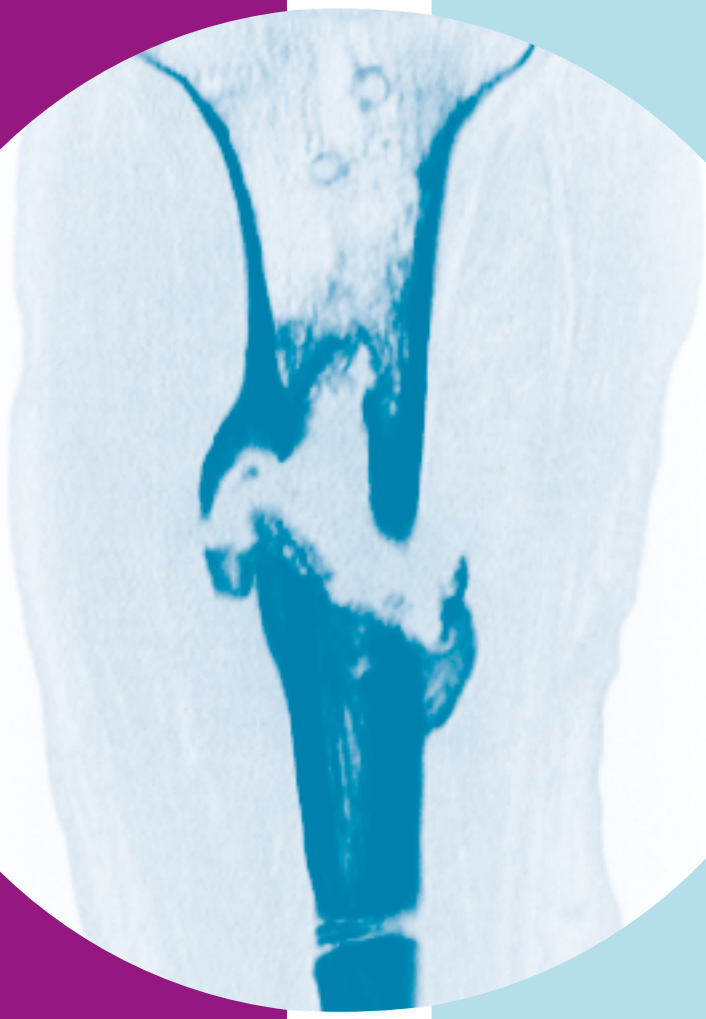
OSTEOmycin V™

SAFE, CLEAN and EFFICIENT!



EUROPEAN CELL AND TISSUE BANK
Österreichische Gewebebank Gemeinnütziger Verein

ECTB

OSTEOmycin V™

BONE ALLOGRAFT

NEW GENERATION PROCESSED CHIPS AND STRUCTURAL BONE ALLOGRAFTS IMPREGNATED WITH VANCOMYCIN

CHIPS, SHAPED FEMORAL HEADS AND BLOCKS

Treatment of chronic bone infection is considered one of the most challenging procedures in orthopaedic surgery. Reduced susceptibility for traditional antibiotic therapy and extensive bone defects make surgical intervention mandatory for a successful outcome.

The European Cell and Tissue Bank (ECTB/ÖGGV) has therefore developed a new product which makes biological reconstruction of bone defects and effective local treatment or prevention of infections with a single surgical intervention feasible. Human allografts are cleaned and processed using modern technologies. The cleaning process is a gentle, safe and efficient cleaning process throughout the whole bone matrix even for structural allografts. Its virus-inactivating effect is validated. Lipids and cellular components are removed completely. Collagen and osteoinductive proteins are treated with care. Mechanical properties are mainly unmodified. Thus incorporation in the recipient is faster and more complete. The allografts are impregnated with antibiotics in a special process that leads to a product with slow elution of antibiotics. Thus higher local antibiotic concentration and longer lasting antimicrobial activity is achieved better than with any other method. [21]

The resulting product **OSTEOmycin V™** offers not only ultimate safety and quality, it makes debridement, complete dead space management, biological reconstruction of bone defects as well as implantation of endoprostheses in debrided bone in a one stage approach feasible. [22] Thus stress for the patient, treatment periods and treatment expenses can be reduced distinctively.

WHY VANCOMYCIN?

