CEMAD-LV Vertebral Radiopaque Bone Cement

INSTRUCTIONS FOR USE

1. Intended Use

It is radiopaque bone cement that especially formulated to perform vertebral augmentation procedures, such as vertebroplasty or kyphoplasty.
Bone cement main features:
• Appropriate viscosity to perform vertebral augmentation procedures, allowing application using a cannula, in the same time, enabling the operator to control cement distribution inside vertebral body
• Optimal application time
• High mechanical performance and limited polymerization heat generation rate according to ISO 5833 standards

The bone cement shall be prepared instantly before its application, using two sterile components, liquid and powder in predefined quantities. Preparation happens in pouring the liquid content of the ampoule into the powder content of the bag, then stirring, in accordance with manufacturer's instructions. Both primary containers of cement components are sterile.

Preparation, handling and application of bone cement must be performed only by qualified healthcare professionals, specifically trained to the procedure and under the direct super vision of the physician responsible for the procedure. Each cement comes in the form of a two component system such as powder and liquid form and once hardened; it assumes a compact structure that enhances the mechanical strength of the implant.

2. Composition

A pack of CEMAD-LV Vertebral Radiopaque Bone Cement contains one bag of cement powder and one glass ampoule of monomer liquid.

Powder Formula	**20 g**
Methyl Polymethacrylate	13.84 g
Barium Sulfate	6.0 g
Benzoyl Peroxide	0.16 g
Liquid Formula	**10 ml**
Methyl Methacrylate	9.96 ml
N,N-dimethyl-p-toluidine	0.04 ml
Hydroquinone	60 ppm

3. Activation Process

When the liquid component is added to the powder the N,N-dimethyl-p-toluidine activates the catalyst benzoyl peroxide. This starts the polymerization process of methacrylic acid methyl ester.

The result is a homogeneous fluid and then dough. This dough, introduced as stabilizing medium inside the vertebral body, within the limit working time prescribed by the manufacturer, will become solid, obtaining the fixation and stabilization of the broken vertebral body.

4. Clinical Indications

Bone cement is used to stabilize and reinforce vertebral body structure in vertebroplasty and kyphoplasty procedures. While treating painful pathologic compression fractures of vertebral body, which do not respond to antalgic therapy, and are caused by:

- Primary and secondary osteoporosis
- Osteolysis coming from tumors in the vertebral body
- Osteolysis coming from symptomatic vertebral hemangiomas

Vertebral augmentation procedures such as percutaneous vertebroplasty and kyphoplasty are only mitigative treatments for stabilizing the vertebral bodies and release pain. They do not cure the underlying illness.

5. Contraindications

CEMAD-LV Vertebral Radiopaque Bone Cement should not be applied when it is known a patient's hypersensitivity to the components of bone cement or to the contrast medium (barium sulfate).

Absolute contraindications:

- During pregnancy or breast-feeding
- Non controllable hemorrhagic diseases
- Local or systemic infections not completely resolved

Main relative contraindications:

- Tumors of vertebral body extended to epidural space
- Tumors extended to spinal canal, with occlusion greater than 20%
- Bone fragment affecting the spinal cord
- Vertebra's anatomic damage causing unsafe access into vertebral body

Other relative contraindications:

- Non collaborating patient, patient unable to follow operator's instructions
- Metabolic diseases which interfere with bone cement polymerization reaction
- Osteomalacia
- Non local infection foci potentially interesting implant
- Hypotension
- Congestive heart disease
- Renal failure

Target Population:
Target Population is Adult humans. CEMAD LV must not be used if it is known or supposed that the patient is hypersensitive to ingredients of the bone cement and during pregnancy or breast feeding.

Target User Group:
Bone cement operations must be performed only by qualified healthcare profes sionals, specifically trained for the procedure and under the direct supervision of the physician responsible for the procedure.

6. Side Effects

The pressure increase in the medullary canal may cause a temporary decrease in blood pressure after implantation of the direct cement and prosthesis or after preparation of the prosthetic bed. In addition to hypertension, cardiac embolism and cardiac arrest with potentially fatal consequences may be encountered. It can cause cardiovascular and respiratory side effects known as this implantation syndrome, and infiltration of bone marrow constructions in the vertebral vascular system. The site of the prosthesis should therefore be rinsed thoroughly with an isotonic solution (e.g. physiological saline) before implantation. Adequate drainage is recommended in the presence of pulmo-vascular diseases to minimize the pressure increase in the medullary canal during implantation of cement and prosthesis. The blood loss should be monitored and anaesthesiological measures may be required e.g. in the event of acute respiratory failure. When recasting the vertebral spines, necrosis of these spines including separation of the cement filling may occur. Components of bone cement can cause local irritations of hypersensitivity reactions in isolated cases.

