Summary of Safety and Clinical Performance

PALACOS® fast R+G

- Patient Section -

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English

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2 Abbreviations / Explanations

ALBC	Antibiotic-loaded bone cement
AUS	Australia
BCIS	Bone cement implantation syndrome
BfArM	Federal Institute for Drugs and Medical Devices (Germany) *[Bundesinstitut für Arzneimittel und Medizinprodukte]*
CAN	Canada
CE	Conformité Européenne
CER	Clinical Evaluation Report
CH	Switzerland
CND	*Classificazione Nazionale dei Dispositivi medici* [National Classification of Medical Devices]
CT	Computed tomography
CS	common specifications as defined in the MDR
DIN	German standard *[Deutsches Institut für Normung]*
EMDN	European Medical Device Nomenclature
EN	European Standard *[Europäische Norm]*
EU	European Union
FDA	Food and Drug Organization (USA)
GER	Germany
IFU	Instructions for Use
ISO	International Organization for Standardization
MDD	Medical Device Directive
MDR	Medical Device Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC and the amendments of 2017/45 (2020/561 and 2023/607)
MHRA	Medicines and Healthcare Products Regulatory Agency in the UK
MRI	Magnetic resonance imaging
N/A	Not applicable
NB	Notified Body
PMCF	Post-Market Clinical Follow-Up
PMMA	poly(methyl methacrylate)
PMS	Post-Market Surveillance
SRN	single registration number for an economic operator
SSCP	Summary of Safety and Clinical Performance
Swissmedic	Swiss Agency for Therapeutic Products (Switzerland)
TGA	Therapeutic Goods Administration (Australia)
TPLC	FDA Total Product Life Cycle (TPLC)
UDI-DI	Unique Device Identification - device identifier
UK	United Kingdom
US/USA	United States of America

3 General Information

This document applies to implantable class IIb, and class III medical devices developed by Heraeus Medical GmbH and is established to comply with the Medical Device Regulation (MDR) 2017/745 (EU) of 5th April 2017, valid from May 2021.
The Summary of Safety and Clinical Performance (SSCP) is intended to provide a summary of clinical data pertinent to the safety and clinical performance of the medical device. The SSCP is an important source of information for intended users – both healthcare professionals and if relevant for patients. It is one of several means intended to fulfil the MDR objectives, to enhance transparency and provide adequate access to information.

3.1 Relevant information for Users/Healthcare Professionals

Please refer to the English language version of this document for the contents of this section.

3.2 Relevant Information for patients

The following chapters provide a summary of the safety and clinical performance of the device intended for patients.

This Summary of Safety and Clinical Performance (SSCP) provides public access to an updated summary of the main aspects of the safety and clinical performance of the device. The information presented below addresses patients or lay persons. The first part of the document shows a more extensive summary of safety and clinical performance prepared for healthcare professionals.

The SSCP does not provide general advice on the treatment of a medical condition. Please contact your doctor/surgeon in case you have questions about your medical condition or about the use of the device in your situation. This SSCP does not replace an Implant Card or the Instruction for Use (IFU) to provide information on the safe use of the device.

3.2.1 Background information

PALACOS® fast R+G is a bone cement. PALACOS® fast R+G is part of the product family PALACOS® +G bone cements. It is based on a biologically safe material called poly (methyl methacrylate) (PMMA). This material has a long history of safe use in humans. PALACOS® R+G was the basis for development of the bone cements PALACOS® MV+G, PALACOS® LV+G, and PALACOS® fast R+G. All four bone cements together comprise the product family PALACOS® +G bone cements.

PALACOS® +G bone cements are used in adults such as elderly patients with degenerative joint disease. Osteoarthritis is an example for such a joint disease. Osteoarthritis is the most common form of arthritis and affects millions of people worldwide. It occurs when the protective cartilage that cushions the ends of the bones wears down over time. Patients with trauma after severe accidents with several fractures in a bone can also be considered for treatment with bone cements. The bone cement is used to anchor total or partial joint endoprostheses. It attaches endoprostheses firmly and stably to the bone. Endoprostheses are medical devices used to replace parts of the inside of your body. Hip, knee, or shoulder joints can be replaced by an endoprostheses, for example.

Arthroplasty is a surgical procedure to restore the function of a joint. Primary arthroplasty refers to the first joint replacement. Revision arthroplasty refers to follow-up surgery on the same joint. In total joint replacement parts of a joint are removed and replaced by an implant, the endoprosthesis. In partial joint replacement artificial surfaces replace only the movable surfaces of a joint. The healthy parts of the joint stay intact.

