OSTEOREMEDIES®
ADVANCED MEDICAL TECHNOLOGIES

SURGEON INFORMATION

REMEDY SPECTRUM® GV HIP SPACER

Temporary Hip Spacer with Gentamicin and Vancomycin

1

Overview

The REMEDY SPECTRUM® GV Hip Spacer is part of the treatment foreseen in a two-stage procedure performed in the event of periprosthetic joint infection (PJI). The REMEDY SPECTRUM® GV Hip Spacer implant is intended for temporary use only (180 days or less). It allows basic joint mobility and the PMMA component 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 the REMEDY SPECTRUM® GV Hip Spacer and replace it with a permanent hip joint implant. The REMEDY SPECTRUM® GV Hip Spacer consists of two individual implants (head and stem) which, when joined, allow to better fit the anatomy of the patient. Each REMEDY SPECTRUM® GV and REMEDY® CoCr Modular Femoral Head can be combined with each REMEDY SPECTRUM® GV Modular Femoral Stem. REMEDY SPECTRUM® GV Modular Femoral Stems are provided in short and long lengths. Modularity is offered by selecting optional neck lengths (offset) and using a threaded connection featured on both implants. REMEDY SPECTRUM® GV Modular Femoral Heads include a monomer (MMA) phial that serves as an adhesive (which binds the head and stem) and "cover cap". The liquid is sterilized by filtration. The REMEDY® CoCr Modular Femoral Heads are secured to the stem using off the shelf bone cement.

See ANTIBIOTIC RELEASE FROM PMMA section for Warnings and Precautions.

REMEDY SPECTRUM® GV PMMA Hip Spacers:

- single-use medical devices/gamma-ray sterile
- formed with bone cement (PMMA), gentamicin and vancomycin
- release gentamicin and vancomycin

REMEDY® CoCr Modular Heads:

- single-use medical device/gamma sterilized
- formed with CoCr Alloy

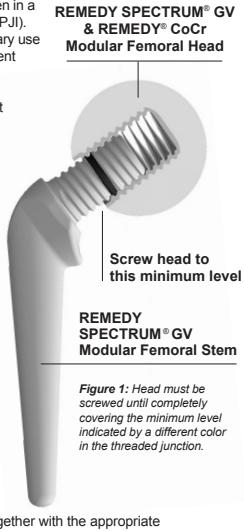


Figure 1: *Head must be screwed until completely covering the minimum level indicated by a different color in the threaded junction.*

REMEDY SPECTRUM® GV Modular Femoral Head

The REMEDY SPECTRUM® GV Modular Femoral Head must be used together with the appropriate REMEDY SPECTRUM® GV Modular Femoral Stem and may be used with the optional PMMA Acetabular Cups. Do **not** combine the REMEDY SPECTRUM® GV Modular Femoral Head with the REMEDY® POLY+PLUS™ Acetabular Cup or REMEDY® POLY+PLUS™ SNAP FIT Acetabular Cup (SNAP FIT Cup). When both head and stem are joined, the form emulates an anatomically correct hip prosthesis. The REMEDY SPECTRUM® GV Hip Spacer is temporary, implantable and composed of gentamicin and vancomycin bone cement.

REMEDY® CoCr Modular Femoral Head

The REMEDY® CoCr Modular Femoral Head must be used together with the appropriate REMEDY SPECTRUM® GV Modular Femoral Stem and may be used with the optional REMEDY® POLY+PLUS™ Acetabular Cups and Snap Fit Cups. Do **not** combine the REMEDY® CoCr Modular Femoral Head with the PMMA Acetabular Cup. The REMEDY® CoCr Modular Femoral Head is made of Cobalt Chrome. When both head and stem are joined, the form emulates an anatomically correct hip prosthesis. The resulting REMEDY SPECTRUM® GV Hip Spacer is temporary, implantable and the stem releases gentamicin and vancomycin antibiotics.

REMEDY SPECTRUM® GV Modular Femoral Stem
The REMEDY SPECTRUM® GV Modular Femoral Stem is made of formed bone cement (PMMA) with gentamicin and vancomycin applied to a stainless-steel reinforcing structure, with a straight profile and an oval cross-section. The combination of a stem with a head generates a device resembling a hip prosthesis. The REMEDY SPECTRUM® GV Hip Spacer is temporary, implantable and composed of gentamicin and vancomycin bone cement.

REMEDY® Hip Spacer Indications
The OsteoRemedies® Hip Spacer System consists of a modular head and stem, and optional acetabular cups. The REMEDY® PMMA 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 antibiotics based on the susceptibility pattern of the infecting micro-organism(s). 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 acetabular cavity 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, fusion etc.).

REMEDY® Hip Spacer Contraindications
- Patient exhibits hypersensitivity (allergy) to PMMA bone cement, CoCr, nickel, molybdenum, manganese, amino-glycosides, gentamicin, glycopeptides or vancomycin.
- Infecting bacteria/pathogens resistant to gentamicin and vancomycin.
- Infecting bacteria/pathogens are not susceptible to gentamicin and vancomycin.
- Patient's two-stage arthroplasty procedure is contraindicated based on decreased immune response or systemic clinical conditions.
- Infection of the THR cannot be confirmed.
- A remote infection (systemic/secondary) is suspected or verified.
- The infected THR devices cannot be removed.
- 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.
- Sufficient bone not available to allow insertion and fixation of the hip spacer.
- Lack of ideal bone disallows support of the prosthesis in the acetabular region or proximal femur.
- 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.
- The REMEDY® CoCr Modular Femoral Heads should not be used with the PMMA REMEDY® Acetabular Cups.
- The PMMA REMEDY® and REMEDY SPECTRUM® GV Modular Femoral Heads should not be used with the REMEDY® POLY+PLUS™ Acetabular Cups or SNAP FIT Cups.

Pregnancy and Breast-feeding
There are no existing data that illustrates the usage safety of the REMEDY SPECTRUM® GV Hip Spacer during pregnancy and breast-feeding. It is recommended that hip revision surgery be avoided during the first three months of pregnancy. The REMEDY SPECTRUM® GV Hip Spacer 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 SPECTRUM® GV Hip Spacer is safe to use in children. The REMEDY SPECTRUM® GV Hip Spacer should only be used in mature adults.

Clinical Study Overview

Prospective and retrospective data were collected outside of the United States on subjects with a diagnosis of periprosthetic joint infection (PJI) who were implanted with an antibiotic spacer during the first stage of a two-stage revision due to a PJI. One antibiotic spacer contained gentamicin and vancomycin ("GV Spacer") having data collected prospectively. The other one contained gentamicin only ("G Spacer") having the majority of its data collected retrospectively but some prospectively. The antibiotic formulation and PMMA in the GV Spacer are identical to the REMEDY SPECTRUM® GV Spacers. The antibiotic formulation and PMMA in the G Spacer are identical to the REMEDY® Spacers. The study included 49 subjects (26 hips and 23 knees) implanted with the GV Spacer, and 81 subjects (51 hips and 31 knees) implanted with the G Spacer which is 510(k)-cleared though has only one antibiotic. The GV and G spacer data were also compared to the predicate hip spacer and literature data.

