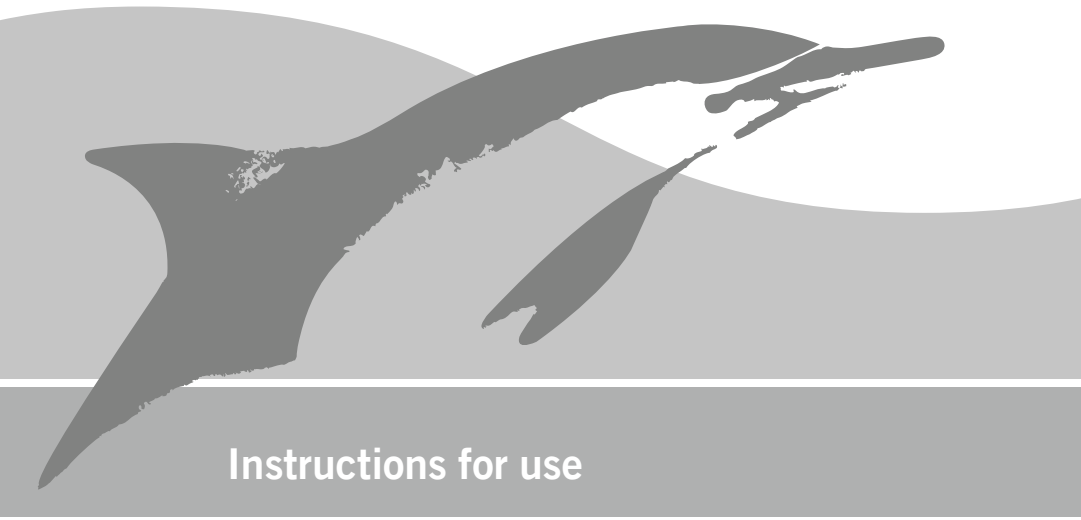
Heraeus

Medical

COPAL® G+V

Radiopaque revision bone cement containing Gentamicin and Vancomycin



Instructions for use

℞ Only

COPAL® G+V

1 General information

1.1 Device description

COPAL® G+V is a standard-setting, high-viscosity, radiopaque, poly(methyl methacrylate)-based (PMMA) bone cement.

It contains the aminoglycoside antibiotic gentamicin and the glycopeptide antibiotic vancomycin to protect the cured bone cement and surrounding tissue from colonization by bacteria that are sensitive to gentamicin and/or vancomycin. 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.

1.2 Device sizes and packaging

Device sizes

COPAL® G+V is available in the size 40.

Package content

- 1 pouch filled with gentamicin- and vancomycin-containing powder
- 1 brown glass ampoule filled with liquid
- 1 set of product stickers for documentation
- 1 instructions for use

Packaging design

The powder is triple packaged and sterilized using gamma irradiation: it is packed first in an inner polyethylene (PE) paper pouch, secondly in an outer PE-paper pouch (peel-off) and last in a protective aluminum pouch. The peel-off pouch contains the sterile inner PE-paper pouch with powder and is sterile on the inside and non-sterile on the outside.

The liquid is single packaged. The ampoule blister is sterilized using ethylene oxide and contains (a) brown glass ampoule(s) with sterile-filtered liquid.

1.3 Composition

Composition	
Powder:	
PMMA copolymer	78 %
zirconium dioxide	14 %
benzoyl peroxide	1 %
gentamicin sulfate	2 %
vancomycin hydrochloride	5 %
Liquid:	
methyl methacrylate	98 %
N, N-dimethyl-p-toluidine	2 %

The data is rounded.

Other constituents:

- Powder: chlorophyll-copper-complex (E141)
- Liquid: chlorophyll-copper-complex (E141), hydroquinone

It cannot be excluded that **COPAL® G+V** contains traces of histamine. **COPAL® G+V** does not contain a radiation source.

Device size	40
Powder:	43.0 g
including gentamicin	0.5 g
including vancomycin	2.0 g
Liquid:	20 ml

The data is rounded.

The mass ratio is about 31 % liquid to 69 % powder.

1.4 Supporting equipment

Mixing equipment is required to mix the two components of **COPAL® G+V**. 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.

