OSTEOREMEDIES®
ADVANCED MEDICAL TECHNOLOGIES

SURGEON INFORMATION

REMEDY® ACETABULAR CUP

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Figure 1: REMEDY® Acetabular Cup

Overview
The REMEDY® Acetabular Cup (Figure 1) is part of the treatment in a two-stage procedure performed in the event of permanent prosthesis infection.

The REMEDY® Acetabular Cup implant is intended for temporary use only (180 days or less) and only in combination with REMEDY® & REMEDY SPECTRUM® GV Modular Head. It allows basic joint mobility and releases antibiotic into the joint area to protect the implant from bacterial colonization. A second surgery will be required at a later date to remove REMEDY® Acetabular Cup and replace it with a permanent hip joint implant.

REMEDY® Acetabular Cup:
- single-use medical device/ethylene oxide sterile
- formed with bone cement (PMMA) and gentamicin
- releases gentamicin

Indications
The OsteoRemedies® Hip Spacer System consists of a modular head and stem, and an optional acetabular cup. The REMEDY® components of the OsteoRemedies® Hip Spacer System include gentamicin and the REMEDY SPECTRUM® GV components include gentamicin and vancomycin.

The OsteoRemedies® Hip Spacer System is indicated for temporary use (maximum 180 days) as an adjunct to total hip replacement (THR) in skeletally mature patients undergoing a two-stage procedure due to a septic process and where gentamicin or gentamicin/vancomycin are the most appropriate antibiotic based on the susceptibility pattern of the infecting micro-organisms.

Following removal of the existing acetabular and femoral components and radical debridement the head and stem components are inserted into the femoral medullary canal and can mate directly with the native acetabulum or an acetabular component which is placed in the acetabular cavity. The device is intended for use in conjunction with systemic antimicrobial antibiotic therapy (standard treatment approach to an infection).

The OsteoRemedies® Hip Spacer System is not intended for use for more than 180 days, at which time it must be explanted and a permanent device implanted or another appropriate treatment performed (e.g. resection arthroplasty, etc.).

Contraindications
Contraindicated for use with:
- Deficiencies in the patient's vascular, nervous or muscular systems.
- Osteoporosis or poor bone quality may cause the implant to fracture existing bone or migrate.
- Patient's two-stage arthroplasty procedure is contraindicated based on decreased immune response or systemic clinical conditions.
- The infected THR devices cannot be removed.
- Patient exhibits hypersensitivity (allergy) to PMMA bone cement, aminoglycosides or gentamicin.

- Lack of ideal bone disallows support of the prosthesis in the acetabular region or proximal femur (e.g. when Burch Schneider reinforcement cage is needed)
- Infection of the THR cannot be confirmed.
- Infecting bacteria/pathogens resistant or not susceptible to gentamicin when coupled with the REMEDY® Hip Spacer.
- Infecting bacteria/pathogens resistant or not susceptible to gentamicin and vancomycin when coupled with the REMEDY SPECTRUM® GV Hip Spacer.
- A remote infection (systemic or secondary) is suspected or verified.
- Patient has myasthenia gravis.
- The patient does not have a THR and the infection is secondary to trauma, septic arthritis or other surgical procedures.
- Patient has neuromuscular disorders disallowing proper control of the hip.
- Patient is unable or rejecting the use of protected weight bearing devices throughout the implantation period (canes, walkers, crutches, etc.).
- Age, weight or activity level, may cause the surgeon to expect possible, early failure of the hip spacer.

Possible Adverse Events
The list provided below addresses serious adverse effects which may be associated with the use of the REMEDY® Acetabular Cup. Note that some effects are not directly associated with the device itself; however, the surgeon should be aware of these possible issues, and be ready to treat them accordingly.

Surgical Risks (General): pulmonary embolism, myocardial infarction, arrhythmias, venous thrombosis, and transitory hypotension.

Surgery Risks (THR): difference in limb length, wound healing issues, femur or acetabulum damage, blood vessel damage, nerve damage, bone bed damage, excessive blood loss, arthrofibrosis, phlebitis, thrombophlebitis, and hematoma

REMEDY® Acetabular Cup Risks: recurrent infection, gentamicin toxicity (ototoxicity/nephrotoxicity), implant breakage, head disassembly, implant loosening, PMMA sensitivity, debris release, difficult device removal, implant dislocation, and foreign body reaction.