Baseline Patient Demographics (Table1):

N=130		GV Spacer			G Spacer		
		N	Mean	SD	N	Mean	SD
Age		49	69.86	9.18	81	71.09	10.18
		N	n	%	N	n	%
Sex	Female	49	30	61.2%	81	40	49.4%
	Male	49	19	38.8%	81	41	50.6%
Cardiopathy	Yes	49	1	2.0%	81	13	16.0%
Hypertension	Yes	49	30	61.2%	81	46	56.8%
Diabetes	Yes	49	8	16.3%	81	19	23.5%
COPD	Yes	49	9	18.4%	81	10	12.3%
Corticoids	Yes	49	0	0.0%	81	3	3.7%
Renal failure	Yes	49	3	6.1%	81	9	11.1%
Rheumatoid arthritis	Yes	49	0	0.0%	81	3	3.7%
Liver Cirrhosis	Yes	49	2	4.1%	81	4	4.9%
Obesity	Yes	48	20	41.7%	71	38	53.5%
Comorbidities	Yes	49	39	79.6%	81	64	79.0%
Joint Treated	Hip	49	26	53.1%	81	51	63.0%
	Knee	49	23	46.9%	81	30	37.0%

Safety – Stage 1 Outcomes

In a clinical study, the following outcomes were identified for subjects implanted with a gentamicin/vancomycin- containing antibiotic spacer ("GV Spacer") during the first stage of a two-stage revision. The Stage 1 outcomes for a gentamicin-containing spacer ("G Spacer") also are reported. Success at Stage 1 is defined as the absence of Girdlestone (hip fusion), arthrodesis (knee fusion), amputation, or spacer-related death.

Table 2: Stage 1 Outcomes

All Subjects	GV Spacer			G Spacer			Diff.	Exact
	N[a]	N[b]	%	N	n	%	%	p-value*
Total Enrolled	**49**			**81**				
Unrelated deaths	**1**			**0**				
Stage 1 Successes	**48**	**44**	**91.7%**	**81**	**69**	**85.2%**	**6.5%**	**0.213**
THA	25	22	88%	51	43	84.3%		
TKA	23	22	95.7%	30	26	86.7%		
Stage 1 Failures	**48**	**4**	**8.3%**	**81**	**12**	**14.8%**	**-6.5%**	
Girdlestone	48	2	4.2%	81	8	9.9%		
Arthrodesis	48	0	0%	81	3	3.7%		
Amputation	48	1	2.1%	81	1	1.2%		
Death	48	1	2.1%	81	0	0%		
Hip Subjects	**GV Spacer**			**G Spacer**			**Diff.**	
	N	**n**	**%**	**N**	**n**	**%**	**%**	
Total Enrolled	**26**			**51**				
Unrelated deaths	**1**			**0**				
Stage 1 THA Successes	**25**	**22**	**88%**	**51**	**43**	**84.3%**	**3.7%**	
Stage 1 Failures	**25**	**3**	**12%**	**51**	**8**	**15.7%**	**-3.7%**	
Girdlestone	25	2	8%	51	8	15.7%		
Death	25	1	4%	51	0	0%		

*Two-sided Fisher's Exact p-value.

[a]N = All subjects implanted with each type of spacer. Definition applies to all tables.

[b]n = All subjects meeting the specified endpoint. Definition applies to all tables.

For the “All Subjects” cohort, the rate of Stage 1 success for the GV Spacer cohort is 91.7% which is higher than the Stage 1 success rate of 85.2% for the G Spacer cohort, though this difference is not statistically significant (two-sided Fisher’s Exact p=0.213). For the “Hip Subjects” cohort, the Stage 1 success rate for the GV Spacer is 3.7% higher than the Stage 1 success rate for the G Spacer.

The outcomes for the GV Spacer were also compared to: (1) a retrospective study of 135 patients implanted with the 2-antibiotic predicate, and (2) literature.

At Stage 1, 6 (4.4%) of the 135 2-antibiotic predicate subjects had a Girdlestone procedure, 12 (8.9%) had persistent/recurrent deep infections, 8 (5.9%) had an intra-operative bone fracture, and 5 (3.7%) had a post-operative bone fracture. Seventeen (17) of the 135 subjects (12.6%) did not have a reimplantation with a definitive implant. These 17 subjects had a retained predicate, received a second spacer device, or died.

A publication from the Rothman Institute reports on 504 hip and knee PJI subjects. When the lost-to-follow-up subjects (n=19) are excluded, the Stage 1 success rate was 89.5% which is comparable to the Stage 1 success rate for the GV Spacer. The 10.5% failure rate included 6 amputations, 5 Girdlestones, 4 arthrodeses, and 36 deaths *(Gomez, et al., 2015).*

Safety – Inter-Stage Reoperations
Inter-stage reoperations included spacer exchanges and debridements.

Table 3: Inter-stage Reoperations

All Subjects	**GV Spacer**			**G Spacer**		
	N	**n**	**%**	**N**	**n**	**%**
Spacer exchange	48	5	10.4%	81	8	9.9%
Spacer debridement	48	3	6.25%	81	0	0%
Hip Subjects	**GV Spacer**			**G Spacer**		
	N	**n**	**%**	**N**	**n**	**%**
Spacer exchange	25	3	12%	51	6	11.8%
Spacer debridement	25	2	8%	51	0	0%

For both the “All Subjects” and “Hip Subjects” cohorts, the GV and G cohorts exhibit similar rates of spacer exchange. The rate of spacer debridement for the GV Spacer is higher than what is reported for the G spacer.

The inter-stage reoperation rates were also compared to the 2-antibiotic predicate study and literature.

Inter-stage Reoperations

Inter-stage Reoperations	**2-Antibiotic Predicate**			**Gomez (2015)**			**Cancienne (2017)****		
	N	**n**	**%**	**N**	**n**	**%**	**N**	**n**	**%**
Spacer exchange	118	8	6.8%	504	60	11.9%	-	-	-
Spacer debridement	135	*	*	-	-	-	7146	775	10.8%

*Although the number of debridement procedures was not identified for the retrospective study of the predicate, a publication *(Wentworth, et al., 2002)* reports that 12 subjects (8.9%) had persistent/recurrent deep infections at Stage 1.

