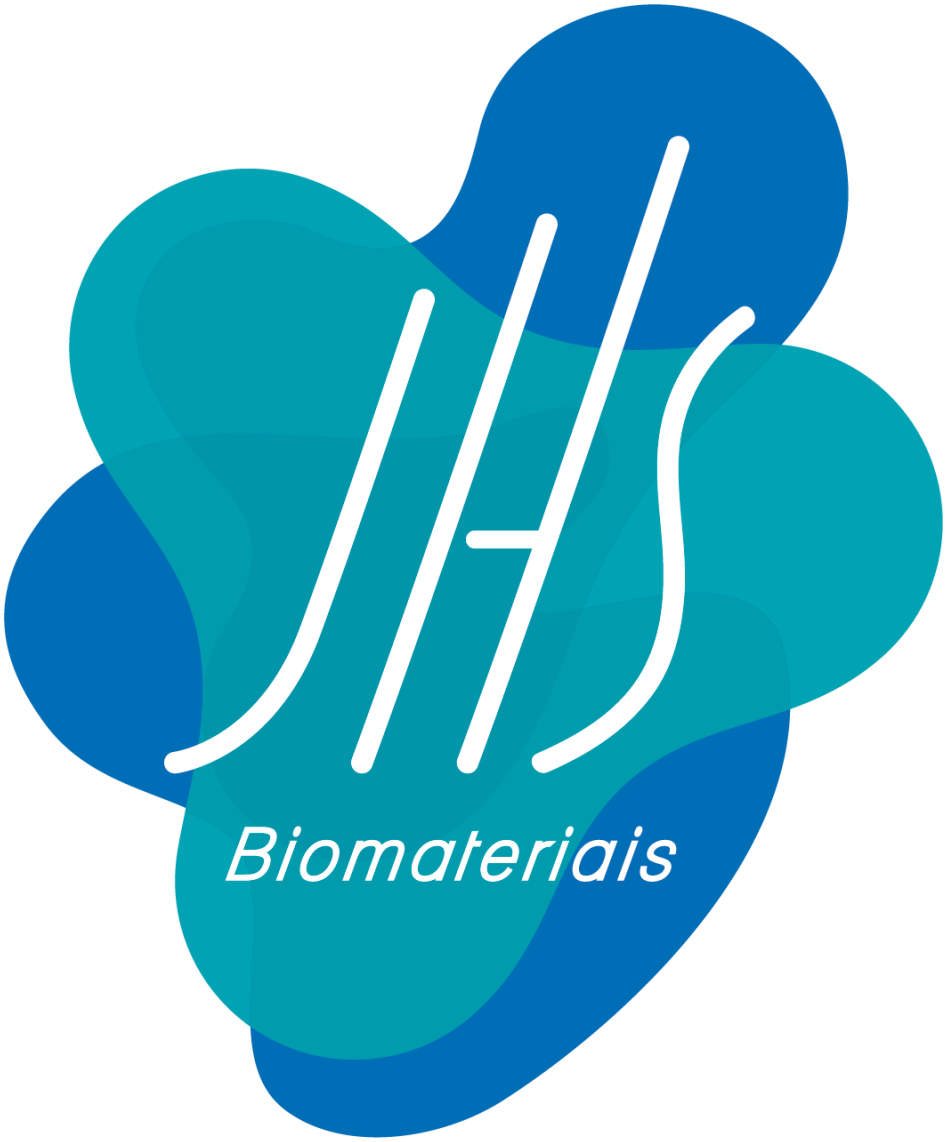

INSTRUCCIONS FOR USE
ACTIVEBONE

ActiveBone

Product Commercial Name: ActiveBone

Technical Product Name: Graft for bones and associated devices

GENERAL INFORMATIONS

Manufactured by: JHS LABORATÓRIO QUÍMICO LTDA

Address: Rua Ouro Branco, 345 - Novo Alvorada ZIP Code. 34650-120

Sabará - MG - Brazil

Phone / Fax: +55 (31) 3484-9355 CNPJ: 71.029.631 / 0001-81

Brazilian Industry NATIONAL MANUFACTURING PRODUCT Operating authorization: ANVISA / MS: 9904LHMY57H9 (8.01499.8) ANVISA registration no.: 80149980013