Bone cements can also treat cases of bone loss. For example, after severe accidents with multiple fractures in a bone. The name of this surgical technique is reconstruction of bone. It restores bone continuity mainly in patients suffering from tumor of the bone or in trauma.

Your doctor/surgeon applies the bone cement during surgery. The instructions for use give directions.

Your doctor/surgeon takes care of the following aspects during your surgery:
- The bone cement is applied to your carefully cleaned, aspirated, and dried bone.
- Your prosthesis is put in place and held until the bone cement has set completely.
- During and immediately after the bone cement is applied, your doctor/surgeon will monitor your blood pressure, pulse, and breathing carefully. This ensures early detection and treatment of adverse events such as low blood pressure and cardiac arrest. Drops in blood pressure have occurred remotely and shortly after application of bone cement. However, consequences such as cardiac arrest are only reported in very few cases.

It is safe to have magnetic resonance tests (MRI) with PALACOS® +G bone cements. But the composition of the prosthesis you receive together with the bone cement may affect your ability to have magnetic resonance tests. You will receive an implant card for the bone cement that was used. Additionally, you will receive an implant card

for the prosthesis. Please keep these documents and provide them in future examinations (e.g., X-ray, CT scan, MRI).

3.2.2 Device identification and general information

3.2.2.1 Products (device trade names) covered by this document

PALACOS® fast R+G

3.2.2.2 Manufacturer name and address

Heraeus Medical GmbH
Philipp-Reis-Str. 8/13
61273 Wehrheim
Germany

3.2.2.3 Basic UDI-DI number of the concerned product

The unique device identification (UDI) consists of a series of numbers with letters. It allows the unmistakable identification of a specific medical device on the market. An UDI device identifier (UDI-DI) is specific to a device, connecting the product to the information on the EUDAMED database.

The following UDI-DI numbers are assigned to the different products:

Product	Basic UDI-DI
PALACOS® fast R+G	4260102130101010002AL

3.2.2.4 Year of first CE-mark

Before a medical device is introduced on the market in the European Union, it needs to show that the product fulfills the requirements. The so-called CE-certification documents the fulfilment, and the CE-mark is placed on the product. The legal requirements for medical devices have changed in May 2021. Then, the Medical Device Regulation (MDR) replaced the Medical Device Directive (MDD).

The following table contains the detailed information about the different products. The table lists the year of the first CE-mark under MDR and under MDD.

Product	Year of first CE-mark under MDR	Year of first CE-mark under MDD
PALACOS® fast R+G	2022	2013

3.2.3 Intended use of the device

3.2.3.1 Intended purpose

PALACOS® fast R+G is intended for stable anchoring of total or partial joint replacements (endoprostheses) in living bone as well as for reconstruction of bone.

3.2.3.2 Indications and intended patient groups

PALACOS® fast R+G is indicated for surgical treatment such as

- anchoring of endoprosthesis in primary and revision arthroplasty procedures of
    - hip
    - knee
    - ankle
    - shoulder

- elbow
- reconstruction of bone via induced membrane technique after tumor surgery and / or trauma

These treatments are typically conducted in adults, predominantly elderly patients with osteoarthritis and patients with trauma.

3.2.3.3 Contraindications/ advice against treatment

PALACOS® fast R+G must not be used in the following cases:

- known or suspected intolerance against parts of the bone cement or against the antibiotic gentamicin
- infection at the site of the body where the surgery is planned
- patients with impaired kidney function
- reconstruction of skull bone defects
- spinal surgery
- children

3.2.3.4 Lifetime of the device

There is no general factor influencing the lifetime of the PALACOS® +G bone cements. The general provisions for the prosthesis they anchor also apply to the bone cements. The actual lifetime of these bone cements can be influenced by factors such as your medical situation and your lifestyle.

3.2.4 Device description

PALACOS® +G bone cements are based on a biologically safe material called poly (methyl methacrylate) (PMMA) which has a long history of safe use in humans.

Composition

The cement consists of two main components, a powder, and a liquid. The table below shows the composition of the components. Mixing of the components starts a chemical reaction. This so-called polymerization forms a soft dough. The dough becomes more and more solid over time. Your surgeon determines the right time for the application of the dough to the bone. There it hardens completely. In addition, the cement contains an antibiotic (gentamicin). Your treating surgeon chose the antibiotic to prevent an infection.