** Cancienne, J. M. et al. Removal of an Infected Total Hip Arthroplasty: Risk Factors for Repeat Debridement, Long-term Spacer Retention, and Mortality. *Journal of Arthroplasty,* Volume 32, Issue 8, 2017, 2519 - 2522.

The inter-stage reoperation rates for the GV Spacer, including spacer exchanges and debridements, are similar to those reported for the predicate and/or literature.

Safety – Acute Kidney Injury (AKI)
In the "All Subjects" cohort, acute kidney injury (AKI) was reported in 5 of the 49 subjects (10.2%) implanted with the GV Spacer, and 3 of the 81 subjects (3.7%) implanted with the G Spacer. These rates are within the range of what is reported in the literature for patients being treated for PJI with antibiotic-loaded spacers (i.e., 8.5%[1] to 20%[2]) *(Reed et al., 2014; Aeng et al., 2015)*. Published literature indicates that high-dose antibiotic spacers made in the operating room, such as the predicate, may be associated with a higher risk of nephrotoxicity when compared to preformed, low-dose antibiotic spacers such as the GV Spacer *(Luu et al., 2013; Edelstein et al., 2018)*. In the "Hip Subjects" cohort, AKI was reported in 4 of 25 subjects (16%) implanted with a GV Hip Spacer, and 3 of the 51 subjects (5.9%) of the subjects implanted with the G Spacer. Again, these are within the range of AKI rates reported in the literature for patients undergoing treatment for PJI. One patient with chronic kidney disease, hypertension, and cardiopathy experienced an AKI-related death.

Patients should be monitored for AKI while undergoing treatment for PJI, as the combination of systemic antibiotics, drugs prescribed to treat any comorbidities, and the antibiotics present in the spacer can all contribute to the risk of AKI. Please refer to the precautions for additional information.

Effectiveness – Stage 2 Outcomes
Success at the second stage of a two-stage revision is defined as the absence of two or more positive cultures of microorganisms at the time of reimplantation.

Safety – Acute Kidney Injury (AKI)

Table 4: Stage 2 Outcomes

All Subjects	**GV Spacer**			**G Spacer**			**Diff.**	**Exact**
	N	**n**	**%**	**N**	**n**	**%**	**%**	**p-value***
Success at Stage 2	43	42	97.7%	69	58	84.1%	13.6%	0.0198
Hip Subjects	**GV Spacer**			**G Spacer**			**Diff.**	
	N	**n**	**%**	**N**	**n**	**%**	**%**	
Success at Stage 2	22	21	95.5%	43	34	79.1%	16.4%	

* One-sided Fisher's Exact Test.

For the "All Subjects" cohort, the Stage 2 success rate for the GV Spacer of 97.7% is statistically superior to the success rate for the G Spacer of 84.1% (one-sided Fisher's Exact p = 0.0198). For the "Hip Subjects" cohort, the Stage 2 success rate for the GV Spacer was 95.5%, which is 16.4% higher than the Stage 2 success rate for the G Spacer subjects of 79.1%.

In the retrospective study of the 2-antibiotic predicate, a successful *treatment outcome* was defined as no growth of a microorganism on any culture obtained from the operative site during the second stage surgery. A successful *clinical outcome* was defined as implantation of a total hip prosthesis at the second stage surgery with no growth of a microorganism on any culture obtained from the operative site and no reoperations resulting from a recurrent or persistent infection of the affected hip at a minimum of one month postoperatively. Of the 135 subjects enrolled in the retrospective study, 116 were included in the evaluation of Stage 2 success. Of these, 96 (83%) were considered a treatment success. Note: Seventeen (17) of the 135 subjects (12.6%) did not have a reimplantation with a definitive implant. These 17 subjects had a retained spacer device, received a second spacer device, or died. Two additional subjects were excluded from the evaluation of Stage 2 outcomes because their intraoperative cultures could not be confirmed. Successful clinical outcomes were reported for 91.7 percent (89/97) of the cases with the minimum required one-month follow-up.

In the Rothman Institute publication (Gomez, et al., 2015), the Stage 2 success rate was calculated to be 80.7% (268/332). The Stage 2 success rate for the GV Spacer compares favorably to the rate reported by Gomez.

Composite Endpoint (Stage 1/Stage 2 Success)
Success for the composite endpoint required both Stage 1 and Stage 2 success.

Table 5: Composite Success (Stage1 / Stage 2 Success)

All Subjects	GV Spacer			G Spacer			Dif.	
	N	n	%	N	n	%	%	p-value
Composite – All Evaluable (N=129)[1]	48	43	89.6%	81	58	71.6%	18%	0.0126[2]
Composite – MI (N=130)[3]	49	---	89.2%	81	58	71.6%	17.6%	0.0105[4]
Hip Subjects	GV Spacer			G Spacer			Dif.	
	N	n	%	N	n	%	%	p-value
Composite (N=76)	25	21	84%	51	34	66.7%	17.3%	

[1] For this comparison, one patient with good clinical status but with no reimplantation with a definitive implant was defined as a composite success and one patient with unrelated death prior to reimplantation with a definitive implant were censored.

[2] One-sided Fisher's Exact Test.

[3] The number of successes is not reported for GV Spacer under MI (multiple imputation). 89.2% is the average across 20 MIs. For this comparison, the outcome for one GV patient with unrelated death prior to reimplantation with a definitive implant was imputed.

[4] One-sided T-test from MI taking into account between and within imputation variance.

For the "All Subjects" cohort, the composite success rate for the GV Spacer is significantly higher than the composite success rate for the G Spacer for both the "all evaluable" and "multiple imputation" analyses. For the "Hip Subjects" cohort, the composite success rate for the GV Spacer is 17.3% higher than the composite success rate for the G Spacer.

A composite endpoint based on Stage 1 and Stage 2 outcomes was not defined for the retrospective study of the 2-antibiotic predicate. Nonetheless, it is reasonable to consider the absence of persistent/recurrent infection at both Stage 1 and Stage 2 as a composite endpoint. At Stage 1, the absence of infection rate is 91.1% (123/135); at Stage 2, the rate is 89.3% (100/112). Combined, the predicate success rate is 82.2% for Stage 1 and Stage 2 which is comparable to the composite success rate for the GV Spacer.

In the Rothman Institute publication *(Gomez, et al., 2015)*, "Retrospective multi-center study on outcomes of PJI patients treated with various antibiotic cement spacers", outcomes were captured for 504 hip and knee PJI subjects. A Stage 1 success rate was calculated using the same definition used in the GV vs. G study (i.e., absence of Girdlestone, arthrodesis, amputation, or death). When the lost-to-follow-up subjects (n=19) are excluded, the Stage 1 success rate was calculated to be 89.5% (434/485) which includes 417 subjects who were reimplanted and 17 patients with retained spacers who were considered to be treatment successes. When the lost-to-follow-up subjects (n=85) are excluded, the Stage 2 success rate was calculated to be 80.7% (268/332). Overall composite success requires success at both stages. When the lost-to-follow-up subjects are excluded at both stages, the overall composite success rate for Stage 1 and Stage 2 was calculated to be 71.3% (285/400) which is lower than the composite success rate for the GV Spacer.