Technical Responsible: Dámiana Máximo Brandão CRF / MG 26.315

PRODUCT DESCRIPTION

ActiveBone Granules is composed of a resorbable and synthetic bioceramic composed of natural elements present in the bone (Ca, Si, P, O). It is a synthetic, bioactive, osteoconductive and osteoinductive material. Its function is to temporarily fill a bone defect of traumatic, pathological or surgical origin in anticipation of bone regeneration.

During its implantation, **ActiveBone** has the property of forming a layer of calcium phosphate on the surface whose composition and structure are substantially close to the mineral phase of human bone.

In aqueous solution (eg body fluids), **ActiveBone** works by loosening or releasing ions and consequently developing a layer of silica gel that acts as a model for a calcium phosphate precipitate (CaP). CaP crystallizes to form hydroxyapatite, which resembles the mineral phase of natural bone due to its chemical composition and structure, thus allowing the chemical bonding of ActiveBone to the surrounding bone and promoting the formation of new bone in the implanted area.

COMPOSITION

ActiveBone is a synthetic, alloplastic, osteoconductive, osteoinductive and osteostimulant material. It is formed by 58S bioactive glass with a 58%SiO2-33% CaO-9% P2O5 mass composition (equivalent to the 60% SiO2- 36% CaO-4% P2O5 molar composition).

RECOMMENDATION

ActiveBone is indicated for filling and restoring bone losses, as well as for the maintenance of anatomical structures (bone part), maxillofacial reconstruction; filling of bone cavities in regions resulting from injuries, segmental losses, sinking, dehiscence, pseudoarthrosis, bone infectious processes, osteomyelitis, osteolysis, cysts and tumors; filling of the alveolar crest due to atrophies; filling of the maxillary sinus; base of the maxillary sinus; periodontal intraosseous injuries; periapical injuries; substitute for uninfected surgical bone defect; defects after surgical removal and corrective osteotomies; reconstructive surgery on injured bone areas; atrodesis (vertebral arthrodesis with the help of Cage); aesthetic repairs to the bone.

Thus it has applications and indications, for bone formation, in the areas of orthopedics and traumatology, neurosurgery, surgery and traumatology, buccomaxillofacial, bone

reconstructive plastic surgery, cranial-facial surgery, dental surgery, ophthalmology, otolaryngology. **ActiveBone** does not offer mechanical resistance to withstand load-bearing defects prior to the formation of hard tissue. If a fracture requires load-bearing fixation, internal or external stabilization techniques must be used to achieve rigid stabilization in all planes.

The implantation of an implant immediately after insertion of **ActiveBone** is the responsibility of the surgeon.

PREPARATION

- The product can be used alone or mixed with patient's saline, blood, PRF (Plasma rich in fibrin) or autologous bone.
- When placing **ActiveBone**, it is recommended to completely fill the cavity.
- To allow better vascularization of the site, enliven the receiving cortical bone walls.
- The combination of the entire drug substance with **ActiveBone** during implantation is the responsibility of the surgeon.
- The general principles of asepsis work and patient medication must be respected when using **ActiveBone**.
- It is necessary to follow the usual post-operative treatment and rehabilitation procedures associated with bone grafts.