7. Warnings

• It should be always used the all content of one powder bag mixed with the entire content of one ampoule. It is not permitted mixing of more than one powder bag and one ampoule at a time.
• It is single use device. This device cannot be re-used.
• It should not be added any other material to bone cement. Addition of unapproved ingredients (powder, water solutions) severely effect physical and chemical characteristics of bone cement both in preparation phase and after implant.
• During preparation and application of bone cement, higher temperature accel erates hardening, while lower temperatures slow it down.
• Rare severe adverse events, associated with the use of bone cements include myocardial infarction, cardiac arrest, cerebro vascular accident, and pulmonary embolism.
• In case of cardiovascular or pulmonary complications it is necessary to control and re-establish an appropriate level of volemia.
• Be careful during bone cement mixing phase and strictly follow the instructions.

• In case of acute respiratory or cardiac failure, apply appropriate resuscitation techniques to restore vital functions.
• Monitor the patient carefully for any change in blood pressure during and immediately following the application of bone cement. Adverse patient reactions affecting the cardiovascular system have been associated with the use of bone cements. Hypotensive reactions have occurred between 10 and 165 seconds following application of bone cement; they have lasted from 30 seconds to 5 or more minutes. Some have progressed to cardiac arrest. Patients should be monitored carefully for any change in blood pressure during and immediately following the application of bone cement.
• Prior to implanting bone cement it is necessary to exclude risky or contraindicating conditions (see absolute and relative contraindications). In particular an accurate XR control of vertebral fracture morphology, of fractured vertebral body possible vascularization or presence of eodema.
• Prior to implanting bone cement, as safeguard measure, it should be previewed the possibility of an immediate surgical action to correct percutaneous procedure complications.
• It is mandatory to execute vertebral augmentation procedure under real time XR imaging guidance, to see the distribution of bone cement in the entire extension of vertebral body and enabling the operator to avoid leakage outside of vertebral body.
• Uncompleted filling of vertebral body may imply insufficient symptoms corrections and long term reduced stability of the treated vertebra.
• In case of bone cement leakage outside vertebral body, paravertebral structures may be damaged, potentially causing spinal cord compression, intercostal pain, leakage in the intervertebral space, perivertebral blood vessels filling, with risk of embolism, infections and post surgical pain.
• In case of treatment of hemangioma, a preliminary vascular sclerotization with percutaneous alcohol application may help in preventing bone cement penetration in blood vessels.
• Avoid direct operator's skin or eye contact of liquid component of dough and reduce as possible the exposition to monomer vapors, which may cause irritation of air ways, of eyes and, in rare cases, affect liver.
• Ventilate the room to eliminate monomer vapors. Liquid component is volatile and flammable. In presence of monomers vapors do not use electrocautery instruments or other high temperature sources.
• Do not use latex gloves or other latex devices. Liquid component is a lipid solvent which can cause glove perforation and may damage exposed tissues. PVP gloves (three layers: polyethylene, vinyl copolymer, polyethylene) or Viton®-butile gloves give an adequate protection for a long period. In case surgical synthetic rubber gloves are going to be used, it is advisable to wear a second pair of gloves upon, adapted to bone cement handling.

• Operators wearing contact lenses shall not mix bone cement or be exposed to monomer vapors.
• Polymerization of bone cement is an exothermic reaction which finish only when bone cement becomes hard inside vertebral body. Respect waiting time before application and consider that generated heat may damage bone tissue o other tissues in contact with bone cement.
• During the exothermic free-radical polymerization process, the cement heats up.This polymerization heat reaches temperatures of around 82-86 °C in the body. This temperature is higher than the critical level for protein denaturation in the body. The cause of the low polymerization temperature in the body is the relatively thin cement coating, which should not exceed 5 mm, and the temperature dissipation via the large prosthesis surface and the flow of blood.
• The quantity of bone cement to be implanted is related to the number of vertebras to be treated and depends on the anatomical proportions of each individual patient.

8. Preparation and Application

It is necessary while preparing bone cement:
• Sterile working surface
• Sterile bowl made of ceramic, stainless steel, polypropylene or other material specifically approved to get in contact with bone cement dough
• Sterile spoon or spatula made of ceramic, stainless steel, polypropylene or other material specifically approved to get in contact with bone cement dough

Only after a confirmation of the integrity of the packaging, an assistant will open the external blister and extract the internal blister containing the bag and the ampoule, maintaining sterile condition.

Internal blister can be laid on the sterile working surface. Bag and ampoule must be opened only in condition of absolute sterility, right before preparation of bone cement and subsequent application. A dose is prepared by pouring the entire content of the liquid component ampoule into a bowl containing the entire quantity of powder included in one bag.

The preparation and application of bone cement is applied through four subsequent phases:
I. Mixing
II. Waiting
III. Application
IV. Setting
(Fig.1)

Mixing:

It is advisable to first measure out the liquid and then add the powder. If this order is reversed, powder nests are more likely to form as a result of polymerization commencing immediately at the surface. Both components, i.e. the relative proportions of powder and monomer, are precisely matched. The

pouch and ampoule must therefore be emptied completely if an optimal mix is to be achieved.