Secondary Outcome – Antibiotic Usage
Success at Stage 2 was associated with a shorter mean total duration of systemic antibiotic usage after the second stage surgery.

Table 6: Duration of Antibiotic Usage after Stage 2 (Days)

% (n)	0 - <7	7 - <14	14 - <30	30 - <90	>365	Total
GV Spacer	**93%** (39)	**0%** (0)	**2%** (1)	**2%** (1)	**2%** (1)	42
G Spacer	**25%** (17)	**54%** (37)	**3%** (2)	**16%** (11)	**1%** (1)	68
Total	56	37	3	12	2	110

As shown, 93% of the GV subjects were finished with their antibiotic course within a week. In contrast, only 25% of the G subjects were completed with antibiotics within the first post-operative week after the second stage surgery. A Mann-Whitney U test indicates that overall antibiotic use in the GV group is lower than in the G group with p= <0.001.

NOTES
The surgeon should be aware of the possible negative effects of bone cement, as the device must be affixed with it. Infections that recur, though rare, have been known to reappear even with I.V. antibiotic use. Gentamicin and vancomycin application may trigger negative reactions of this antibiotic following systemic use, as shown in the next paragraphs.

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

REMEDY SPECTRUM® GV Hip Spacer Risks
- recurring infection which can lead to joint fusion, amputation, or death
- gentamicin and/or vancomycin toxicity (ototoxicity/nephrotoxicity)
  - ***Patients should be monitored for ototoxicity and nephrotoxicity while undergoing treatment for PJI, as the combination of systemic antibiotics, drugs prescribed to treat any comorbidities, and the antibiotics present in the spacer can all contribute to the risk of these adverse events.***
- implant breakage
- head disassembling
- implant loosening
- PMMA sensitivity
- debris release
- difficult device removal
- implant dislocation
- foreign body reaction

Surgical Risks (General)
- pulmonary embolism
- myocardial infarction
- arrhythmias
- venous thrombosis
- 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
- hematoma

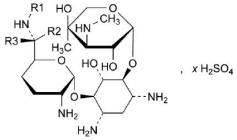
ANTIBIOTIC AND PMMA

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 SULPHATE

Chemistry/Structure

Gentamicin is an aminoglycoside antibiotic derived by the growth of an actinomycete, Micromonospora purpurea. Gentamicin is a complex of the gentamicins C1, C1a, C2 C2a and C2b as shown. The molecular weight is 449.55. The compound is supplied as sulphate.



Gentamicin	Mol. Formula	R1	R2	R3
C1	$C_{21}H_{43}N_5O_7$	CH_3	CH_3	H
C1a	$C_{19}H_{39}N_5O_7$	H	H	H
C2	$C_{20}H_{41}N_5O_7$	H	CH_3	H
C2a	$C_{20}H_{41}N_5O_7$	H	H	CH_3
C2b	$C_{20}H_{41}N_5O_7$	CH_3	H	H

Mechanism of action

Gentamicin is rapidly bactericidal. It binds to the prokaryotic ribosome and interferes with protein synthesis by causing misreading and premature termination of mRNA translation leading to altered cell membrane permeability, progressive disruption of the cell envelope as well as other vital processes and cell death.

Antibacterial activity
Gentamicin activity is primarily directed against aerobic, gram negative bacilli. The action against most gram positive bacteria is limited. In vitro it is bactericidal against Gram-positive and Gram-negative bacteria.

Gentamicin is active against susceptible strains of enterococci and streptococci at concentrations that can be achieved clinically only when combined with a penicillin or vancomycin. Gentamicin has been shown to be active against most strains of the following organisms both in vitro and in clinical infections.

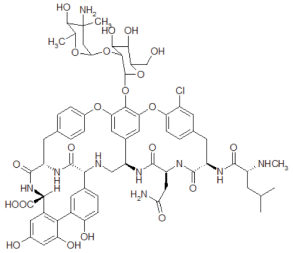
Table 7: Common susceptible pathogens (*)

Gram positive bacteria	Gram negative bacteria
Staphylococcus aureus	Citrobacter
Streptococcus pyogenes	Enterobacter
Streptococcus pneumoniae	Escherichia coli
Streptococcus faecalis	Klebsiella spp.
Listeria monocytogenes	Proteus mirabilis
	Proteus vulgaris
	Morganella morganii
	Providencia spp.
	Salmonella spp.
	Serratia Shigella spp.
	Pseudomonas aeruginosa
*Kucers A, Bennett N. The use of antibiotics 4th Ed. 1987, Butterworth-Heinemann Ltd	

Bibliography

- Goodman & Gilman's. The Pharmacological Basis of Therapeutics - 2011, XII Ed., Chapter 54 (Henry F. Chambers); McGraw Hill, New York.
- Kucers A, Bennett N. The use of antibiotics - 4th Ed. 1987, Butterworth-Heinemann Ltd (*)

VANCOMYCIN HYDROCHLORIDE
Chemistry/Structure
Vancomycin hydrochloride is a tricyclic glycopeptide antibiotic derived from Streptococcus orientalis. The molecular weight is 1449.22. The compound is supplied as hydrochloride.



Mechanism of action
Vancomycin is bactericidal. It inhibits the synthesis of the cell wall in sensitive bacteria by binding with high affinity to the cell wall precursor units. This binding occurs at a different site of action from that of penicillin. The result is an alteration of bacterial cell wall permeability. In addition, RNA synthesis is inhibited.

Antibacterial activity
Vancomycin is primarily active against gram-positive bacteria. Strains are considered susceptible at MICs of 2 µg/ml for Staphylococcus aureus, 4 µg/ml for S. epidermidis and 1 µg/ml for streptococci. Vancomycin is particularly useful against penicillin- and methicillin-resistant staphylococcal infections and for treating gram- positive infections in penicillin-allergic patients. All species of gram-negative bacilli and mycobacteria are resistant to vancomycin. The combination of an aminoglycoside with a cell-wall synthesis inhibitor is the only reliably bactericidal regimen for treatment of enterococcal infections.