INSTRUCTIONS FOR USE

- Exclusive use by qualified professionals (doctors and dentists) and with knowledge of surgical and grafting techniques.
- The patient must undergo preoperative evaluation so that the best set of materials and surgical techniques are determined for the use of the product.
- **ActiveBone must be used in an aseptic environment.**
- It is supplied in a sterile state and must be opened in an aseptic environment (surgical, ambulatory, dental office or medical clinic) at the time of application.
- After necessary surgical techniques, prepare the recipient bed so that the product is applied in contact with the healthy and bleeding bone. Necrotic areas, with infection, must be treated before grafting the material.
- Use only support materials and sterile surgical instruments.
- Direct application of **ActiveBone** to the site to be grafted is recommended.

- The surgeon must adopt classic prophylactic treatment described in the literature for immediate and late pre- and postoperative periods.
- It is recommended to use a maximum of 30.0 grams of product per procedure. If there is a need to use an amount greater than the maximum recommended, the professional must analyze the risk / benefit, being the responsibility of the same to adopt the additional amount to be used.

PRECAUTIONS

- Check the information regarding the validity of the product, as well as the integrity of the packaging.
- The product is for single use, marketed sterile ready for use, packaged so that it can be used only once, without the need to be processed for use.
- Do not use the product if it has expired.
- If the product (packaging) has suffered damage, malfunctions, characteristics of adulteration, has been poorly stored and / or handled, it must not be used and must be mischaracterized and discarded, once the primary packaging is opened, the product cannot be returned to the manufacturer / distributor.
- The surgical use of **ActiveBone** is restricted to qualified professionals, knowledgeable of the surgical techniques and procedures indicated; since improper application can result in relative failure and / or migration of the product.
- Preoperative evaluation, the correct indication of materials and the use of compatible surgical techniques and procedures, as well as postoperative monitoring and controls, are essential for the desirable results.
- As it is a sterile product, the packaging (surgical-grade paper) should only be opened at the time of use. Its use requires appropriate asepsis techniques.
- The region that will receive the product must be exposed and curetted, where the infected and / or necrotic tissues must have been removed.
- Use only support materials and sterile surgical instruments.

STERILE PRODUCT, SINGLE USE, PROHIBITED TO REUSE, PROHIBITED TO RESTERILIZE, PROHIBITED TO REPROCESS, DO NOT USE IF THE EXPIRATION DATE IS EXPIRED OR THE PACKAGE IS VIOLATED, EXCLUSIVE USE OF QUALIFIED PROFESSIONAL, STERILIZATION BY ETHYLENE OXIDE.

RESTRICTIONS

- The product can only be used by professionals trained in the surgical area (dentists and doctors).
- Graft load restrictions:

This product is not designed to withstand load. Repetitive efforts, stress, support / loading activities can result in fractures or damage to the implanted area.
This product cannot be screwed and / or used as an implant support base.

- Bone Support

The product must be grafted into a healthy and bleeding bone region, the quality of the bone region must be estimated at the time of surgery. The bone region is decisive for the success of the product. The evaluation of bone support must be made by the surgeon, for each patient.

- Combination with implants

The product can be used with metallic implants. The need to use and combine these products is at the surgeon's discretion.

- Utilization

The product can only be used if it is within the expiration date, has been stored as intended and with its integral packaging.
It is recommended to use a maximum of 30.0 grams of product per procedure. If there is a need to use a larger quantity than the stipulated one, it must be determined previously, being the professional's responsibility the decision to use the larger quantity.

WARNING

- Only qualified medical and dental professionals with full knowledge of the necessary surgical and asepsis techniques can use the product.
- The surgical techniques adopted and the material used is the responsibility of the surgeon.
- Unused product (surplus) in the surgical procedure must be disposed of, disposed of as hospital waste.
- **ActiveBone** is manufactured in order to facilitate the handling of its products in the surgical act, but it is IMPORTANT to emphasize that it is friable, liable to deformation, but its physical-chemical characteristics, as well as its biocompatibility and biofunctionality ARE NOT CHANGED, when any change in its format occurs.