Bone cement can be mixed by these methods:

Preparation mixing by hand:

Cement components must be filled in the mixing bowl just before mixing. Filling and mixing should always be done under sterile conditions. The mixing time is 30 seconds. During this time, the two components are mixed together evenly. As a result, a homogeneous pulp compound is obtained if rubber gloves are no longer complied with. Always mix the powder polymer completely with a monomer liquid ampoule.

Mixing can be done a vacuum mixing:

The liquid and powder are mixed in a vacuum to provide a mixture of air intake minimized. For this, an airtight mixing system should be used, which ensures a sufficient vacuum in the mixing under sterile conditions. The mixing time is 30 seconds. For details on the mixing technique, see the instructions of the mixing system in use.

The result is a homogeneous pulp compound that can now work when it is not sticking to rubber gloves. The entire contents of a bag is mixed with the entire contents of a monomer liquid ampoule.

Application must be only performed using approved devices for vertebroplasty or kyphoplasty procedures.Apply a regular stirring action, not too fast, and continue for one minute. Do not exceed mixing time.Viscosity increases progressively as a consequence of polymerization reaction, during the phases from II to IV. The cement needs to be aspired into a syringe approved for vertebral augmentation treatments immediately after mixing phase, because in this phase the viscosity is low and fluid can be easily transferred into the syringe. Keep waiting until completion of phase II (waiting phase) and then proceed with the application (phase III, the cement has become dough). Use cannula needles with mandrel, with internal diameter higher than 1.8 mm. Cemad-LV bone cement shall be introduced into vertebral body by a syringe approved for percutaneous vertebral augmentation treatments, which allows to inject the cement with constant and regular flow and to verify total volume injected. Follow syringe and access devices manufacturer's instructions. During applicati ons it is mandatory to be supported by a real time XR monitoring. In case of paravertebral escape of bone cement, operator must interrupt immediately cement injection, wait, and continue only when the cement has reached a higher viscosity. If the filling of vertebral body is insufficient and not correctly distributed, it is advisable to proceed with a contralateral access and complete filling of vertebral body. When cement injection is concluded, introduce the mandrel into the cannula needle, in such a way that, after taking out the needle and the mandrel, there will be no cements residuals in contact with the soft tissues of access canal. Patient must be remain motionless until bone cement is completely set. (end of phase IV).

9. Storage

Cemad-LV Vertebral Radiopaque Bone Cement must be stored:

- In its sealed original package
- Inside a dry and clean storage room
- Between 5°C and 25°C

10. Expiry Date, Disposal

- Expiry date is written on the external box and on the secondary outer blister labels.
- The Bone Cement must be used before expiry date.
- The Bone Cement is sterilized by ethylene oxide and cannot be re-sterilized.
- If the package is unsealed or the secondary blister is damaged, the Bone Cement cannot be used.
- Opened or damaged package of bone cement must be disposed with all their content.
- A yellowish color of the powder or of the liquid are not normal, in this case the cement cannot be used and must be disposed.
- Dispose the remaining of bone cement and the content of partially utilized, expired, not usable or damaged packages, following rules and procedures applicable to this kind of hospital waste.

11. Packaging and Sterility

Manufacturing and packaging process of bone cement is performed under strict quality procedures in controlled environment.

Liquid component is sterilized by filtration; powder component is sterilized by ethylene oxide. The sterile liquid is contained in an amber glass ampoule packed in a blister pack in sterile conditions and subsequently sterilized by ethylene oxide. The powder is packed in two bags in sterile conditions.

The internal bag in medical-grade paper and polyethylene containing the powder component is inserted in an other bag in Tyvek and polyethylene and both are sterilized by ethylene oxide. The two bags are packed in a non-sterile protective aluminum wrapping.

Before using, it is necessary to control carefully the integrity of the packaging. If the packaging is uncompleted, damaged, unsealed, the cement cannot be used and must be discarded.

After the opening of the package on, it is mandatory, and responsibility of the operator, to use an aseptic handling technique. Any error in handling and during the transfer into the sterile field might affect bone cement sterility, the sterility of the surgical intervention and imply the risk of severe complications for the patient, such as infections and sepsis.

12. Shelf Life

The shelf life of the sterilized product is 3 (three) years when the products store at between 5˚C and 25˚C.The expiry date is printed on the outer box, on the protective aluminium packaging and on the inner sachet. CEMAD-LV

Vertebral Radiopaque Bone Cement must not be used after expiry date.The contents of opened or damaged aluminium sachets or ampoule blisters must not be resterilized and thus must be discarded.If the cement powder has turned to yellow do not use CEMAD-LV Vertebral Radiopaque Bone Cement.