PALACOS® R+G pro
Radiopaque ready-to-mix bone cement containing Gentamicin

Instructions for use
PALACOS® R+G pro

Uses and properties
PALACOS® R+G pro is a poly(methylmethacrylate) based bone cement, packed in a closed mixing and application system ready for processing (ready-to-mix).

PALACOS® R+G is a fast setting polymer containing gentamicin, for use in bone surgery. Mixing of the two components 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.

Features of the PALACOS® R+G pro mixing and application system
In PALACOS® R+G pro the bone cement powder and the monomer component are packed in a closed mixing and application system ready for use. The PALACOS® R+G pro system thus reduces direct contact with the bone cement components. It also makes it possible to process the bone cement quickly and easily. All the components of the system are in a sterile inner plastic pack, which is sealed in a transparent bag. The bag is in turn sealed in an aluminium bag, which protects the sterile product against humidity. The monomer liquid has been filled aseptically. The accessory bag with its vacuum hose and activated charcoal/sterile filter has been sterilised by irradiation.

The polymer powder and the monomer glass ampoule of PALACOS® R+G as well as the mixing and application system are all sterilized with ethylene oxide.

Constituents of PALACOS® R+G pro
- Mixing cartridge filled with PALACOS® R+G bone cement (polymer powder)
- Brown glass ampoule filled with monomer liquid
- Application nozzle
- Femoral pressurizer
- Vacuum hose with an activated charcoal / sterile filter, packed into an aluminium pouch
- Product sticker for patient documentation
- Instructions for use

All constituents are not made with natural rubber latex and all constituents that come into contact with bone cement are not made with PVC.

Accessories required
To be able to use PALACOS® R+G pro, the Heraeus Medical vacuum pump (connector as per ISO 4414, DIN EN 983) and cement gun as well as compressed air hoses described under Accessories are required.

Indications
PALACOS® R+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® R+G must not be used during pregnancy or the nursing period.
PALACOS® R+G must not be used in patients with infectious arthritis.
PALACOS® R+G must not be used in active infection of the joint or joints to be replaced.
PALACOS® R+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 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 sciatric nerve entrapment due to extrusion of the bone cement beyond the region of its intended application, and adhesions and structure of the ileum due to the heat released during polymerization.

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 thor-
oughly 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 and anaesthe-
siological measures may be required e.g. in the event of
acute respiratory failure. The gentamicin content of
PALACOS® R+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. How-
ever, these adverse reactions are very unlikely to occur as
the serum levels required to cause damage are not
reached.

Precautions
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 com-
ponents 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.
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.

Monitoring:
(1) patients receiving gentamicin should be periodical-
lly monitored with peak and trough levels of the antibi-
otic, serum electrolytes, serum renal function, urinal-
ysis, 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;
(l) Colistin;
(g) Cisplatin; and
(h) Vancomycin.

<table>
<thead>
<tr>
<th>Composition</th>
<th>PALACOS® R+G pro net 75</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 pouch of 61.2 g powder contains:</td>
<td></td>
</tr>
<tr>
<td>poly(methyl acrylate, methyl methacrylate)</td>
<td>50.3g</td>
</tr>
<tr>
<td>zirconium dioxide</td>
<td>9.0g</td>
</tr>
<tr>
<td>Hydrous benzoyl peroxide</td>
<td>0.67g</td>
</tr>
<tr>
<td>Gentamicin base (as sulphate)</td>
<td>0.75g</td>
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<tr>
<td>1 ampoule of 30 ml liquid contains:</td>
<td></td>
</tr>
<tr>
<td>Methyl methacrylate</td>
<td>27.6g</td>
</tr>
<tr>
<td>N,N-dimethyl-p-toluidine</td>
<td>0.6g</td>
</tr>
<tr>
<td>Other constituents:</td>
<td>In the powder: chlorophyll VIII</td>
</tr>
<tr>
<td>In the liquid: chlorophyll VIII in an oily solution, hydroquinone</td>
<td></td>
</tr>
<tr>
<td>Amount of bone cement available for the application (net)</td>
<td>75g</td>
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</table>
Pediatric use
There is very little experience with children and adolescents, therefore it is not recommended to use PALACOS® R+G pro. If no other option is available, for example with present surgical trauma, the decision whether to use PALACOS® R+G pro lies with the attending surgeon.

Warnings
PALACOS® R+G is considered most unlikely to cause gentamicin overdosage, since only low (< 1 μg/ml) 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. 1984 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® R+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® R+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. However, PALACOS® R+G pro was developed so that as little liquid and gaseous monomer as possible can escape into the environment.

• 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-vinylalcohol-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.

Interactions
Owing to the administration of muscle relaxants and ether, the neuromuscular blocking properties of gentamicin may be intensified. However, this is unlikely on account of the very low serum levels reached.

Amount required
The amount of bone cement required depends on the patient's anatomy and on the implant used. At least one additional pack of PALACOS® R+G pro should be available before commencing the operation.

