**DESCRIPTION**

GENERATION 4® Bone Cement System is comprised of two sterile components (liquid and powder) mixed in the VacPac® delivery system forming poly(methyl methacrylate) (PMMA) bone cement for use in orthopedic applications.

The liquid component is comprised of:
- Methyl methacrylate monomer
- N,N-dimethyl-p-toluidine
- Hydroquinone

The powder component is comprised of:
- Methyl methacrylate-styrene copolymer
- Barium sulfate, U.S.P.

**INDICATIONS**

GENERATION 4® Bone Cement is indicated for the fixation of prostheses to living bone in orthopedic musculoskeletal surgical procedures for osteoarthritis, rheumatoid arthritis, traumatic arthritis, osteoporosis, avascular necrosis, collagen disease, severe joint destruction secondary to trauma or other conditions and revision of previous arthroplasty procedures.

**CONTRAINDICATION**

Absolute contraindications include: use in the presence of active or incompletely treated infection that could involve the site where the device will be implanted and in patients allergic to any of the cement components or implant materials.

Relative contraindications include:

1. uncooperative patient or patient with neurologic disorder who are incapable of following directions
2. metabolic disorders which may impair bone formation
3. osteomalacia
4. distant foci of infections which may spread to the implant site
5. rapid joint destruction, marked bone loss or bone resorption
6. vascular insufficiency, muscular atrophy, or neuromuscular disease.
WARNINGS
Surgeon training and experience: Prior to using the GENERATION 4R Bone Cement System surgeons should, by specific training and experience, be thoroughly familiar with the properties, handling characteristics, and application of the PMMA bone cement. (See Precautions and Mixing Technique) Because the handling and curing characteristics of this cement varies with temperature and mixing technique, they are best determined by the surgeon's actual experience.

Adverse cardiovascular reactions, including hypotension, hypoxemia, cardiac arrhythmia, bronchospasm, cardiac arrest, myocardial infarction, pulmonary embolism, cerebrovascular accident and possible death. Hypotensive reactions can occur between 10 and 165 seconds after application of PMMA bone cement and can last for 30 seconds to 5 or more minutes. Some hypotensive reactions have progressed to cardiac arrest. The blood pressure of patients should be monitored carefully during and immediately following the application of the PMMA bone cement. In addition, overpressurization of the PMMA bone cement should be avoided during the insertion of the PMMA bone cement and implant in order to minimize the occurrence of pulmonary embolism.

Pulmonary fat embolism and the severity of all Bone Cement Implantation Syndrome (BCIS) complications can be reduced by meticulous irrigation and drying of the intramedullary canal. In high-risk patients, for example those sustaining hip fractures, care should be taken not to over pressurize the cement and to insert the prosthesis slowly.

Device volatility and flammability and electrocautery devices: The operating room should be adequately ventilated to eliminate monomer vapors. Ignition of monomer vapors caused by use of electrocautery devices in surgical sites near freshly implanted bone cements has been reported.

Irritation of the respiratory tract, eyes, and the liver: Caution should be exercised during the mixing of the liquid and powder components of the PMMA bone cement to prevent excessive exposure to the concentrated vapors of the liquid component, which may produce irritation of the respiratory tract, eyes, and possibly the liver. Personnel wearing contact lenses should not mix PMMA bone cement or be near the mixing of the PMMA bone cement.

1. DO NOT USE if there is loss of sterility of the cement.
2. Discard and DO NOT USE opened or damaged packages of the bone cement. Use only product packaged in unopened and undamaged containers.
3. Expired cement must be mixed according to Instructions for Use (steps 1 – 5) and disposed of immediately.
4. Loosening and fracture of either the cement or the prosthesis, or both, can occur due to disease, trauma, inadequate cementing technique, mechanical failure of the materials or latent infection.
5. The liquid and powder components of this cement must be mixed thoroughly before using. Inadequate mixing will lead to inhomogeneity which will compromise the mechanical properties and clinical performance of the cement. Strict adherence to the Instructions For Use is absolutely required.
6. DO NOT USE cement after expiration date. This product has a 6 month shelf-life.