Note: Heraeus Medical GmbH has not tested the compatibility of **COPAL® G+V** with devices of other manufacturers and does not assume any liability for this. The use of mixing equipment of other manufacturers is done in the sole discretion and responsibility of the user.

1.5 MRI safety information

COPAL® G+V is MR safe.

2 Directions for use

2.1 Intended use
COPAL® G+V is a PMMA bone cement intended for fixation of **COPAL® exchange G hip spacer** to the host bone.

2.2 Intended patient population
Adult population, predominantly elderly patients with periprosthetic joint infection.

2.3 Intended user
Healthcare professionals in a clinical context and experienced in the handling of the product.

The surgeon and nurse 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, a test mix should be performed to gain familiarity with its characteristics.

2.4 Indications
COPAL® G+V (gentamicin and vancomycin) is a PMMA bone cement intended for fixation of **COPAL® exchange G hip spacer** to the host bone.

2.5 Contraindications
COPAL® G+V must not be used in the following cases:
- suspected or proven hypersensitivity to components of the bone cement including gentamicin, other aminoglycoside antibiotics, or vancomycin
- 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 and vancomycin non-sensitive strains
- spinal surgery
- children

2.6 Adverse events and residual risks
Adverse events

General

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.

Gentamicin and Vancomycin

Where gentamicin and vancomycin are used, it is possible, in principle, for the antibiotics to trigger typical adverse events:
- Damage to the auditory and vestibular nerves
- Nephrotoxicity
- Neuromuscular blockade
- Rarely paresthesia, tetany and muscle weakness
- Rarely allergic reactions (exanthema, urticaria, anaphylactic reactions)

Gentamicin and vancomycin are also potentially nephrotoxic and/or ototoxic. Although an accumulation is hardly to be expected because of the minimal systemic concentration, caution is advised, and serum levels of gentamicin should be monitored in patients with severe renal impairment.
As gentamicin and vancomycin have neuromuscular blocking properties, caution is advised with patients, in particular, if they also have a history of renal insufficiency:
- having a history of neuromuscular disease
- treated concomitantly with the administration of muscle relaxants

Allergic reactions may occur regardless of the dosage.

Residual risks
Residual risks listed below are procedure related risks which are beyond the control of the manufacturer because they are procedure or user related.

Nervous System
- numbness

Muscoskeletal System
- loosening
- loss of range of motion
- ambulation difficulties

Infection
- bacterial infection including cellulitis, and/or osteomyelitis

Generalized Disorders
- inflammation
- swelling/edema
- fibrosis

2.7 Warnings

Regarding intended users

Caution should be exercised during the mixing of the two components of **COPAL® G+V** 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. Eye protection is recommended while mixing the bone cement to protect the eye from any glass fragments or monomer liquid when opening the ampoule.

Do not allow the liquid component to contact rubber or latex gloves. The liquid component is a powerful lipid solvent. Should contact occur, the gloves may dissolve and tissue damage may occur. Wearing a second pair of gloves and strict adherence to the mixing instructions may diminish the possibility of hypersensitivity reactions. The mixed bone cement should not make contact with the gloved hand until the cement has acquired the consistency of dough. This usually occurs between one and two minutes after the liquid and powder components are mixed.

The monomer is not for injection.

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 PMMA spacer.

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 tissues.
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 PMMA spacer may occur leading to PMMA spacer failure. Long-term follow-up is advised for all patients on a regularly scheduled basis.

Note: COPAL® G+V 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

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 are in particular linked to the pressurization of bone cement and the subsequent implantation of the cemented stem. Hypotensive reactions have occurred shortly after application of bone cement. However, consequences such as cardiac arrest are only reported in very few cases.

2.8 Precautions

Regarding intended users

Do not use this product after the expiration date printed on the folding box. 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.

Do not use the bone cement if its consistency is inhomogeneous as this can lead to early loosening of the spacer.

Fixation of **COPAL® exchange G hip spacer** with **COPAL® G+V** is used primarily to stabilize the spacer. Deep penetration of the bone cement into the bone structure is not desirable and can make subsequent explantation of the spacer more difficult. Excess bone cement must be removed.