Preparation and Mixing
Before using PALACOS® R+G pro the surgeon must be thoroughly familiar with its properties, handling and use, and must have read the relevant literature. 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.

Beyond the handling procedure described below, the system must not be tampered with (opening of the system, addition of substances, removal of components, etc.) or there would be no guarantee of correct use and there may also be a considerable detrimental effect on the physical properties of the cement.

For the use of PALACOS® R+G pro a constant vacuum of approx. 100 mbar is required. It must be provided by a suitably powerful vacuum pump (see Accessories). The vacuum enables the transfer of monomer liquid to the mixing cartridge with polymer powder. In addition, mixing in a vacuum reduces the number of air inclusions in the PALACOS® R+G bone cement.

Remember that PALACOS® R+G pro may only be removed from the aluminium pack just before use. The constituents are mixed under sterile conditions.

The mixing times, waiting times, working times and curing times of PALACOS® R+G pro are shown on the diagram at the end of these instructions. Please note that they are stated for guidance only, because the working time and curing time depend on temperature, mixing and humidity, whereby direct ambient temperatures also have an influence. Higher temperatures or high humidity shorten the waiting, working and curing times. It is not recommended to pre-cool PALACOS® R+G pro. The initial viscosity of pre-cooled PALACOS® R+G is lower than that of a bone cement that has not been pre-cooled and the processing time is significantly prolonged. If PALACOS® R+G pro is used pre-cooled the user is strongly recommended to familiarise themselves in advance with the pre-cooled product in terms of the initial viscosity, as well as waiting, application and curing times.
Use of the bone cement
After mixing the cement powder with the monomer liquid, a fast-curing ductile dough develops which is introduced to bone cavities for fixation and/or filling purposes.

Joint endoprosthetics
To ensure adequate fixation, the prosthesis must be introduced within the time window allowed for working and immobilised until the bone cement has set completely. Remove any surplus cement as long as it is still soft.

Storage
Do not store above 25°C (77°F).

Shelf life/sterility
The expiration date is printed on the outer carton and on the outer plastic tray. PALACOS® R+G pro must not be used after the expiration date. The contents of unused but opened or damaged packs must not be resterilized and are therefore to be discarded. PALACOS® R+G pro is sterilized with ethylene oxide gas and must not be resterilized. 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.

Information status: 2018-05
PALACOS® is a trademark of Heraeus Medical GmbH, Germany.

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Accessories

<table>
<thead>
<tr>
<th>Description</th>
<th>Composition</th>
<th>Sets per sales unit</th>
<th>REF</th>
</tr>
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<tbody>
<tr>
<td>PALAMIX® cement gun</td>
<td>Reusable application gun</td>
<td>1</td>
<td>66036163</td>
</tr>
<tr>
<td>PALAMIX® vacuum pump</td>
<td>Reusable vacuum pump with one way valve</td>
<td>1</td>
<td>66036748</td>
</tr>
</tbody>
</table>
Handling

1. Disengage lock ( unfavorably).
2. Slide back the advancing rod until it stops
3. Engage lock ( favorably).

1. Push the mixing rod twice through the powder to loosen up possibly compacted powder and return in its initial position.
2. Push sealing ring into cartridge.

Connect the vacuum hose to the sealing ring.

Connect the activated charcoal filter to the vacuum pump.

Apply pressure on the vacuum indicator (green) with the left thumb and quickly and fully turn down the scoring lever with the right hand.

Operate the vacuum pump and initiate monomer transfer. As soon as the vacuum indicator retracts, monomer transfer is complete (approx. 10 s). Continue to operate the vacuum pump.

Mix cement with consistent rotary up and down motions of the mixing rod over the entire length of the cartridge for at least 20 seconds (1 stroke per second) until a homogeneous dough develops.

1. Pull up the mixing rod until it stops, and
2. turn it to the right and left briefly.
1. Switch off the vacuum pump
2. Remove the vacuum hose from the mixing head.
3. Break the mixing rod off the mixing head at the predetermined breaking point.

1. Press the cartridge securing device down.
2. Unscrew the cartridge.

Screw the application nozzle into the cartridge.

Screw the cartridge onto the cement gun with a short rotary motion.

Advance cement up to the tip of the nozzle. Cement should now be applied quickly.

After application:
Squeeze the grip of the gun and undo the locking screw (•).
Then let go of the grip and unscrew the cartridge.

Break off the nozzle at the predetermined breaking point.

If necessary, attach femoral pressurizer.

Expel the cement remaining in the nozzle with the aid of the mixing rod.
Test conditions: 55% humidity.
Symbols

#### Manufacturer

Sterilized using aseptic processing techniques

Sterilized using ethylene oxide

Sterilized using irradiation

Consult instructions for use

Keep away from sunlight

Keep dry

Do not store above 25 °C (77 °F)

Do not re-use

Do not resterilize

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

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

Catalogue number