Vancomycin is one of the antibiotics with intracellular bactericidal activity and therefore should cover small colony variants of staphylococci. [2] Remnants of biofilm may be covered as well, [12, 13, 15] especially those of MRSA. [16] Vancomycin shows the least cytotoxic effect of all commonly used antibiotics [6] and is not likely to cause systemic side effects after local application. [3] Vancomycin shows very poor tissue penetration, [10, 14] inhibiting absorption from the implanted site into the vascular system, keeping local tissue levels high and systemic levels low.

INDICATIONS

OSTEOmycin V™ is favourably used as filler after debridement of osseous sites infected with grampositive bacteria. Indications include osteitis after trauma or surgery, hematogenic osteomyelitis and infected joint replacement. In cases of mixed infections (grampositive and gramnegative) and chronic infections with inexplicit cultures combination with **OSTEOmycin T™** is advisable, taking advantage of the synergistic activity of the two antibiotics. [11, 20]

OSTEOmycin V™ is not suitable for treatment of soft tissue infection.

INNOVATIVE PROCESSING METHOD FOR INNOVATIVE PRODUCTS

The bone tissue is procured, tested and processed according the EU Directives and Austrian Tissue Law *Österreichisches Gewebesicherheitsgesetz.*

The essential characteristic of processing is that supercritical CO_2 technology is used, currently the most gentle and effective technology of cleaning bone allografts. CO_2 is used under a pressure of 250 bar with a temperature of 50°C which puts it into supercritical state. Supercritical means that CO_2 has the characteristics of both a gas and a fluid. In this state CO_2 has the ability of high penetration throughout the whole bone matrix combined with high potential to solve lipids and cellular components associated with lipids. [7] Using this technology lipids and bone marrow are removed, while the collagen matrix consisting of collagen and minerals is mainly maintained. Osteoinductive proteins are treated with care. The native composition of the matrix promotes osteocunduction. [9] The virus-inactivating effect of the process has been validated several times. [8] By removing fat and cellular components antigens are removed [17] and immunological reactions are avoided.

The purified matrix is impregnated with high loads of vancomycin, a glycopeptide with superior activity against staphylococci and other grampositive bacteria which are the most common cause of bone infection. Due to the proprietary impregnation technique vancomycin is deposited throughout the whole graft, mainly in the lacunae of the spongy matrix. **OSTEOmycin V™** elutes vancomycin slowly. Thus higher local antibiotic concentration and longer lasting antimicrobial activity is achieved better than with any other method. Release of the antibiotic is completed after several weeks and such is not likely to create resistances or initiate the formation of small colony variants. Concentrations in the immediate surrounding reach levels between 100 and 1000 times the levels reachable with systemic antibiotic therapy. [21]

Because of the unique properties of supercritical CO_2 this innovative processing technology enables efficient and gentle cleaning of human bone allografts – also for cortical and structural allografts – and guarantees ultimate biological safety and quality of the products. Due to the special impregnation technique vancomycin is eluted slowly. Higher local antibiotic concentration and longer lasting antimicrobial activity is achieved better than with any other method.

SAFE, CLEAN and EFFICIENT!

ADVANTAGES

- The validated virus-inactivation grants ultimate safety. [8]
- Extraction of lipids and cellular components takes place deep into the bone matrix.
- The collagen matrix consisting of collagen and minerals is mainly maintained and osteoinductive proteins are treated with care.
- The native composition of the matrix promotes osteoconduction. [9]
- The mechanical and structural qualities are mainly equal to those of unprocessed bone tissue. [18]
- Using impaction grafting the primary stability of purified allografts is favourable compared to not purified, fatty transplants. [4, 5]
- The cleaning process uses only non-toxic solvents.
- Processed chips, femoral heads and blocks have no immune response of the recipient.
- Incorporation at the recipient therefore takes place faster and more complete. [1, 9, 19]
- Due to the special impregnation technique vancomycin is eluted slowly. Higher local antibiotic concentration and longer lasting antimicrobial activity is achieved better than with any other method. [21]
- Concentrations of vancomycin in the immediate surrounding reach levels between 100 and 1000 times the levels reachable with systemic antibiotic therapy. [21]
- Release of the antibiotic is completed after several weeks and such is not likely to create resistances or initiate the formation of small colony variants.
- The allografts are double-packaged in blisters or glas vials and sterilized.
- Storage takes place under room temperature conditions for up to 3 years.
- The products are easy to handle and user-friendly shapening saves time in the operating room.