After the bone cement used for fixation is set, the joint space must be cleaned of any bone cement particles. During the cleaning, the spacer should not be rinsed with aqueous solution, nor should the pulse lavage touch the spacer or bone cement because any substances present in the spacer or bone cement may be flushed out as a result.

For more information, please consult the IFU and Surgical Technique of **COPAL® exchange G hip spacer**.

Regarding the intended patient population

Both gentamicin and vancomycin are potentially nephrotoxic and/or ototoxic. Independent of the total amount applied, care should be taken in patients with risk factors for the development of renal failure as well as in patients simultaneously treated with other nephrotoxic drugs; e.g. by periodically monitoring systemic levels of the antibiotic, serum electrolytes and renal function.

The use of **COPAL® G+V** should be limited to patients that are proven to be infected with pathogens sensitive to vancomycin and when solely gentamicin-containing cement is considered inadequate or undesirable.

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 **COPAL®G+V**, the prepared bone should be carefully cleaned, aspirated, and dried just before the bone cement is placed.

Pregnancy and lactation
Gentamicin and vancomycin are known to cross the placenta. In animals, neither gentamicin nor vancomycin produced structural malformations in spite of maternal toxicity at high doses. Limited human experience does not point to an increased risk of structural malformations. Ototoxicity and nephrotoxicity in the fetus are potential hazards, but this has not been confirmed clinically. Gentamicin and vancomycin are excreted in small amounts in human breast milk and absorbed by the nursing child. Because of enhanced intestinal permeability in neonates, accumulation and toxicity cannot be excluded. In view of this data, the benefits for the mother should be weighed against the potential risk to the child before using **COPAL®G+V** during pregnancy and lactation.
In view of this data, the benefits for the mother should be weighed against the potential risk to the child before using **COPAL®G+V** during pregnancy and lactation.

3 Handling

Perform mixing and application of **COPAL®G+V** under sterile conditions. **COPAL®G+V** is mixed in a mixing system with or without vacuum (see 1.4 Supporting equipment).

If **COPAL®G+V** 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 **COPAL®G+V** are shown in the diagrams at the end of the instructions for use (see 7.1 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, **COPAL®G+V** 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).

COPAL®G+V 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/s	sterile

3.1 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 **COPAL®G+V** should be available before commencing the operation.

3.2 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 product stickers.
- Before opening the aluminum pouch, move the content down by shaking or tapping to ensure that when the aluminum pouch is torn open at the top, the content is not damaged.
- Open the aluminum pouch and take out the outer PE-paper pouch.
- Visually inspect the outer PE-paper pouch immediately prior to use in order to determine if breaches in sterile barrier system integrity are evident. Do not use if outer PE-paper pouch is damaged
- 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

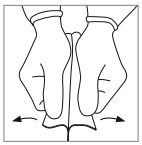


Figure 1

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.

3.3 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.
- Before opening the inner PE-paper pouch, move the content down by shaking or tapping to ensure that when the inner PE-paper pouch is cut open at the top, no powder is lost.
- Open the inner PE-paper pouch 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 ampoules are 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.

3.4 Mixing and application

For mixing and application of **COPAL® G+V**, the instructions for use of the suitable systems must be followed (see 1.4 Supporting equipment).

Mixing the powder and liquid together produces a paste that is used to anchor **COPAL® exchange G hip spacer** to the bone. The hardened bone cement allows fixation of **COPAL® exchange G hip spacer** to the host bone.

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. For adequate fixation of **COPAL® exchange G hip spacer**, please consult IFU of **COPAL® exchange G hip spacer**.

Note: Cleanse all cement-receiving bone surfaces thoroughly using high pressure pulse lavage repeatedly until clear fluid is received in the return line. Deliver the cement to a clean, dry bone bed following pulse lavage. Prevent PMMA spacer – bone cement interface contamination.

4 Storage, transport, shelf life, sterilization

Storage

Do not store above 25 °C (77 °F).
COPAL® G+V must be stored in dry conditions and must not be exposed to direct sunlight, ionizing radiation, extremes of temperature, or particulate contamination. In the case of a not pre-chilled use of **COPAL® G+V** the product must be brought to the temperature of the operating room at least 2 hours before use to achieve the depicted working times.