PALACOS® fast R+G contains:

Table 1: Composition of PALACOS® fast R+G in percentage

Constituents	**PALACOS® fast R+G**
Powder:	
PMMA copolymer *Polymer (powder component)*	81 %
zirconium dioxide *X-ray contrast medium (enabling visualization with X-ray, CT or MRI)*	15 %
benzoyl peroxide *Chemical component initiating the polymerization reaction*	2 %
gentamicin sulfate *(Antibiotic)*	2 %
Liquid:	
methyl methacrylate *Monomer (liquid component)*	98 %
N, N-dimethyl-p-toluidine Chemical component accelerating the polymerization reaction	2 %

The data is rounded

Other constituents:

- Powder: chlorophyll-copper-complex (E141) (Food colorant. Improving visibility of the bone cement in the surgical field)
- Liquid: chlorophyll-copper-complex (E141), hydroquinone (chemical component stabilizing the chemical reaction)

Traces of histamine may be present in these bone cements. But no manufacturing residuals that could pose a risk to you have been found. Be aware that the composition table shows the constituents before mixture of the bone cement components. The methyl methacrylate is completely used up during setting and forms the hardened bone cement. PALACOS® +G bone cements are intended for single-use and are supplied sterile.

3.2.5 Risks and warning

Contact your doctor/surgeon if you believe that you are experiencing side effects. This applies for side effects related to the device or its use and if you are concerned about risks. This document does not replace a consultation with your doctor/surgeon if needed.

Side effects are events that are known when using the device. They can be caused by the device.
Residual risks are risks which cannot be controlled by the device manufacturer. They are mostly related to the surgical procedure in general or to the handling of the user.
Adverse events are events that can occur in a clinical investigation. They have a negative impact mostly on the patient. No causal relationship with the device must be present.

Heraeus Medical GmbH has a risk management process that complies with harmonized risk management guidelines. It ensures that the benefits of using the medical device are greater than any potential risks.

Side effects and residual risks of the device can occur with different frequencies. As an example, if a side effect occurs in less than 1% of cases (< 1%), the side effect will occur in less than 1 in 100 surgeries.

Side effects

Frequencies are taken from literature, < 0.0001% can include potential risks not reported in literature so far.

Table 2: Frequencies of side effects

Frequency	Side effect
Immune system	
4.79%*	• hypersensitivity / allergic reaction and local reaction which may include inflammation, induration, erythema, pruritus, or pain
< 0.0001%	• anaphylactic shock
Kidney and Urinary Tract	
< 0.0001%	• renal impairment
Musculoskeletal System	
36.65%*	• ossification
22.78%*	• osteolysis due to bone cement fragments
Skin and Subcutaneous Tissue	
< 0.0001%	• rash
< 0.0001%	• urticaria

*cases reported to Heraeus Medical GmbH with frequencies lower than from literature

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. Frequencies are taken from literature, < 0.0001% can include potential risks not reported in literature so far.

Table 3: Frequencies of Residual risks

Frequency	Residual Risk
Vascular System, Heart, Respiratory System, Blood and Lymphatic System, Nervous System	
Bone Cement Implantation Syndrome (BCIS): Insertion of bone cement may produce a high medullary pressure that forces bone marrow constituents into the venous vascular system, resulting in fat and marrow emboli. To avoid BCIS, it is recommended that the implantation site is cleaned thoroughly with pulsatile, high pressure, high-volume lavage using an isotonic solution and dried before the bone cement is introduced. The bone cement should be applied retrogradely under sustained low pressure into the medullary canal. Subsequently, the prosthesis should be introduced slowly into the cemented medullary canal. In case of pulmonary or cardiovascular events, it is necessary to monitor blood volume and possibly increase it. In case of acute respiratory failure, anesthesiologic measures should be taken. In general, adverse reactions of BCIS might include low blood pressure/hypotension, hypoxia, bradycardia, tachycardia, pulmonary hypertension, thrombosis, embolism, pulmonary embolism, myocardial infarction, cerebrovascular accident, respiratory arrest, and cardiac arrest.	
25.48%*	BCIS grade 1 moderate hypoxia (SpO2 < 94%) or hypotension [fall in systolic blood pressure > 20%]
8.17%*	BCIS grade 2 severe hypoxia (SpO2 < 88%) or hypotension [fall in systolic blood pressure > 40%] or unexpected loss of consciousness.
3.37%*	BCIS grade 3 cardiovascular collapse, requiring CPR
Nervous System	
< 0.0001%	• numbness
Blood and Lymphatic System	
< 0.0001%	• hypovolemia
Musculoskeletal System	
15.22%*	• aseptic loosening
< 0.0001%	• unequal limb length
0.27%*	• loss of range of motion
< 0.0001%	• ambulation difficulties
Infection	
3.58%*	• bacterial infection including cellulitis, and / or osteomyelitis
Generalized Disorders	
2,56%	• inflammation
< 0.0001%	• swelling / edema
0.94%*	• fibrosis
< 0.0001%	• heat necrosis