NOTES: The surgeon should be aware of the possible negative effects of bone cement, as the device must be affixed with it. Reoccurring infections have been known to present even with intravenous (i.v.) antibiotic use. Gentamicin application may trigger negative reactions of this antibiotic following systemic use, as shown in the next paragraphs.

Gentamicin (and Aminoglycosides) Risks:
All aminoglycosides have the potential to produce reversible and irreversible vestibular, cochlear and renal toxicity when administered systemically.

Ototoxicity:
Both vestibular and auditory dysfunction can follow administration of any of the aminoglycosides. It is more likely to occur in patients with persistently elevated concentrations of drug in plasma. Ototoxicity is largely irreversible. Repeated courses of aminoglycosides can lead to deafness. Older patients may be more susceptible to ototoxicity. Drugs such as ethacrynic acid and furosemide may potentiate the ototoxic effects. Hearing loss is more likely to develop in patients with pre-existing auditory impairment following exposures to these agents. It is recommended that patients receiving high doses and /or prolonged courses of aminoglycosides be monitored carefully for ototoxicity, since initial symptoms may be reversible. However, deafness may occur several weeks after therapy is discontinued.

Nephrotoxicity:
Approximately 8-28% of patient receiving an aminoglycosides for more than several days will develop mild renal impairment, which is almost always reversible: Toxicity correlates with the total amount of drug administered. Other drugs, such as amphotericin B, vancomycin, cisplatin, cyclosporine, cephalotin, furosemide may potentiate aminoglycoside-induced nephrotoxicity. Monitoring drug concentrations in plasma is useful, particularly during prolonged and/or high dose therapy.

Neuromuscular Blockade:
Episodes have occurred in association with anesthesia or administration of other neuromuscular blocking agents. Patients with myasthenia gravis are particularly susceptible to this phenomenon.

Other Untoward Effects:
Aminoglycosides have little allergenic potential; both anaphylaxis and rash are unusual. Rare hypersensitivity reactions, - including skin rashes, eosinophilia, fever, blood dyscrasia, angioedema, exfoliative dermatitis, and anaphylactic shock - have been reported. Allergic reaction may appear independent to dosage.

Pregnancy and Breast-feeding
There are no existing data that illustrates the usage safety of the REMEDY® Acetabular Cup during pregnancy and breast-feeding. It is recommended that hip revision surgery be avoided during the first three months of pregnancy. The REMEDY® Acetabular Cup can be used in the remaining gestation time only when it is determined that it is impossible to save the joint or preserve the patient's life by other means of intervention.

Use in Children
No data or tests support that the REMEDY® Acetabular Cup is safe to use in children. The REMEDY® Acetabular Cup should only be used in mature adults.

Chemistry/Structure - Gentamicin Sulphate
Gentamicin is an aminoglycoside antibiotic derived from the actinomycetes *Micromonospora purpurea.* Gentamicin is a complex of the gentamicins C1, C1a, C2 and C2a as shown in Figure 2. The molecular weight is 449.55. The compound is supplied as sulphate.

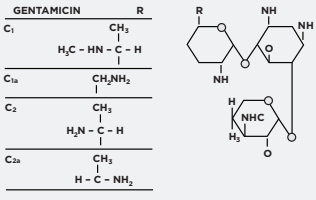

Figure 2: *Molecular formulae of gentamicin main components*

GENTAMICIN SULPHATE RELEASED FROM PMMA

Mechanism of Action
Bacteria tend to adhere to surfaces where they can multiply and create a defensive barrier called a biofilm (complex structure mainly made by extracellular polysaccharides and proteins). Bacteria embedded in a biofilm are more resistant to most antibiotic therapy because the glycoprotein structure is difficult for antimicrobial agents to penetrate. PMMA, due to its surface characteristics, is one of the materials with the highest risk of bacterial colonization. It has been demonstrated in vitro that the presence of antibiotics in PMMA reduces bacterial adhesion.

