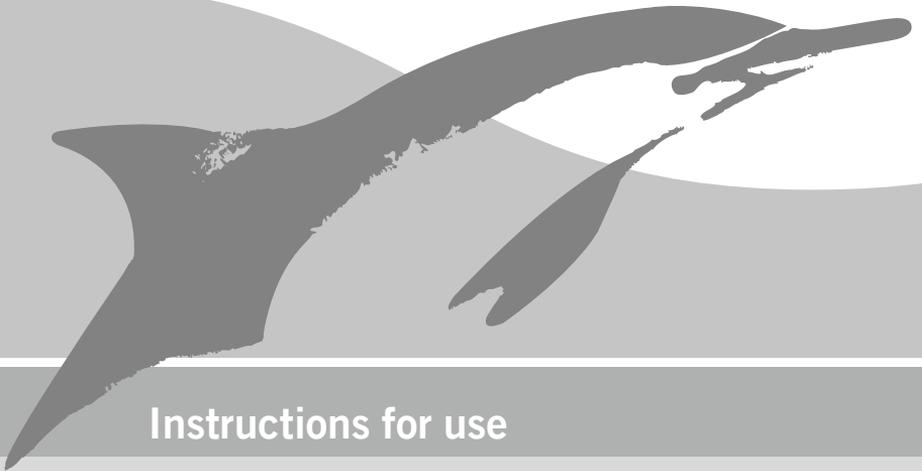


Heraeus

PALACOS[®] LV+G

Low viscosity, radiopaque bone cement
containing gentamicin



Instructions for use

PALACOS® LV+G

Uses and properties

PALACOS® LV+G is a fast setting polymer, for use in bone surgery. It is 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. Mixing of the two component system, consisting of a powder and a liquid, initially produces a liquid and then a paste, which is used to anchor the prosthesis to the bone. The hardened bone cement allows stable fixation of the prosthesis and transfers all stresses produced in a movement to the bone via the large interface. Insoluble zirconium dioxide is included in the cement powder as an X ray contrast medium. The chlorophyll additive serves as optical marking of the bone cement at the site of the operation.

Indications

PALACOS® LV+G is indicated for use as bone cement in arthroplasty procedures of the hip, knee and other joints to fix plastic and metal prosthetic parts to living bone when reconstruction is necessary. The cement 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® LV+G must not be used during pregnancy or the nursing period.

PALACOS® LV+G must not be used in patients with infectious arthritis.

PALACOS® LV+G must not be used in active infection of the joint or joints to be replaced.

PALACOS® LV+G must not be used in cases of known hypersensitivity to gentamicin or to other constituents of the bone cement. A history of hypersensitivity or serious toxic reactions to other aminoglycosides may contraindicate use of gentamicin because of known cross-sensitivity of patients to drugs in this class.

Relative contraindications include:

- (1) uncooperative patient or patient with neurologic disorder who is incapable of following directions
- (2) metabolic disorders which may impair bone formation
- (3) osteomalacia
- (4) distant foci of infections which may spread to the implant site

(5) rapid joint destruction, marked bone loss or bone resorption, vascular insufficiency, muscular atrophy, or neuromuscular disease

- (6) hypotension
- (7) congestive heart failure
- (8) renal impairment

Adverse effects

Neurotoxicity

(1) manifested as both auditory and vestibular ototoxicity, including irreversible hearing loss;

- (2) numbness;
- (3) skin tingling;
- (4) muscle twitching; and
- (5) convulsions.

Nephrotoxicity

- (1) usually in patients with pre-existing renal damage; and
- (2) also in patients with normal renal function to whom aminoglycosides are administered for longer periods or in higher doses than recommended, the symptoms of which may manifest after cessation of therapy.

Disclaimer

It has not been clinically proven that the antibiotic effect of the drug gentamicin holds for the gentamicin-loaded bone cement.

Side effects

After preparation of the prosthesis bed or directly after the implantation of the cement and prosthesis, pressure rise in the medullary canal may cause a temporary fall in blood pressure. In addition to hypotension, pulmonary embolism and cardiac arrest with their potentially fatal consequences have been encountered in rare cases. These cardiovascular and respiratory side effects known as the implantation syndrome are caused by infiltration of bone marrow constituents into the venous vascular system.