- The patient's ability and willingness to follow medical recommendations is of paramount importance for the success of the graft. Patients affected by senility, mental illness, alcoholism, and drug abuse may be at high risk of failure of the procedure, as they are more likely to ignore the recommendations and restrictions.
- **ActiveBone** has a white color, if it is different, do not use the product and contact the manufacturer.
- To patients:

Physical activities are restricted during the recovery period, and must be evaluated by the surgeon, according to the type of surgery, extent of the lesion and place of application.

- The patient must abstain from smoking, alcoholic beverages and drugs of abuse, for a period of at least 4 weeks, with the surgeon being able to change this period.

CONTRAINDICATIONS

- The product should not be used in case of infection (acute or chronic) and / or inflammation, especially at the surgery site.
- Do not use **ActiveBone** in the presence of infected and/or necrotic tissues not removed.
- No tests were performed on pregnant women, lactating women, so use in this group is not recommended.
- Patient with immature skeletal development (bone immaturity).
- Applications to support efforts.
- Surrounding bone is not viable or unable to support or support graft.
- Metabolic and/or inflammatory disease that can prevent bone formation.
- Immunological and / or systemic disorders that hinder wound healing or calcium metabolism.
- Severe neurological or vascular diseases.
- Uncooperative patients who are unwilling or unable to follow postoperative instructions, including individuals who use drugs or alcohol.
- Smoking patiets.
- Patients that use alcohol and/or drugs.

- In immunosuppressed patients, with diabetes mellitus, in corticosteroid therapy or affected by diseases that lead to bone demineralization, they may not present the predictable results, due to the systemic involvement of the patient himself.
- The product is intended for bone formation, studies on aesthetic surgery (subcutaneous filling, among others) have not been carried out, so the product is not indicated and should not be used for procedures other than bone formation.
- All cases not included in the indications.

INFORMATION TO THE PATIENT

- The patient must be informed by the surgeon about the potential risks and undesirable effects during implantation and give his agreement regarding the proposed intervention.
- Surgeons must inform the recipient of this implant that the success of the implantation depends on their behavior.
- The patient must report any episode to his surgeon that could compromise the proper integration of the implant and undergo postoperative controls.
- Physical activities are restricted during the recovery period, and must be evaluated by the surgeon, according to the type of surgery, extent of the lesion and place of application.
- The patient must abstain from smoking, alcoholic beverages and drugs of abuse, for a period of at least 4 weeks, with the surgeon being able to change this period.

ADVERSE EFFECTS

In the safety studies, no adverse effects were found. Common complications in implant surgery (grafting) can occur as:

- Infection.
- Sepsis.
- Swelling.
- Osteomyelitis.
- Pain in the first days after grafting at the same site.
- Anesthesia-related complications

IN THE OCCURRENCE OF ADVERSE EFFECTS RELATED TO THE PRODUCT IT IS NECESSARY TO CONTACT THE MANUFACTURER JHS BIOMATERIAIS THROUGH THE TELEPHONE +55 (31) 3484-9355. IT MAY BE PROCEEDED, ALSO WITH THE NOTIFICATION OF THESE IN THE COMPETENT SANITARY BODY, ANVISA, THROUGH THE WEBSITE WWW.ANVISA.GOV.BR OR THROUGH THE TELEPHONE 0800 - 642 9782.

STORAGE CONDITIONS, TRANSPORT AND MANIPULATION

It must be transported and stored away from direct sunlight, sources of heat and humidity.

- The product should preferably be kept at temperatures in the range of 15-30 °C and maximum relative humidity of 80% RH).
- It must be stored in order to maintain the physical integrity of the packaging, without damaging it.
- No heavy or sharp objects should be placed on or near the product to avoid damaging its packaging and endangering the physical integrity and sterility of the product.
- As it is a sterile product, the packaging should only be opened at the time of use. Its use requires appropriate asepsis techniques.
- When expired or the packaging is violated, the product must be discarded and the product must be completely uncharacterized.
- Ensure that the storage environment is free of dust and weather that may affect the conservation of the stored product.