Table 8: Most common susceptible pathogens (*)

Gram positive bacteria	Gram negative bacteria
Actinomyces sp.	Not effective
Bacillus cereus	
Bacillus sp.	
Bacillus subtilis	
Clostridium difficile	
Clostridium sp.	
Corynebacterium jeikeium	
Corynebacterium sp.	
Enterococcus faecalis	
Enterococcus faecium	
Enterococcus sp.	
Lactobacillus sp.	
Listeria monocytogenes	
Staphylococcus aureus	
Staphylococcus epidermidis	
Streptococcus agalactiae	
Streptococcus bovis	
Streptococcus pneumoniae	
Streptococcus pyogenes	
Viridans streptococci	
*Kucers A, Bennett N. The use of antibiotics 4th Ed. 1987, Butterworth-Heinemann Ltd	

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- Kucers A, Bennett N. The use of antibiotics - 4th Ed. 1987, Butterworth-Heinemann Ltd (*)

ANTIBIOTIC RELEASE FROM PMMA
Patients should be monitored for ototoxicity and nephrotoxicity while undergoing treatment for PJI, as the combination of systemic antibiotics, drugs prescribed to treat any comorbidities, and the antibiotics present in the spacer can all contribute to the risk of these adverse events.

Antibiotic warnings
Although in vitro elution studies (microbiological method) have shown that the daily combined release of gentamicin and vancomycin never exceeds the recommended systemic adult dose for gentamicin (5-7 mg/kg/day) – and vancomycin (30 - 45 mg/Kg/day) according to Goodman and Gilman's recommendations (adults with normal renal function), the presence of these two antibiotics will increase systemic exposure levels. The amount of gentamicin and vancomycin released from the REMEDY SPECTRUM® GV Hip Spacer and absorbed locally will result in serum levels some in the range associated with Acute Kidney Injury (AKI). The GV and G spacer clinical data found 5 of 49 (10.2%) of the GV subjects and 3 of 81 (3.7%) of the G spacer subjects had an acute kidney injury (AKI) based on serum creatinine levels.

Systemic administration of gentamicin and vancomycin
When administered systemically, plasma trough concentrations of gentamicin which exceed 2mg/ml for longer than 10 days have been associated with toxicity. Due to the presence of two antibiotics in the REMEDY SPECTRUM® GV Hip Spacers, which may impact systemic levels, patients should be closely monitored while the hip spacer is implanted.

Auditory impairment, which is frequent, although not permanent, may follow the use of vancomycin. Ototoxicity is associated with excessively high concentration of the drug in plasma (60 to 100 mg/ml). Nephrotoxicity due to vancomycin is unusual when appropriate doses are used, as judged by renal function and determinations of the antibiotic concentration in blood. Due to the presence of two antibiotics in the REMEDY SPECTRUM® GV Hip Spacer, which may impact systemic levels, patients should be closely monitored while the hip spacer is implanted.

Special caution must be exercised if the patient
Has kidney problems, is elderly, has hearing difficulties, will have a general anesthetic, is taking medicines such as other antibiotics that can affect the kidneys (streptomycin, neomycin, gentamicin, kanamycin, amikacin, tobramycin, polymyxin B and colistin; water tablets, e.g. ethacrynic acid and furosemide; cholestyramine).

Monitoring
Patients receiving REMEDY SPECTRUM® GV Hip Spacer should be periodically monitored while the two-antibiotic spacer is implanted with peak and trough levels of the antibiotics, 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, Aminoglycosides, Vancomycin, Glycopeptides use). Elderly patients may have reduced renal function that may not be evident in the results of routine screening tests, such as BUN or serum creatinine. A creatinine clearance determination may be more useful. Monitoring of renal function during treatment with aminoglycosides and glycopeptides is particularly important in such patients.The inactivation of gentamicin and other aminoglycosides by ß-lactam type antibiotics (penicillins, cephalosporins) has been demonstrated in vitro and in patients with severe renal impairment. Such inactivation has not been found in patients with normal renal function who have been given the drugs by separate routes of administration.

The use of REMEDY SPECTRUM® GV Hip Spacer may result in overgrowth of non-susceptible organisms. If overgrowth of non-susceptible organism occurs, appropriate therapy should be initiated.

There may be increased risk of ototoxicity from gentamicin, if other ototoxic drugs such as cisplatin (an antineoplastic agent) and vancomycin (another antibiotic) are given at the same time. There also appears to be a synergistic effect of loop diuretics, such as furosemide or ethacrynic acid, and also loud noise, when combined with gentamicin.

Local administration of gentamicin and vancomycin
The local release of both antibiotics produces increased serum concentrations. Therefore, the REMEDY SPECTRUM® GV Hip Spacer should be used with caution (mainly in the first days of implantation of the spacer) when used in conjunction with other nephrotoxic or ototoxic drugs administered systemically. The device should be used with caution in patients who are predisposed to or who have preexisting clinical conditions that would put them at risk for gentamicin and vancomycin toxicity (e.g. renal dysfunction, dehydration, advanced age etc.).

All patients at risk (renal insufficiency) should be monitored for blood levels of gentamicin, vancomycin nephrotoxicity and ototoxicity during implantation of the device. This is especially important in elderly subjects and in those receiving other systemic nephrotoxic and/or ototoxic drugs.

GENTAMICIN (and Aminoglycosides) Risks
All aminoglycosides have the potential to produce reversible and irreversible vestibular, cochlear and renal toxicity.

Ototoxicity: Vestibular and auditory dysfunction can follow the 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 and results from progressive destruction of vestibular or cochlear sensory cells, which are highly sensitive to damage by aminoglycosides. Repeated courses of aminoglycosides can lead to deafness. Older patients may be more susceptible to ototoxicity. Drugs such as ethacrynic acid and furosemide potentiate the ototoxic effects of the aminoglycosides in animals, but data from humans implicating furosemide are less convincing. 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 8-26% of patient receiving an aminoglycoside for several days will develop mild renal impairment that is almost always reversible. Toxicity is correlated with the total amount of drug administered. Other drugs, such as amphotericin B, vancomycin, angiotensin-converting enzyme inhibitors, cisplatin and cyclosporine may potentiate aminoglycoside-induced nephrotoxicity. Monitoring drug concentrations in plasma is useful, particularly during prolonged and/or high dose therapy.

Neuromuscular blockade: Neuromuscular blockade generally has occurred after intrapleural or intraperitoneal instillation of large doses of an aminoglycoside; however, the reaction can follow intravenous, intramuscular and even oral administration of these agents. Most episodes have occurred in association with anesthesia or administration of other neuromuscular blocking agents. Patients with myasthenia gravis are particularly susceptible to neuromuscular blockade by aminoglycoside.

Other untoward effects: Aminoglycosides have little allergenic potential; anaphylaxis and rash are unusual. Rare hypersensitivity reactions, - including skin rashes, eosinophilia, fever, blood dyscrasia, angioedema, exfoliative dermatitis and anaphylactic shock - have been reported as cross-hypersensitivity among drugs in this class.