*cases reported to Heraeus Medical GmbH with frequencies lower than from literature

Please contact your healthcare professional if you have any questions.

Reporting of side effects, residual risks, or adverse events

If you experience any of these side effects or residual risks, or if you notice any adverse events not listed in this document, contact your doctor/surgeon immediately. You can also contact Heraeus Medical GmbH directly using the following email-address: hm.vigilance.medical@heraeus.com

3.2.6 Summary of clinical evaluation and post-market clinical follow-up

PALACOS® R+G was the first bone cement with an antibiotic introduced in 1972. All further products of the PALACOS® +G product family like PALACOS® fast R+G are based on PALACOS® R+G. They own few modifications in terms of product characteristics. PALACOS® fast R+G was developed and placed on the market in 2013. PALACOS® +G bone cements treated a total of about 30 million patients worldwide so far. The product range of PALACOS® +G bone cements can be considered as state-of-the-art in the field of stable anchoring of joint endoprostheses as well as for reconstruction of bone.

The manufacturer performs the analysis of any clinical data regularly. Sources can be endoprosthesis registries and scientific publications, for example. These activities are called post-market clinical follow-up measures. They allow the continuous proof of the benefit/risk ratio of the medical device. Registries are databases which collect long-term results after application of products in patients. These databases can be initiated by governmental authorities, medical societies, or manufacturers. In most cases they collect data from hospitals or private practices on a regional or national level.

The following clinical benefits and outcome parameters relate to the use of the bone cements:

- Stable fixation of the endoprosthesis with a low risk of revision surgery. This is evaluated based on long-term data from regional or national registries.
- Improvement of impaired body function with a high patient satisfaction. This is evaluated based on quality-of-life data from registries.
- Relief of symptoms related to the surgical procedure with high patient success. This is evaluated based on quality-of-life data from registries.
- Application of bone cements in combination with an antibiotic with a low risk of infection. This is evaluated based on revisions that are caused by infections, compared to the overall number of revisions (based on data from registries).
- Local use of an antibiotic within the bone cement can result in a reduced risk for side effects compared to oral or intravenous administration of the antibiotic. This is evaluated based on complaints reported to manufacturer, evaluation of databases and data regarding the development of the medical device.
- The reconstruction of bone via induced membrane technique can result in the preservation of function of the limb or of the limb itself. This is evaluated by determination of the union of bone defects after tumor surgery and / or trauma.

The above-mentioned clinical benefits and clinical outcome parameters are important to decide on the benefit/risk ratio of PALACOS® fast R+G. The manufacturer evaluates the achievement of these clinical benefits.

The analysis revealed that PALACOS® fast R+G performed as expected in all aspects of the above-listed outcome parameters:

- Stable fixation was analyzed by the rate at which operations needed to be repeated (revision rate). The rate was in a range comparable with the current state-of-the-art. For example, the revision rate of PALACOS® fast R+G was reported to be 1.4% for primary hip and 1.7% for primary knee, which is better than benchmark standards (range for hip: 2.0 – 3.8% after 5 years; range for knee: 2.4 – 5.5% after 5 years).
- Impaired body function was evaluated through questionnaires. In these, patients have reported on how much they are impacted in their daily activities. In all cases, PALACOS® fast R+G was comparable to or better than current state-of-the-art.
- Relief of symptoms was evaluated through questionnaires. In these, patients have reported on how much better their joint was after the surgery. In all cases, PALACOS® fast R+G were comparable to the current state-of-the-art.
- The number of re-operations because of an infection at the site of surgery was comparable to the current state-of-the-art in patients who underwent their first operation with PALACOS® fast R+G and for revision surgeries.
- PALACOS® fast R+G contains an antibiotic that can also be given directly into the veins. From this it is known that too high amounts can cause severe side effects. In a clinical study, it was measured how high

up the blood concentrations of antibiotics released from the bone cement would go after an operation with PALACOS® fast R+G. The result was that the values remained far below the levels which can lead to severe side effects.