Transport

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

Shelf life

The shelf life of **COPAL® G+V** is printed on the folding box. Do not use **COPAL® G+V** if the date indicated has expired.

Sterilization

Powder and its packaging have been sterilized using gamma irradiation. Liquid has been sterilized by sterile filtration and its packaging by ethylene oxide. 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 **COPAL® G+V**.

5 Disposal

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.

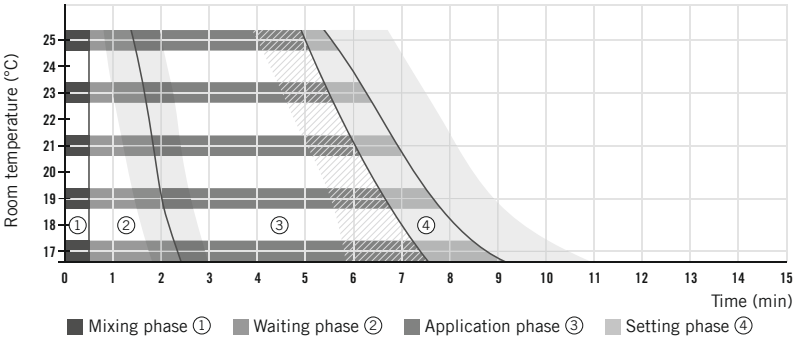
6 Disclaimer of liability

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

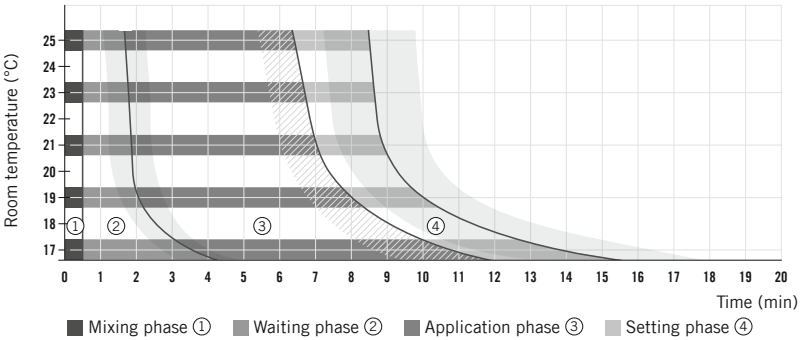
7 Appendix

7.1 Working times

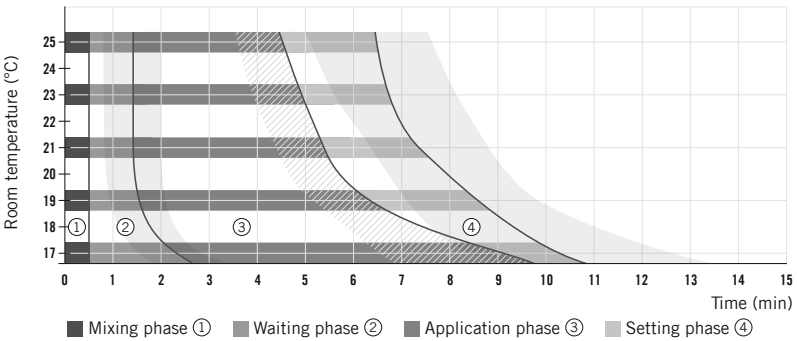
Working times for manual mixing (not pre-chilled bone cement)



Working times for vacuum mixing (pre-chilled bone cement)



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



Note: The working times 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.

Symbols


Manufacturer

Country and date of manufacture (DE=Germany)

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


Use-by date

Batch code

Catalogue number

Do not resterilize


Do not use if package is damaged and consult instructions for use

Sterilized using aseptic processing techniques

Sterilized using ethylene oxide

Sterilized using irradiation


Single sterile barrier system


Single sterile barrier system with protective packaging outside


Keep away from sunlight


Keep dry

Upper limit of temperature
25 °C (77 ° F)


Do not re-use


Consult instructions for use


Caution


Contains a medicinal substance

Medical Device

Unique Device Identifier


Causes skin irritation


Flammable liquid

MR safe

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