Note: Allergic reaction may appear independent to dosage.

VANCOMYCIN Risks
Nephrotoxicity: Nephrotoxicity, formerly very problematic due to the impurities in earlier formulations of vancomycin, has become less common with modern formulations at standard dosages. However, the more aggressive dosing regimens recently advocated have been demonstrated to increase nephrotoxicity risk.

In a recent observational study, nephrotoxicity occurred in 33% of patients with initial vancomycin trough concentrations of >20 µg/mL, compared to 5% among patients with trough concentrations of <10 µg/mL.

Ototoxicity: Auditory impairment, sometimes permanent, may follow the use of vancomycin. Ototoxicity is associated with excessive high concentrations of the drug in plasma (60 – 100 µg/mL of vancomycin).

Hematologic: Anemia, reversible neutropenia, thrombocytopenia, reversible agranulocytosis, leukopenia are frequency not reported.

Miscellaneous: Among the hypersensitivity reactions produced by vancomycin and teicoplanin are macular skin rashes and anaphylaxis. Phlebitis and pain at the site of intravenous injection are relatively uncommon. Chills, rash, and fever may occur. Rapid intravenous infusion of vancomycin may cause erythematous or urticarial reactions, flushing, tachycardia, and hypotension. The extreme flushing that can occur called "red- neck" or red-man syndrome. This is not an allergic reaction but a direct toxic effect of vancomycin on mast cells, causing them to release histamine.

Note: Allergic reaction may appear independent to dosage.

Precautions
Review of the OsteoRemedies LLC surgical technique for hip arthroplasty revision surgery and familiarity with the proper use of the REMEDY SPECTRUM® GV Hip Spacer is required for successful implantation of the device. Only surgeons who have studied the REMEDY SPECTRUM® GV Hip Spacer surgical technique and are aware of the limitations of its application are allowed to perform the procedure. The surgeon is not allowed to adjust or modify the device in any way (do not add additional antibiotics as the effects structurally and pharmacologically 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 SPECTRUM® GV Hip Spacer 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. Always use the largest component size possible to ensure ideal performance. 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 the greater trochanter and 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 prior to implantation of the REMEDY SPECTRUM® GV Hip Spacer following a fine needle aspiration from the joint site. 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 SPECTRUM® GV Hip Spacer is single-use intended for an individual patient. Do not resterilize and/or reuse. Resterilization of the components can cause 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 that could cause a malfunction with serious health risks for the patient.

Implants should not be reused once removed, though they may appear not damaged as this could cause contamination and aggravation of patient infection. The removal of the device may damage the implant itself, and cement residues may remain adhered as well to the device. By not following these recommendations

there will be an increased likelihood of wear, loosening, poor function, fracture or premature failure. Excess material is deemed as surgical waste and must be removed/destroyed at the conclusion of the surgical procedure.

The REMEDY SPECTRUM® GV Hip Spacer should not be implanted if the existing implant cannot be completely removed.

The REMEDY SPECTRUM® GV Hip Spacer is comprised of two components (head and stem). It is important not to use the individual components alone within the anatomy.

The REMEDY SPECTRUM® GV Hip Spacer must not be rinsed or cleaned with liquids prior to implanting.

The REMEDY SPECTRUM® GV Hip Spacer should not be used in areas that contain osteosynthesis implants that may interfere with the device and its mechanical function.

The REMEDY SPECTRUM® GV and REMEDY® CoCr Modular Femoral Head must be torqued/screwed at least to the blue colored line indicated on the stem neck (see Figure 1).

The REMEDY SPECTRUM® GV Modular Femoral Head is intended for use with the optional REMEDY® Acetabular Cup (PMMA) and the REMEDY® CoCr Modular Femoral Head is intended for use with the optional REMEDY® POLY+PLUS™ Acetabular Cup or SNAP FIT Cup (UHMWPE XL with Vitamin E).

Do **not** combine the REMEDY SPECTRUM® GV Modular Femoral Head with the REMEDY® Poly+Plus Cup or SNAP FIT Cup. Do **not** combine the REMEDY® CoCr Modular Femoral Head with the REMEDY® Acetabular Cup (PMMA).

MMA liquid is provided within packaging to affix the PMMA head to the PMMA stem. Excessive vapor inhalation of the liquid component may cause drowsiness: prolonged exposure to vapors may irritate the respiratory system and eyes. Avoid monomer contact with the mucous membranes and skin (wear a second pair of surgical gloves to reduce reactions created by hypersensitivity). Susceptible patients have been observed to experience contact dermatitis. The liquid component should not come into contact with accessories made of rubber or elastomers. The liquid component is flammable and volatile and for this reason, the operating theatre must be correctly ventilated. The liquid component and/or its vapors must never be directly exposed to naked flames or heated materials.

The REMEDY SPECTRUM® GV Hip Spacer 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 (fusion, 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. Correct sizing of the REMEDY SPECTRUM® GV Hip Spacer depends on the selection and judgment of 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 SPECTRUM® GV Hip Spacer surgery, and (C) study and become informed regarding the use of instrumentation for sizing and implantation of the devices. Proper sizing and selection of components can be determined by use of REMEDY® Hip Trial devices available to ensure the implant has been correctly sized for the patient's anatomy.

Warning: The REMEDY SPECTRUM® GV Hip Spacer must be proximally cemented with gentamicin and vancomycin loaded cement. The use of bone cement is compulsory to avoid rotation and to limit the risk of dislocation or spacer loosening.

Head Size Selection
To avoid possible dislocation, the largest head size should be chosen. Choose the REMEDY® Head Trial size based on the dimension of the removed prosthesis.

Note: When utilizing an optional acetabular cup, the head size will be dictated by the cup size selected to fit the acetabulum. The cup may be implanted so that proper trialing for the head offset can occur.

The acetabular dome may be reamed in relation to the quality of the residual bone thus allowing the use of a larger diameter head. This is ideal as it aids in the removal of any existing infected tissue while deepening the spacer head which may prevent possible painful dislocation in the future. Choose the REMEDY® POLY+PLUS™ Head Trials for use with REMEDY® POLY+PLUS™ Acetabular Cup and REMEDY® POLY+PLUS™ Snap Fit Cup or use the REMEDY® Radel Head Trials for use with the REMEDY Acetabular Cups (PMMA), see Trial Compatibility Table below (Table 1).

Stem Selection
The choice of the stem size depends on the dimensions of the femoral canal and on the stability achieved. Choose the REMEDY® Radel® Stem Trial based on the dimension of the removed prosthesis. The size measurement can be determined with the use of REMEDY® Hip Trials provided. When a distal anchorage is needed, a long stem is recommended: this occurs in case of absence of proximal support, in presence of a vast metaphyseal damage, or after a transfemoral approach for device removal. The lower protrusion of the stem collar shall rest on the proximal diaphysis cortex.