The site of the prosthesis should therefore be rinsed thoroughly with an isotonic solution (e.g. physiological saline) before implantation. To minimize the large pressure increase in the medullary canal during the prosthesis implantation, suction drainage is recommended. In the presence of pulmocardiovascular disturbances, the liquid volume must be monitored as appropriate

Composition	PALACOS® LV+G
	1 pouch of 41.7 g powder contains:
poly(methyl acrylate, methyl methacrylate)	33.3 g
zirconium dioxide	6.3 g
hydrous benzoyl peroxide	0.4 g
gentamicin base (as sulphate)	1.0 g
	1 ampoule of 20 ml liquid contains:
methyl methacrylate	18.4 g
N,N-dimethyl-p-toluidine	0.4 g
Other constituents:	In the powder: chlorophyll VIII In the liquid: chlorophyll VIII in an oily solution, hydroquinone

and anaesthesiological measures may be required e.g. in the event of acute respiratory failure. The gentamicin content of **PALACOS® LV+G** may cause hypersensitivity reactions in isolated cases.

Application of gentamicin may, in principle, trigger the typical adverse reactions of this antibiotic, which are in particular, damage to hearing and to the kidneys. However, these adverse reactions are very unlikely to occur as the serum levels required to cause damage are not reached.

Precautions

Monitoring:

- (1) patients receiving gentamicin 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).
- (2) Use of gentamicin should be avoided in the following situations:
 - (a) concurrent/sequential use of other neurotoxic/nephrotoxic antibiotics;
 - (b) Other aminoglycosides;
 - (c) Cephaloridine;
 - (d) Viomycin;
 - (e) Polymixin B;
 - (f) Colistin;
 - (g) Cisplatin; and
 - (h) Vancomycin.

Do not use this product 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 monomer 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.

It has been recommended by manufacturers of soft contact lenses that such lenses should be removed "in the presence of noxious and irritating vapors". Since soft contact lenses are quite permeable, they should not be worn in an operating room where methyl methacrylate is being mixed.

Pediatric use

A pediatric use of **PALACOS® LV+G** should be thought over well by the surgeon. The cement should be used only if the risk/benefit analysis gives a clear indication.

Warnings

PALACOS® LV+G is considered most unlikely to cause gentamicin overdose, since only low and shortlived serum concentrations are obtained during the first few postoperative hours from the high local gentamicin concentrations (Wahlig et al.: Pharmacokinetic study of Gentamicin-loaded cement in total hip replacements. Comparative effects of varying dosage. J. Bone Joint Surg. 66-B: 175-179).

Since the concentration of gentamicin may reach the nerve and the kidney, ototoxic and nephrotoxic reactions may happen

following the use of **PALACOS® LV+G** bone cement. Monitor patients carefully for any change in blood pressure during and immediately following the application of bone cement. Adverse patient reactions affecting the cardiovascular system have been associated with the use of bone cements. Hypotensive reactions have occurred between 10 and 165 seconds following application of bone cement; they have lasted from 30 seconds to 5 or more minutes. Some have progressed to cardiac arrest. Patients should be monitored carefully for any change in blood pressure during and immediately following the application of bone cement.

Using **PALACOS® LV+G** 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. Follow the handling, mixing and canal preparation instructions carefully.

- Caution should be exercised during the mixing of the two components 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.
- Polymerization of the bone cement is an exothermic reaction, which occurs while the cement is hardening in situ. The released heat may damage bone or other tissues surrounding the implant.
- Inadequate fixation or unanticipated postoperative events may affect the cement-bone interface and lead to micro motion of cement against bone surface. A fibrous tissue layer may develop between the cement and the bone, and loosening of the prosthesis may occur leading to implant failure. Long-term followup is advised for all patients on a regularly scheduled basis.
- When working with the monomer or the cement, gloves must be worn to ensure adequate protection against the penetration of the monomer (methyl methacrylate) into the skin. PVP (three-layer polyethylene, ethylene-vinyl alcohol-copolymer, polyethylene) and Viton/Butyl gloves have proved to provide good protection over an extended period. Putting on two pairs of gloves – one pair of polyethylene surgical gloves over a pair of standard latex surgical gloves has also proved to offer adequate protection.

The use of latex or polystyrene-butadiene gloves, however, must be avoided. Please request the confirmation of your glove supplier whether the respective gloves are suitable for the use of this cement.

Avoid over-pressurization of 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 tissues. 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.