PRECAUTIONS
Strict adherence to good surgical principles and technique are required during use of the cement. Deep wound infection is a serious postoperative complication and may require total removal of the prostheses and embedded cement. Deep wound infection may be latent and not manifest itself for several years postoperatively.

a. Contact dermatitis: The liquid component (monomer) has caused contact dermatitis in those handling and mixing PMMA bone cement. Strict adherence to the instructions for mixing the powder and liquid components may reduce the incidence of contact dermatitis.

b. Hypersensitivity reaction: The liquid component of the PMMA bone cement is a powerful lipid solvent. It should not contact rubber or latex gloves. Double gloving and strict adherence to the mixing instructions may diminish the possibility of hypersensitivity reactions. The mixed PMMA bone cement should not contact the gloved hand until the cement has acquired the consistency of dough, several minutes after mixing.

c. Inadequate post-operative fixation: Inadequate fixation or unanticipated postoperative events may affect the
PMMA bone cement-bone interface and lead to micro-motion of cement against the bone surface. A fibrous tissue layer may develop between the PMMA bone cement and the bone that may cause loosening of the prosthesis. Thus, continued, periodic follow-up is advised for all patients.

d. **Exothermic reaction:** Polymerization of the PMMA bone cement is an exothermic reaction that occurs while the PMMA bone cement is hardening in situ. The released heat may damage bone or other tissue adjacent the implant.

e. **Extrusion:** Extrusion of the PMMA bone cement beyond the region of its intended application may occur resulting in the following complications: hematuria; dysuria; bladder fistula; delayed sciatic nerve entrapment from extrusion of the bone cement beyond the region of its intended use; local neuropathy; local vascular erosion and occlusion; and intestinal obstruction because of adhesions and stricture of the ileum from the heat released during the exothermic polymerization.

f. **Use in pregnant women and children:** The safety and effectiveness of the PMMA bone cement in pregnant women or children has not been established.

g. **Expiration dating:** PMMA bone cement should not be used after the expiration date because the effectiveness of the device may be compromised.

h. **Disposal:** Expired cement should be mixed according to Instructions for Use (steps 1 – 5) prior to disposal. Because of the volatility and flammability of the liquid monomer of the PMMA bone cement, liquid monomer that has leaked or is leaking from a VacPac® package should be collected and evaporated in a well-ventilated hood or absorbed by an inert material and transferred in a suitable container (one that does not react with the PMMA bone cement) for disposal.

### ADVERSE EVENTS

The most serious adverse events, including death, reported with the use of acrylic bone cements are:

- Cardiac arrest
- Myocardial infarction
- Pulmonary embolism
- Cerebrovascular accident
- Sudden death

The most frequent adverse events reported are:

- Transitory fall in blood pressure
- Thrombophlebitis
- Hemorrhage and hematoma
- Loosening or displacement of the prosthesis
- Superficial or deep wound infection
- Trochanteric bursitis
- Short-term cardiac conduction irregularities

Other adverse events reported are:

- Heterotopic new bone formation
- Trochanteric separation

Other potential adverse events reported include:

- Pyrexia due to an allergy to bone cement
- Hematuria
- Dysuria
- Bladder fistula
- Local neuropathy
- Local vascular erosion and occlusion
- Intestinal obstruction due to extrusion of the bone cement beyond the region of its intended application
IMPORTANT PHYSICIAN INFORMATION

ADVERSE REACTIONS AFFECTING THE CARDIOVASCULAR SYSTEM HAVE BEEN ATTRIBUTED TO LEAKAGE OF UNPOLYMERIZED LIQUID MONOMER INTO THE CIRCULATORY SYSTEM. DATA INDICATE THAT THE MONOMER UNDERGOES RAPID HYDROLYSIS TO METHACRYLIC ACID AND THAT A SIGNIFICANT FRACTION OF THE CIRCULATING METHACRYLATE IS IN THE FORM OF THE FREE ACID, RATHER THAN OF THE METHYL ESTER. CORRELATION BETWEEN CHANGES IN CIRCULATING CONCENTRATIONS OF THE METHYL METHACRYLATE/METHACRYLIC ACID AND CHANGES IN BLOOD PRESSURE HAS NOT BEEN ESTABLISHED.

HYPOTENSIVE EPISODES REPORTED APPEAR TO OCCUR PRIMARILY IN PATIENTS WITH ELEVATED OR HIGH NORMAL BLOOD PRESSURE IN HYPOVOLEMIA AND IN PATIENTS WITH PREEXISTING CARDIOVASCULAR ABNORMALITIES. IF A HYPOTENSIVE REACTION OCCURS, THE ONSET MAY APPEAR 10-165 SECONDS FOLLOWING APPLICATION OF THE BONE CEMENT. ITS DURATION MAY LAST FROM 30 SECONDS TO 5-6 MINUTES. ELEVATIONS IN PLASMA HISTAMINE LEVELS SUBSEQUENT TO INTRODUCTION OF CEMENT HAVE ALSO BEEN REPORTED.