Gentamicin activity is primarily directed against aerobic, gram-negative bacilli. The action against most gram-positive bacteria is limited. Gentamicin is active against susceptible strains of enterococci and streptococci at concentrations which can be achieved clinically only when combined with a penicillin. Gentamicin is active *in-vitro* against more than 90% of strains of S. aureus and 75% of S. epidermidis. Gentamicin has been shown to be active against most strains of the following organisms both in vitro and in clinical infections.

Common Susceptible Pathogens
Gram positive bacteria
Staphylococcus aureus; Streptococcus pyogenes; Streptococcus pneumoniae; Streptococcus (Enterococcus) faecalis; Listeria monocytogenes

Gram Negative Bacteria
Citrobacter; Enterobacter; Escherichia coli Klebsiella spp.; Proteus mirabilis; Proteus vulgaris; Morganella morganii; Providencia spp.; Salmonella spp.; Serratia; Shigella spp.; Pseudomonas aeruginosa

Bibliography
Goodman & Gilman's *The Pharmacological Basis of Therapeutics* 2005, XI Ed., Chapter 45 (Henry F. Chambers) pp.1155-1170; McGraw Hill, New York.

Antibiotic Warnings
The release of gentamicin from in vitro studies has been shown to be below the recommended adult dose of 3-5 mg/kg/day (or 1.0 -1.7 mg/Kg/8 hours) according to the US Pharmacopoeia (gentamicin sulphate monograph). Toxic levels are not expected when gentamicin is released locally from the REMEDY® Acetabular Cup. However, trough concentrations exceeding 2 µg/ml for longer than 10 days have been associated with toxicity (systemic administration). Therefore, patients should be monitored closely during the first day of implantation of the REMEDY® Acetabular Cup when used in conjunction with other ototoxic or nephrotoxic drugs. The device should be used with caution in patients predisposed to or who have preexisting medical conditions that would put them at risk for gentamicin toxicity (dehydration, renal dysfunction, advanced age, etc.). All patients should be monitored for toxic blood levels of gentamicin, nephrotoxicity and ototoxicity while the device is in situ: this is especially critical for elderly patients and those receiving other ototoxic and/or nephrotoxic drugs.

Precautions
Review of the OsteoRemedies® LLC surgical technique for hip arthroplasty revision surgery and familiarity with the proper use of the REMEDY® Acetabular Cup is required for successful implantation of the device. Only surgeons who have studied the REMEDY® & REMEDY SPECTRUM® GV Hip Spacer surgical technique, including the additional steps for the use of the acetabular component, and are aware of the limitations of its application, should perform the procedure. The surgeon should not adjust or modify the device in any way (do not add antibiotics to the device as the structural and pharmacological effects cannot be known).

The user must protect the device from harm as any damage to the implant may reduce fatigue strength and may result in failure under load thus possibly affecting the patient. If particulate debris becomes detached (loose fragments of bone or bone cement) the wear rate of component contact surface is greatly accelerated as debris acts as an abrasive and damaging anomaly. The REMEDY® Acetabular Cup may be compromised in an overweight or obese patient and/or one who does not limit the amount of activity and weight placed on the hip. It is essential that the patient use mobility-assisted devices (e.g. crutches, walker, cane) during the implantation period.

Care should be taken in placing the spacer to preserve other remaining bony tissue during the implantation procedure. Implantation methods which are deemed aggressive are not needed for proper placement of the spacer. Any damage to the device may affect the fatigue strength and lead to failure under load, therefore do not subject the device to excessive forces (mallet strikes). Antibiotic susceptibility testing should be performed using a fine needle aspiration from the joint site prior to implantation of the REMEDY® Acetabular Cup. Patients should be informed of the limitations of the implant and the requirement for additional surgery to implant a permanent hip prosthesis. Patients should be instructed to adjust their activities and be informed that postoperative care is essential.

The REMEDY® Acetabular Cup is single-use, intended for an individual patient. Do not resterilize and/or reuse. Resterilization can cause a risk of infection to the patient and may change the morphology of the device, the effectiveness of the antibiotic component and mechanical properties of the implant, which could cause a malfunction with serious health risks for the patient. The implant must not be reused once removed, though it may appear undamaged, as this could cause contamination and aggravation of patient's infection. By not following these recommendations there will be an increased likelihood of wear, loosening, poor function, fracture or premature failure. The removed device is a surgical waste and must be discarded once explanted at the end of its lifetime.