Interactions

Concurrent administration of muscle relaxants and ether may potentize the neuromuscular blocking properties of gentamicin. However, due to the low serum concentrations this is unlikely to happen.

Incompatibilities

Aqueous (e.g. antibiotic-containing) solutions must not be mixed with the bone cement, as this reduces the strength considerably.

Adverse Events

Serious adverse events, some with fatal outcome, associated with the use of acrylic bone cements include myocardial infarction, cardiac arrest, cerebrovascular accident, and pulmonary embolism.

The most frequent adverse reactions reported with acrylic bone cements are a transitory fall in blood pressure, thrombophlebitis, hemorrhage and hematoma, loosening or displacement of the prosthesis, superficial or deep wound infection, trochanteric bursitis, and short-term cardiac conduction irregularities. Other reported adverse reactions include heterotopic new bone formation and trochanteric separation.

Other reported adverse events for acrylic bone cements include pyrexia due to an allergy to the bone cement, hematuria, dysuria, bladder fistula, delayed sciatic nerve entrapment due to extrusion of the bone cement beyond the region of its intended application, and adhesions and stricture of the ileum due to the heat released during polymerization.

Instructions and Training

The surgeon should, by specific training and experience, be thoroughly familiar with the properties, handling characteristics, and application of bone cements. Because the handling and curing characteristics of this bone cement vary with temperature, humidity, and mixing technique, they are best determined by the surgeon's actual experience.

Dosage

The amount of bone cement required depends on the patient's anatomy and on the implant used. One or more complete units (the contents of one pouch and one ampule) must always be mixed together. In practice, more than four dose units per implantation are only rarely used.

Notes on use

Before using **PALACOS® LV+G** the surgeon must be thoroughly familiar with its properties, handling and use, and must have read the relevant literature. For special mixing and application techniques (e.g. vacuum mixing, vacuum application, use of a femoral cement restrictor), the relevant instructions of these mixing and application system must be consulted. Before using **PALACOS® LV+G** for the first time, a test mixing should be carried out to become familiar with the characteristics of **PALACOS® LV+G**.

To mix, the protective aluminum packaging and outer non sterile polyethylene pouch ("peel off" package) and the ampule packaging should be opened, maintaining sterility, by the circulating nurse. The ampule and powder pouch are then taken out under sterile conditions and placed on a sterile working surface. The ampule is opened by breaking the neck and the inner pouch is cut open with sterile scissors. Do not open the ampoule over the mixing device to prevent contamination of the cement with glass fragments.

Opening under sterile conditions:



The opening flaps from the bag top assist to detach the foil from the paper. In order to grip as much of the opening flaps as possible, the side of the paper/foil should be kept between thumb, index and middle finger.

Please use the whole thumb surface to grip foil and paper side and take off each side evenly.

Mixing

PALACOS® LV+G can be mixed by two different methods:

- Mixing without vacuum
- Mixing under vacuum

Mixing without vacuum

First pour all the liquid from the ampoule into a sterile mixing device and add all the powder. Stir carefully with a sterile mixing rod until a homogeneous mass is obtained. The mixture should not be mixed longer than 30-sec, irrespective of the room temperature. The temperature/time diagrams must be consulted.

Vacuum mixing

To obtain a bone cement with lower porosity the components must be mixed under vacuum. This method requires an airtight closed system and rapid generation of sufficient vacuum (approx. 200 mbar [150 mmHg] absolute pressure) in the mixing device. The stirring time for vacuum mixing is the same as for mixing without vacuum (30 sec). Method of mixing is given in the instructions for the system used and must be consulted.

Use in joint surgery

An appropriate up to date cementing technique should be used with **PALACOS® LV+G** to limit side effects and to achieve a stable and long lasting anchorage of the prosthesis. A prerequisite for this is careful preparation of the prosthesis site by thorough rinsing (e.g. with physiological saline solution) before application of the cement. Suction drainage could be used to avoid any pressure build up in the medullary canal during implantation. Further prerequisites for better prosthesis anchoring include filling of the entire medullary canal with cement (using a femoral cement restrictor), the production of a cement mantle completely surrounding the implant (ideal thickness 3–5 mm), and biomechanically optimal siting of the implant in bone.