REPORTS OF SOMETIME FATAL CARDIAC ARREST SUGGEST THAT ELDERLY OSTEOPOROTIC PATIENTS UNDERGOING HIP REPLACEMENT SURGERY FOR FRACTURES OF THE FEMORAL NECK ARE AT GREATER RISK THAN THOSE RECEIVING ELECTIVE JOINT REPLACEMENT FOR ARTHRITIC DISEASE. RISK IS ALSO HIGHER IN PATIENTS WITH PRE-EXISTING CARDIOVASCULAR DISEASE. ALTHOUGH THE ETIOLOGY OF CARDIAC ARREST IS UNCLEAR, IT MAY WELL BE EITHER DIRECT EMBOLIC EFFECTS OR SECONDARY TO HYPOXIA PRODUCED BY PULMONARY EMBOLIC PHENOMENA. CLINICAL EXPERIENCE HAS SHOWN THAT FAT, BONE MARROW AND AIR EMBOLI CAN BE SIGNIFICANTLY REDUCED BY SCRUPULOUS CLEANING OF THE MEDULLARY CAVITY PRIOR TO INSERTING THE CEMENT.

INTRODUCTION OF LIQUID CEMENT UNDER PRESSURE INTO A CLEAN MEDULLARY CANAL HAS BEEN SHOWN TO APPRECIABLY ENHANCE THE FILLING OF THE BONE CAVITIES WITH MARKED IMPROVEMENT IN THE SECURITY OF THE BONE CEMENT INTERFACE. CARE MUST BE EXERCISED IN INTRODUCING THE CEMENT CONTINUOUSLY FROM DISTAL TO PROXIMAL TO AVOID LAMINATIONS IN THE CEMENT.

POSSIBLE ADVERSE EFFECTS

The following adverse effects are associated with major surgery in general.

1. Risks associated with anesthetic include brain damage, pneumonia, blood clots, heart attack, and death.
2. Damage to blood vessels, hematoma, delayed wound healing, and/or infection.
3. Material sensitivity reactions. Implantation of foreign material in tissues can result in histological reactions.
4. Loosening or migration of the prosthesis can occur due to loss of fixation, trauma, malalignment, bone resorption, and excessive activity.
1. Deliver the VacPac® System to the sterile field using standard techniques.

2. With the vacuum reservoir tube directed downward, peel the flexible cord (black) away from the rigid clamp and remove the clamp.

3. Holding the tab at the liquid end of the VacPac® bag, pull the tube down to initiate mixing. The monomer liquid will wet the entire powder mass in about 15–30 seconds and will soften by 30–60 seconds.

4. Manipulate the VacPac® bag to move about ⅔ of the cement to the empty end, and then back. Repeat the manipulation to progressively move ½, ⅓, and then all of the cement from end to end. Move all cement from end to end at least three times.

5. Collect the cement in the tube end of VacPac® bag and fold over the empty portion of the bag.

6. Then fold the VacPac® bag lengthwise and load into the cartridge of the applicator. (Must use VacPac® delivery gun.)

7. Slide the end cap over the vacuum reservoir tube and screw onto the cartridge.

8. Carefully pull vacuum reservoir tube out of end cap and cut off through wetted cement. (This tube is not a delivery nozzle.)
HANDLING & SETTING OF GENERATION 4® BONE CEMENT

![Diagram showing handling and setting process]

Data on file at Biomet.

The GENERATION 4® Cement’s doughing, working and setting times are similar to those of Simplex® P. As with all PMMA bone cements, high ambient or component temperatures will decrease and low ambient or component temperatures will increase GENERATION 4R Cement’s doughing, working and setting times. See the above graph and table.

STERILITY
GENERATION 4® Bone Cement powder is sterilized by exposure to a minimum 25 kGy dose of electron beam radiation. The liquid component is sterile filtered. The exterior surface of the VacPac® is sterilized by exposure to vaporous hydrogen peroxide. Do not reuse. DO NOT RESTERILIZE. Do not use cement after expiration date.

STORAGE
Store package in a dark, dry, ventilated place between 6° and 23°C (43° to 74°F). Improper exposure to light or high temperatures may result in full or partial polymerization of monomer liquid, or reduction in initiator (benzoyl peroxide) content in powder component. These changes could significantly affect cement handling properties, mechanical properties,
and clinical result.

**CAUTION:** Federal Law (USA) restricts this device to sale by or on the order of a physician.

Comments regarding this device can be directed to Attn: Regulatory Dept., Biomet, P.O. Box 587, Warsaw, IN 45681 USA, Fax: 574-372-1683.

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