The REMEDY® Acetabular Cup must not be implanted if the existing implant cannot be completely removed.

The REMEDY® Acetabular Cup must not be rinsed or cleaned with liquids prior to implanting.

The REMEDY® Acetabular Cup should not be used in areas that contain osteosynthesis implants that may interfere with the device and its mechanical function.

The REMEDY® Acetabular Cup must not remain implanted for more than 180 days. The operative area should be rigorously irrigated and rinsed after device extraction to remove all cement debris prior to implantation of the permanent prosthesis or other surgical procedures (resection arthroplasty, etc.). Survival of the revision implant may be jeopardized if cement and/or bone debris are not thoroughly removed. The device has specific indications for use. Thus its use under conditions other than the intended ones is unlikely to provide any benefit to the patient, and increases the risk of developing drug-resistant bacteria.

Implantation/Utilization
Aseptic surgical techniques are critically important based on clinical study data. The use of the REMEDY® Acetabular Cup is checked by the surgeon in relation to the patient's anatomy and need. In order for the surgeon to effectively implant the device, the surgeon shall: (A) study available literature, (B) properly and thoroughly train on the techniques required for the REMEDY® Acetabular Cup surgery, and (C) study and become informed regarding the use of instrumentation for sizing and implantation of the devices. REMEDY® Acetabular Cups must be used in combination with REMEDY® & REMEDY SPECTRUM® GV Modular Head sizes Small or Extra-Small.

NOTE: REMEDY® Acetabular Cup must be combined with a new implant only. REMEDY® Acetabular Cup Trial/Handle is also available to ensure that the implant is correctly sized for the patient's anatomy.

Warning: REMEDY® Acetabular Cup must be cemented with gentamicin loaded bone cement.

NOTE: It is recommended to use High Viscosity bone cement for implant fixation. This will facilitate explantation at the second stage surgery.

Application Instructions
All routes of access to the hip may be utilized for the insertion of the REMEDY® Acetabular Cup. The operative site must be irrigated with Ringer's or physiological solution. Also, thorough debridement must be executed after removal of the prosthesis and before inserting the REMEDY® Acetabular Cup. Excess cement or debris from the previous device must be removed to ensure a clear operative area.

REMEDY® Acetabular Cup Trial/Handle Use

Trialing
REMEDY® Acetabular Cup Trial/Handle is provided to check the dimensions of the native acetabulum using the TRIAL end (Figure 3 and 4), and to establish the level of reaming needed. Check the correct cup positioning. Note: that the thickness generated by the cement is not reflected in this trial.

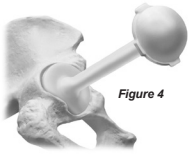

Figure 4

Implant Positioning
When the correct position has been determined, cement should be applied to the backside of the REMEDY® Acetabular Cup (Figure 5). The device should be implanted using hand pressure only with the IMPLANT end of the REMEDY® Acetabular Cup Trial/Handle as shown in Figure 3 and 6. Note: do not use excessive pressure for device positioning.

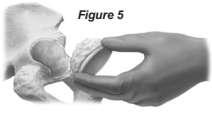

Figure 5

***Figure 3:** REMEDY® Acetabular Cup Trial/Handle*

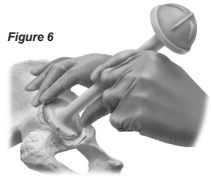

Figure 6

REMEDY® Acetabular Cup Use
Open the package of the REMEDY® Acetabular Cup. Using gentamicin loaded acrylic bone cement, apply the cement to native acetabulum and the backside of REMEDY® Acetabular Cup (Figure 5). Place the acetabular cup in the acetabulum by hand. Using the REMEDY® Acetabular Cup Trial/Handle, position the cup into the desired orientation within the native acetabulum (Figure 6). For the following three hours the patient must not move their leg to ensure correct fixation of the whole REMEDY® & REMEDY SPECTRUM® GV implant(s). To prevent dislocation, the same measures utilized for a permanent total hip replacement should be adopted, plus other specifics such as:

- Instructions, techniques or guides for the spacer device.
- Placement with appropriate joint tension of the soft tissues around the hip joint (offset adjustment.)
- Acquiring ideal cup support in the event of severe acetabular bone loss.
- In cases at risk consider the use of an abduction brace (possibly articulated) to assist flexion to avoid the risk of dislocation.