- Reconstruction of bone via induced membrane technique was analyzed by the rate of successful bone union after two-stage reconstruction. The performance of PALACOS® R+G was comparable to the state-of-the-art.

Additionally, the scientific literature for PALACOS® R+G and PALACOS® fast R+G was thoroughly evaluated, and 77 scientific publications were identified and analyzed. It can be summarized that all data show favorable clinical results for PALACOS® R+G and PALACOS® fast R+G.

In conclusion, the success rates of the clinical benefits were comparable to or better than the current state-of-the-art.

Therefore, the manufacturer confirms that the benefits outweigh the risks for the indications of PALACOS® fast R+G:

- anchoring of endoprosthesis in primary and revision arthroplasty procedures of
  - hip
  - knee
  - ankle
  - shoulder
  - elbow
- reconstruction of bone via induced membrane technique after tumor surgery and / or trauma

The following activities are planned to ensure safety and performance of PALACOS® +G bone cements:

- Device Registry Analysis, to monitor the safety and performance of PALACOS® +G bone cements
- Screening of Scientific Literature, to monitor the safety and performance of PALACOS® +G bone cements
- Authority Databases (adverse events and recalls), to monitor the safety of PALACOS® +G bone cements

The same activities are performed for similar products, in order to detect potential safety or performance issues early. The results will be summarized in reports. These activities will be conducted on an annual basis in connection with the continuous updates of the clinical evaluations.

3.2.7 Possible diagnostic or therapeutic alternatives

General information

Contact your doctor/surgeon when you consider alternative treatments. Depending on your individual situation, two treatment approaches are possible. On the one hand conservative treatment such as physiotherapy or pain medication without surgery is possible. On the other hand, surgical treatment such as joint surgery like hip replacement surgery could be reasonable. Choice of treatment depends on your specific condition and your doctor's opinion.

Joint surgery

If possible, your doctor/surgeon will try to treat defective joints by other means. If all other treatment options fail, a reconstructive joint surgery may be necessary. This means, the complete joint or only parts of the joint are replaced by an endoprosthesis. Joint surgeries and endoprosthesis revision operation as well as the use of PMMA bone cements are very well-established procedures in joint replacement surgery.

PMMA is widely and successfully used for the fixation of various endoprostheses since decades. At present, PMMA is still the most commonly used fixation material in primary joint surgeries. Uncemented procedures have also been used in primary joint surgeries. However, current data do not allow to determine if cementless or cemented generally perform better in joint surgeries. The advantage of the cemented procedures using PMMA is the long-term experience with this material. Also, the majority of orthopedic surgeons is familiar with the use of PMMA. Furthermore, bone cement can apply local antibiotics. This allows for infection prevention in patients at risk for

infection. In addition, bone cements generally spread the force of movement evenly into the bone. Especially in patients with poor bone substance this is an advantage. Your doctor/surgeon will decide on the procedure that fits to your specific clinical condition best.

There is no other treatment option than a surgery in patients with suspected or confirmed infection of the implanted device (so-called prosthetic joint infections). Such a revision surgery can be either a one-stage or a two-stage surgery. A so-called one-stage surgery takes place in a single surgical step. The surgeon removes the infected prosthesis and bone cement, cleans the surgical site thoroughly, and places a new prosthesis. A so-called two-stage approach consists of two separate surgeries. During the first surgery, the surgeon removes the infected prosthesis and bone cement, cleans the surgical site thoroughly, and places a provisional spacer. This ensures proper treatment of the infection. The spacer also provides a limited range of motion during the time until the second operation. After the infection is cured, the second surgery takes place. The surgeon removes the provisional spacer and places a new permanent prosthesis. The attending surgeon will choose the appropriate surgical approach according to the patient's situation.

Reconstruction of bone

Oncological treatment or trauma may lead to bone loss. PMMA bone cement is able to fill certain bone defects depending on the depth and surface of the defect. The method "Induced Membrane Technique" can support new bone growth in an area where part of a bone had to be removed due to cancer or was lost due to trauma. For this approach bone cement is only placed between the ends of a defect for a short period of time. The bone cement is not fixed to the bone.

For larger defects further therapy options have to be considered. Therapy options like human tissues from donors, metal implants or custom-made protheses are available. The attending surgeon will choose the appropriate surgical approach according to the patient's situation.

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