PRE, INTRA AND POST-OPERATIVE CARE

In the pre and intraoperative evaluation, the correct indication of materials and the use of compatible techniques and procedures, as well as post-operative monitoring and controls, are essential for the desirable results.

PREOPERATIVE CARE

All patients who will undergo a surgical procedure should be carefully examined and evaluated, with a view to determining the clinical and radiographic status, as well as dental or bone or soft tissue deficits that may influence the final outcome of the intervention.

INTRA-OPERATIVE CARE

After necessary surgical techniques, prepare the recipient bed so that the product is applied in contact with the healthy and bleeding bone. The region that will receive the product must be exposed and curetted, where the infected and / or necrotic tissues must have been removed.

POST-OPERATIVE CARE

The product must not be exposed to the external environment in the immediate postoperative period. There must be a good fit of the edges of the surgical flap, in order not to expose the product, which will compromise the result of the surgery. Exposure to the external environment drastically reduces the absorption time. Observe postoperative care for surgical procedures. Analgesics, antibiotics, rest in the first 24-48 hours may be prescribed, depending on the procedure and professional technical conduct.

CRITERIA FOR PRODUCT SELECTION

The product should only be used by qualified professionals with knowledge in surgical grafting techniques. The professional must be able to select the quantity and type of product for each specific situation as well as the instruments required for each application.

DISPOSAL CONDITIONS

Unused or non-compliant products must be disposed of in accordance with hospital disposal rules, following the criteria of potentially hazardous products. The disposal methods and procedures must ensure the complete de-characterization of the product, preventing any possibility of reuse. The de-characterization of the product is the sole responsibility of the hospital, as well as the disposal procedures and methods used.
ActiveBone according to RDC 306 of 2004 generates waste from group D and because it is used in a surgical environment it must be disposed of in hospital waste.

STERILIZATION

ActiveBone is sterilized by ethylene oxide. The sterilization method to which the product is submitted must be checked on its labels.

EXPIRATION DATE

- The shelf life of the product is two (2) years after sterilization. This information is contained on the cartridge, product label and control labels.
- The cartridge is not sterile, sterile items are those stored inside surgical-grade paper.

RACEABILITY

Within the packages, 5 (five) labels are provided, according to the applicable legislation through resolution nº 1804 of 11/09/2006 of the Federal Council of Medicine, and these must be filed:

- In the patient's medical record.
- In the report delivered to the patient.
- In the tax documentation that generates the charge in the Hospitalization Authorization (AIH), in the case of a patient treated by SUS, or in the sales invoice, in the case of a patient treated by the complementary health system.
- With the company that supplied it - distributor (historical distribution record - RHD).
- With the surgeon in charge.
- The labels contain the following information: Business name;
  Manufacturer identification / company logo;
  Lot number;
  Registration number with ANVISA;
  Product presentation
  Expiration date
  Sterilization method

- Once the packaging is opened, it is necessary to fix the labels in their respective locations. The surgeon must inform the patient of the existence of the tags, the information contained and instruct him to keep it.

NOTE: Dentists surgeons, when using the material should proceed as described above, the product's traceability depends on the above-mentioned labels.

ActiveBone is presented in the following forms:

ACTIVEBONE SMALL GRANULES

Composition	Dimensions	Code	Net weight (g)	Primary package
BG 58S	0,04 a 1,00 mm 	AB05MS	0,5 g	
		AB10MS	1,0 g	
		AB20MS	2,0 g	
		AB50MS	5,0 g	
		AB100MS	10,0 g	

ACTIVEBONE LARGE GRANULES

Composition	Dimensions	Code	Net weight (g)	Primary package
BG 58S	0,5 a 2,00 mm 	AB05ML	0,5 g	
		AB10ML	1,0 g	
		AB20ML	2,0 g	
		AB50ML	5,0 g	
		AB100ML	10,0 g	

RESPONSÁVEL LEGAL
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