Working procedure

After careful preparation of the medullary canal, **PALACOS® LV+G** can be applied manually or using a cement syringe or some alternative application system. Method of application is given in the instructions for the system used and must be consulted. The working time and the rate of polymerization are strongly dependent on ambient temperature and on temperature of the components. The hardening time is shorter at high temperatures and longer at low temperatures. Viscosity increases as polymerization progresses, i.e. as the cement hardens.

Manual application

The working phase starts when the doughy paste no longer adheres to the instruments or surgical gloves and ends when the paste becomes rubbery/elastic with visible separation lines while kneading. The cement and the prosthesis must be applied within the working phase. Applying the cement after the end of the working phase may cause an uneven and inadequate filling of the medullary canal, thereby resulting in possible early loosening of the implant (see graphs).

The cement and the prosthesis must be applied within the working phase. After positioning of the implant any movement must be avoided, to ensure the anchoring of the prosthesis.

Application with a cement syringe

After mixing, the cement is poured directly into a cement syringe. The working time depends on the ambient temperature and the temperature of the components (see graphs). The times may vary depending on the syringe system used.

Storage

Do not store above 25°C (77°F).

Shelf life/sterility

The expiration date is printed on the outer carton, the protective aluminum packaging and the inner pouch. **PALACOS® LV+G** must not be used after the expiration date. The contents of unused but opened or damaged packs must not be re-sterilized and are therefore to be discarded. **PALACOS® LV+G** is sterilized with ethylene oxide gas and must not be re-sterilized. If the polymer powder shows a yellow discoloration, it must not be used.

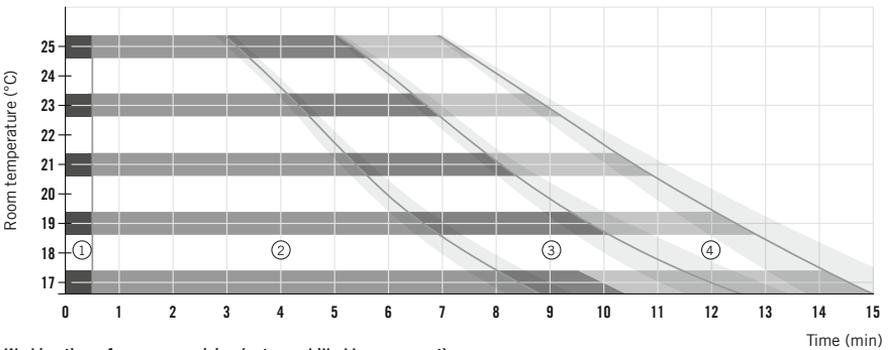
Disposal

Single components of the bone cement, cured solid material as well as (uncleaned) packaging material must be disposed by following the regulations of the local authorities. Dispose of the polymer component in an authorized waste facility. The liquid component should be evaporated under a well-ventilated hood or absorbed by an inert material and transferred in a suitable container for disposal.

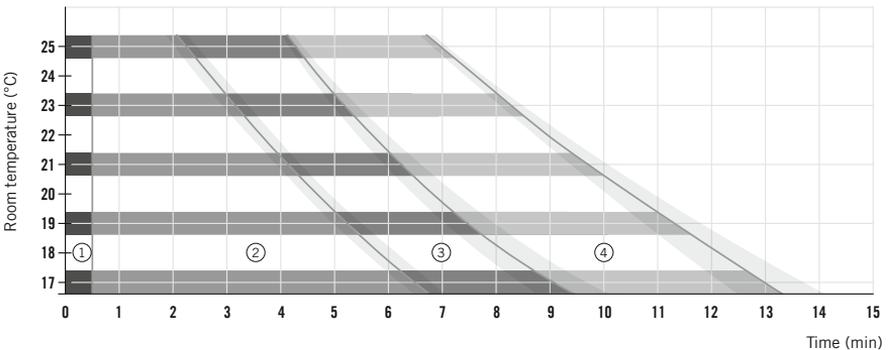
Information status 2020-01

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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



Sterilized using aseptic processing techniques



Sterilized using ethylene oxide



Consult instructions for use



Keep away from sunlight



Keep dry



Do not store above 25 °C (77 °F)



Do not re-use



Do not re-sterilize



Do not use if the product sterile barrier system or its packaging is compromised



Catalogue number



Use by date



Batch code



Flammable liquid – Flashpoint 10 °C



Causes skin irritation



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

Heraeus

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