Offset Selection
Connect the selected REMEDY® Head Trial and REMEDY® Radel® Stem Trial by screwing the head onto the threaded end of the REMEDY® Radel® Stem Trial completely (reaching the end of the thread).

Note: When trialing for the REMEDY® POLY+PLUS™ Acetabular Cup System the RRTHDXS is oversized and will not mate with the REMEDY® POLY+PLUS™ Acetabular Cup. The REMEDY® POLY+PLUS™ Head Trials can be used with the REMEDY® POLY+PLUS™ Acetabular Cup and REMEDY® POLY+PLUS™ Snap Fit Cup. REMEDY® POLY+PLUS™ Head Trials will be slightly undersized when used with the REMEDY® POLY+PLUS™ Acetabular Cup. See Trial Compatibility Table below (Table 1).

Test the device in the patient to determine if the prosthesis is anatomically correct and stable. By unscrewing the REMEDY® Head Trial the required offset may be obtained. The goal is to achieve ideal soft tissue tensioning by following the patient's anatomy to reduce the risk of painful dislocation.

Note: the maximum offset possible is the one achieved once the colored thread is completely covered by the head. This same minimum level is indicated also in the corresponding implantable device. The stem shall not be obstructed by additional devices within the diaphysis canal. Check the correct offset by screwing in or out the head to discover the best fit. When the correct offset has been selected remove the trial, and use it as a reference to prepare the REMEDY® Hip Spacer or the REMEDY SPECTRUM® GV Hip Spacer device which will be implanted. Count the number of threads not included in the head. Note: The thickness generated by the implantation cement is not reflected in the stem trials.

After use, the trial devices must be cleaned and reprocessed per OST002.

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

Trial Compatibility Chart

Implant Heads	Implant Cups						Trial Heads
	REMEDY® POLY+PLUS™ Acetabular Cup 40mm ID/48mm OD RHPAC40	REMEDY® POLY+PLUS™ Acetabular Cup 44mm ID/54mm OD RHPAC44	REMEDY® POLY+PLUS™ SNAP FIT Cup 40mm ID/48mm OD RHSFAC40	REMEDY® POLY+PLUS™ SNAP FIT Cup 44mm ID/54mm OD RHSFAC44	REMEDY® Acetabular Cup 40mm ID / 48mm OD RHAC05	REMEDY® Acetabular Cup 46mm ID / 54mm OD RHAC06	
REMEDY® CoCr Fem. Head 40mm RHCCH40	✓	-	✓	-	-	-	REMEDY® POLY+PLUS™ Head Trial 40mm RRHHD40
REMEDY® CoCr Fem. Head 44mm RHCCH44	-	✓	-	✓	-	-	REMEDY® POLY+PLUS™ Head Trial 44mm RRHHD44
REMEDY Spectrum® GV Fem. Head 40mm GVHD40	-	-	-	-	✓	-	REMEDY® RADEL® Head Trial 40mm RRTHDXS
REMEDY Spectrum® GV Fem. Head 46mm GVHD6M	-	-	-	-	-	✓	REMEDY® RADEL® Head Trial 46mm RRTHDSM
REMEDY Spectrum® GV Fem. Head 54mm GVHD4D	-	-	-	-	-	-	REMEDY® RADEL® Head Trial 54mm RRTHDMD
REMEDY Spectrum® GV Fem. Head 60mm GVHDLG	-	-	-	-	-	-	REMEDY® RADEL® Head Trial 60mm RRTHDLG

REMEDY SPECTRUM® GV Hip Spacer Use

REMEDY SPECTRUM® GV Modular Femoral Heads



- Open the package of the selected REMEDY SPECTRUM® GV Modular Femoral Head size and remove the monomer vial.
- Carefully break the vial open and pour all the monomer into the opening of the head.
- Seal the head with the cover cap and shake the head for 60-seconds, ensuring the threads are fully covered with liquid.
- Remove the cover cap and dispose of the remaining liquid.
- In a clockwise motion, screw the head onto the threaded portion of the stem until the reference thread chosen with the trial components is reached. Make sure the colored line on the stem is completely covered. Monomer provides fixation between the two components.

REMEDY® CoCr Modular Femoral Heads

- Open the package of the selected REMEDY® CoCr Modular Femoral Head size and prepare gentamicin and vancomycin loaded acrylic bone cement.
- Carefully apply doughy cement to the threads on the stem and apply a generous amount of doughy cement to the internal threaded region within the CoCr Head. When applying to the stem, at a minimum, fully fill the exposed threads above the safety line.
- In a clockwise motion, screw the head onto the threaded portion of the stem until the reference thread chosen with the trial components is reached. Make sure the colored line on the stem is completely covered. The bone Cement secures the two components. Ensure any residual cement is removed from the surface of the CoCr head before reduction into the acetabulum.
- Using gentamicin and vancomycin loaded acrylic bone cement, apply the cement to the proximal aspect of the stem and place the stem within the femoral canal in the correct position as previously verified with the trial components. The lower protrusion of the stem collar should rest on the proximal diaphysis cortex and the stem should not be obstructed by additional devices within the diaphysis canal.
- Reduce the head into the acetabulum.



Note

- The remaining offset space and threads of the stem, up to the femoral head, must be filled with gentamicin and vancomycin loaded bone cement.
- Bone cement can also be applied once the stem is seated within the femoral canal.

For the following three hours, the patient must not move the leg to ensure correct fixation of the REMEDY SPECTRUM® GV Modular Femoral Head. To prevent dislocation, the same measures utilized for a permanent total hip replacement should be adopted.

Additional considerations include:
- instructions, techniques or guides for the spacer device.
- options for ideal head diameter and correct stem length.
- placement with appropriate joint tension of the soft tissues around the hip joint (offset adjustment.)
- acquiring ideal head support in the event of severe acetabular bone loss.
- in cases at risk consider the use of an abduction brace (possibly articulated) to assist in flexion to lower the risk of dislocation.
- proximal cementation (with gentamicin and vancomycin-loaded acrylic cement) of the stem (neck region).

MRI Safety Information
The REMEDY SPECTRUM® GV Hip Spacer has not been evaluated for safety and compatibility in the MR environment. It has not been tested for heating, migration, or image artifact in the MR environment. The safety of REMEDY SPECTRUM® GV Hip Spacer in the MR environment is unknown. Scanning a patient who has this device may result in patient injury.