Postoperative Treatment
Postoperative treatment is comparable with a total hip implant; however, weight-bearing can be only partial (use of canes, crutches, etc.). It is recommended that partial weight-bearing be assessed on an individual basis in relation to the anatomic conditions of the femur and acetabulum, bone trophism and the clinical conditions of the patient during rehabilitation stages. Excessive weight bearing or forced mobilization which could cause the implant to damage the biological structure must be avoided. If needed, an abduction brace (possibly articulated) to assist flexion may be suggested in cases at risk of dislocation.

Explantation
The REMEDY® Acetabular Cup must be removed within 180 days of implantation and is not intended for use as a permanent prosthesis. Revision instruments (mallets, osteotomes, etc.) can be used in the surgical procedure. The wound site should be thoroughly cleaned of all bone cement debris prior to implantation of a definitive implant or performing an alternative surgical procedure (e.g. resection arthroplasty etc.). Cement or bone debris may shorten the survival of the revision implant if not removed.

Disposal
Disposal of the device should be in accordance with local waste regulations.

Patient Precautions (surgeon-to-patient instructions):
- Pain, discomfort or trauma with the affected limb must be communicated to the surgeon.
- Canes, crutches, walkers, etc., (protected weight-bearing mobility devices) must be used at all times while the device is implanted.
- The REMEDY® Acetabular Cup must be removed after temporary implantation (not to exceed 180 days).
- Excessive loading/weight on the REMEDY® Acetabular Cup must be avoided (sports activity, obesity, falling, unprotected weight bearing, etc.).

The patient's anatomic conditions of the hip district, bone trophism and other relevant clinical conditions during the rehabilitation phase should be periodically reviewed as the REMEDY® Acetabular Cup was designed for temporary implantation under protected load bearing conditions.

How Supplied
The REMEDY® Acetabular Cup implants are packaged and distributed sterile. Do not resterilize. All packages should be inspected for integrity prior to use. If a package is opened, contaminated or damaged it should not be used.

Caution
Store in a cool and dry environment.
Do not use if the inner container is damaged or opened.
Federal law restricts this device to sale by or on the order of a physician.

Information
For further product information, please contact Customer Service.

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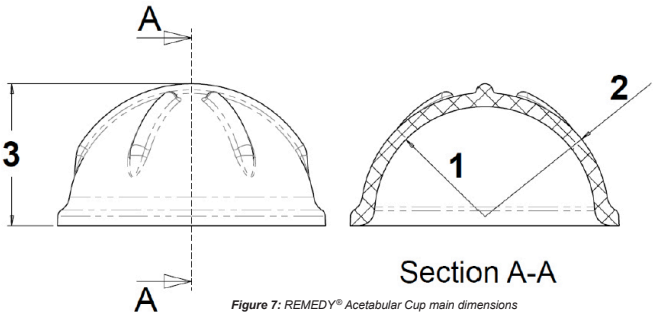

Figure 7: *REMEDY® Acetabular Cup main dimensions*

Component Description	Ref Code	1(mm)	2(mm)	3(mm)	Gentamicin Base (g)
REMEDY® Acetabular Cup 40mm ID/48mm OD	RHACXS	Ø41	Ø47	27.5	0.27
REMEDY® Acetabular Cup 46mm ID/54mm OD	RHACSM	Ø48	Ø54	31	0.3

Figure 8: *REMEDY® Acetabular Cup main dimensions and gentamicin base*

Symbols:

REF Catalog Number	LOT Batch Number	Consult Instruction For Use	Do Not Reuse	Do Not Use If Package Is Damaged	Use By Date	Caution	Do Not Resterilize	Sterilized Using Ethylene Oxide

OsteoRemedies®
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