of temperature, or particulate contamination.
PALACOS® MV+G must be brought to room temperature of the operating room at least 2 hours before use.

Transport
Care shall be exercised during transport and handling of the **PALACOS® MV+G** to avoid any damage or alteration to the performance characteristics of the **PALACOS® MV+G** and its packaging as received. Do not remove the **PALACOS® MV+G** from the sterile packaging until immediately before use. Do not use if packaging is damaged.

Shelf life
The shelf life of **PALACOS® MV+G** is printed on the folding box, the protective aluminum pouch, and the inner PE-paper pouch. Do not use **PALACOS® MV+G** if the date indicated has expired.

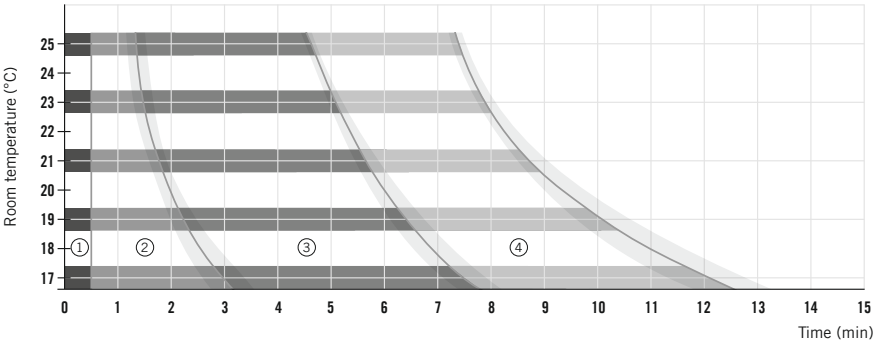
Sterilization
Powder and packaging have been sterilized using ethylene oxide and the liquid by sterile filtration. The product must not be re-sterilized. Non-sterility may cause an infection in the patient. If the powder has turned yellow, do not use **PALACOS® MV+G**.

Disposal
Single components of the **PALACOS® MV+G**, set solid material as well as packaging material must be disposed of as clinical waste in compliance with local regulations.
For separate disposal of liquid or powder, contact your local disposal authority. Mixed bone cement should be allowed to set before disposal with other clinical waste.

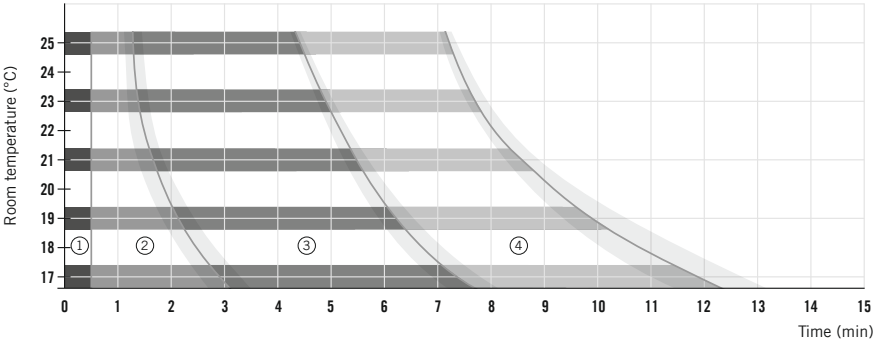
Disclaimer of liability
Any serious incident that has occurred in relation to the device should be reported to the manufacturer and the competent authority.

Information status: 2020-07

Working times for manual mixing (not pre-chilled bone cement)



Working times for vacuum mixing (not pre-chilled bone cement)



Mixing ① Waiting ② Application ③ Setting ④

Test conditions: Not pre-chilled vacuum mixing system PALAMIX®, 55 % humidity.

Symbols


Manufacturer


Date of manufacture


Use-by date

Batch code

Catalogue number

Sterilized using aseptic processing techniques

Sterilized using ethylene oxide

Sterilized using irradiation

Do not resterilize


Do not use if package is damaged

Non-sterile


Fragile, handle with care


Keep away from sunlight


Keep dry

Do not store above 25 °C (77 °F)


Do not re-use


Consult instructions for use


Caution


Causes skin irritation


Flammable liquid

Federal law restricts this device to sale, distribution, and use by or on the order of a physician

MR safe

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