Post-operative treatment
Postoperative treatment is comparable with a primary 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 tropism and the clinical conditions of the patient during rehabilitation stages. Avoid weight bearing or forced mobilization which could cause the implant to damage the biological structure. If needed, an abduction brace (possibly articulated) to assist flexion may be suggested in cases at risk of dislocation.

Explantation
The REMEDY SPECTRUM® GV Hip Spacer 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 thoroughly be cleaned of all bone cement debris prior to implantation of a definitive implant or performing an alternative surgical procedure (e.g. resection arthroplasty, fusion, 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 SPECTRUM® GV Hip Spacer must be removed after temporary implantation (not to exceed 180 days). The device was tested to be safely used for not more than 6 months. If this period is extended for too long this can lead to wear, development of debris and eventually to breakage that can cause pain, inflammation and bone re-absorption.
- Excessive loading/weight on the REMEDY SPECTRUM® GV Hip Spacer must be averted (sports activity, obesity, falling, unprotected weight bearing, etc.).

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

How supplied
The REMEDY SPECTRUM® GV Hip Spacer 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 please do not use. If the device appears damaged, it must not be used.

The REMEDY® trials are provided non-sterile. Before and after each use, the devices must be cleaned, sterilized, and visually inspected per OST002.

Caution
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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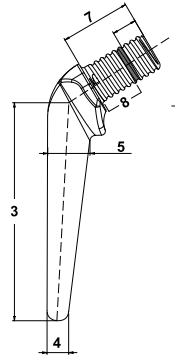
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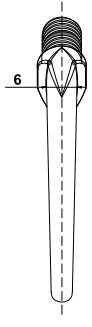
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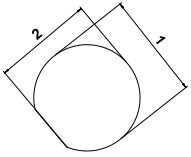
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Component Description	Reference	1(mm)	2(mm)	3(mm)	4(mm)	5(mm)	6(mm)	7(mm)	8(mm)	Gentamicin Base (g)	Vancomycin Base (g)
REMEDY® CoCr Modular Femoral Head - 40 mm	RHCCH40	40	35.9	–	–	–	–	–	–	–	–
REMEDY® CoCr Modular Femoral Head - 44 mm	RHCCH44	44	40	–	–	–	–	–	–	–	–
REMEDY SPECTRUM® GV Modular Femoral Head - 40 mm	GVHDXS	40	35	–	–	–	–	–	–	0.46	0.46
REMEDY SPECTRUM® GV Modular Femoral Head - 46 mm	GVHDSM	46	42.3	–	–	–	–	–	–	0.9	0.9
REMEDY SPECTRUM® GV Modular Femoral Head - 54 mm	GVHDMD	54	50.9	–	–	–	–	–	–	1.6	1.6
REMEDY SPECTRUM® GV Modular Femoral Head - 60 mm	GVHDLG	60	57.3	–	–	–	–	–	–	2.3	2.3
REMEDY SPECTRUM® GV Modular Femoral Stem - Small	GVSTSM	–	–	111	10	16.5	11.3	35.6	17	0.5	0.5
REMEDY SPECTRUM® GV Modular Femoral Stem - Medium	GVSTMD	–	–	112	11	21.7	15.5	35.6	17	0.6	0.6
REMEDY SPECTRUM® GV Modular Femoral Stem - Large	GVSTLG	–	–	117	11.5	24	16.5	35.6	17	0.7	0.7
REMEDY SPECTRUM® GV Modular Femoral Long Stem - Small	GVLSSM	–	–	227	10	16.5	11.3	35.6	17	0.6	0.6
REMEDY SPECTRUM® GV Modular Femoral Long Stem - Medium	GVLSMD	–	–	227	11	21.7	15.5	35.6	17	0.8	0.8
REMEDY SPECTRUM® GV Modular Femoral Long Stem - Large	GVLSLG	–	–	231	11.5	24	16.5	35.6	17	0.9	0.9

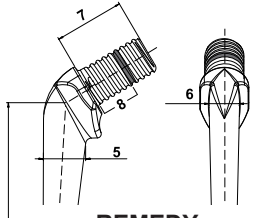


REMEDY SPECTRUM® GV
Modular Femoral Stem

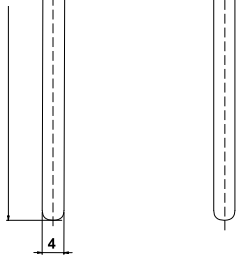




REMEDY SPECTRUM® GV
& REMEDY® CoCr
Modular Femoral Head



REMEDY
SPECTRUM® GV
Modular Femoral
Long Stem



REMEDY® Radel® Hip Trial Tray

Component Description	Reference
REMEDY® Radel® Head Trial 40mm*	RRTHDXS*
REMEDY® Radel® Head Trial 46mm	RRTHDSM
REMEDY® Radel® Head Trial 54mm	RRTHDMD
REMEDY® Radel® Head Trial 60mm	RRTHDLG
REMEDY® Radel® Stem Trial Small	RRTSTSM
REMEDY® Radel® Stem Trial Medium	RRTSTMD
REMEDY® Radel® Stem Trial Large	RRTSTLG
REMEDY® Radel® Long Stem Trial Small	RRTLSSM
REMEDY® Radel® Long Stem Trial Medium	RRTLSMD
REMEDY® Radel® Long Stem Trial Large	RRTLSLG
REMEDY® Radel® Hip Spacer Trial (kit)	RRKITHPLOGO

* RRTHDXS is only available upon request and is not included in RRKITHPLOGO.

REMEDY® POLY+PLUS™ Hip Trial Tray

Component Description	Reference
REMEDY® POLY+PLUS™ Head Trial 40mm	RRPHDT40
REMEDY® POLY+PLUS™ Head Trial 44mm	RRPHDT44
REMEDY® Radel® Stem Trial Small	RRTSTSM
REMEDY® Radel® Stem Trial Medium	RRTSTMD
REMEDY® Radel® Stem Trial Large	RRTSTLG
REMEDY® Radel® Long Stem Trial Small	RRTLSSM
REMEDY® Radel® Long Stem Trial Medium	RRTLSMD
REMEDY® Radel® Long Stem Trial Large	RRTLSLG
REMEDY® POLY+PLUS™ Hip Tray Kit with Trials	RKITPH

Symbols:



Catalog Number



Batch Number



Consult Instruction For Use



Do Not Reuse



Do Not Use If Package Is Damaged Or Opened



Sterilized Using Irradiation



Do Not Resterilize



Caution



Use By

Additional symbols for REMEDY SPECTRUM® Modular Femoral Head only:



Sterile



Sterilized Using Aseptic Processing Techniques



Sterilized Using Ethylene Oxide



Flammable Liquid

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For Internal Use

Manufactured By:

OSTEOREMEDIES®
ADVANCED MEDICAL TECHNOLOGIES

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