APPLICATION

Radical debridement is a prerequisite for cure in any orthopaedic infection. All unvascularized bone must be removed down to slightly bleeding surfaces. The site should be rinsed thoroughly with saline until all macroscopically visible debris is cleared. Osseous dead space and bony defects are then filled up with **OSTEOmycin V™**, using mild to moderate impaction forces, depending from the required effect. Mild impaction will result in accelerated incorporation, moderate forces increase primary stability. Insertion of osteosynthetic material or endoprostheses may precede or follow the grafting procedure, according to local circumstances. Drainage preferably should be performed without suction.

QUALITY GUARANTEE

The allografts are recovered aseptically from donors who are selected according to strict criteria including the patient medical record and other exposures or habits to exclude risc factors. They are tested to exclude the presence of viruses and bacteria. The donor screening includes infectious, malignant, neurological, and autoimmune disease and other exposures or habits of the donor that might result in unsatisfactory tissue. The screening is in accordance with the recommendations of the competent authorities, regulatory agencies and Associations of Tissuebanks. The donor's serum is screened for the following: HIV-1/2-Ab, HTLV-I/II-Ab, HbsAg, HBc-Ab, HCV-Ab, TPPA; utilizing qualified and licensed testing laboratories. In addition, the screening for HIV and hepatitis is performed with nucleic-acid amplification (NAT, PCR).

The allografts are processed with supercritical CO_2 technology, dried, double-packaged in blisters or glas vials and sterilized with gamma irradiation of minimum 25 kGy. All processes are performed using qualified technologies, all critical processes are validated.

The processing laboratory is in possession of the necessary permits and licenses and is GMP-certified. National and international health inspectors of the competent authorities inspect the laboratory at regular intervals and have issued a permit to process bone tissue, respectively to bring the processed allografts on the market.

ECTB/ÖGGV

The European Cell and Tissue Bank (ECTB/ÖGGV) is a *Entnahmeeinrichtung* and *Gewebebank* according to Austrian Tissue Law *Österreichisches Gewebesicherheitsgesetz* which complies with a Tissue Establishment according to EU Directive. ECTB is based in Wels, Austria, and is a non-profit organisation. Its main focus is the procurement, storage, processing and distribution of human bone allografts for implantation as well as research and development of new technologies for processing of innovative tissue products for applications in human medicine. The main objective of ECTB is to supply hospitals with high-quality tissue products meeting the demand of ultimate safety.

Ordering Information

Sp. Chips 1.5-10 mm, 1.8 g, ca. 10 cm³, plus 1.0 g Vancomycin	OMCT10.G1.8
Sp. Chips 1.5-10 mm, 5.4 g, ca. 30 cm³, plus 3.0 g Vancomycin	OMCT10.G5.4
Sp. Cylinder Ø 10 mm, L 25 mm, 2 parts, plus 1.0 g Vancomycin	OMCYV02.M1025
Sp. Cylinder Ø 12 mm, L 25 mm, 2 parts, plus 1.0 g Vancomycin	OMCYV02.M1225

Product offer depends on country approval and availability. For further information please refer to the contact details below.

LITERATURE

1. Aspenberg P, Thoren K. Lipid extraction enhances bank bone incorporation. An experiment in rabbits. Acta Orthop Scand 1990; 61-6:546-8.

2. Barcia-Macay M, Lemaire S, Mingeot-Leclercq MP, Tulkens PM, Van Bambeke F. Evaluation of the extracellular and intracellular activities (human THP-1 macrophages) of telavancin versus vancomycin against methicillin-susceptible, methicillin-resistant, vancomycin-intermediate and vancomycin-resistant Staphylococcus aureus. J Antimicrob Chemother 2006;58-6:1177-84.

3. Buttaro MA, Gimenez MI, Greco G, Barcan L, Piccaluga F. High active local levels of vancomycin without nephrotoxicity released from impacted bone allografts in 20 revision hip arthroplasties. Acta Orthop 2005;76-3:336-40.

4. Cornu O, Bavadekar A, Godts B, Van Tomme J, Delloye C, Banse X. Impaction bone grafting with freeze-dried irradiated bone. Part I. Femoral implant stability: cadaver experiments in a hip simulator. Acta Orthop Scand 2003; 74-5:547-52.

5. Cornu O, Bavadekar A, Godts B, Van Tomme J, Delloye C, Banse X. Impaction bone grafting with freeze-dried irradiated bone. Part II. Changes in stiffness and compactness of morselized grafts: experiments in cadavers. Acta Orthop Scand 2003; 74-5:553-8.

6. Edin ML, Miclau T, Lester GE, Lindsey RW, Dahners LE. Effect of cefazolin and vancomycin on osteoblasts in vitro. Clin Orthop Relat Res 1996-333:245-51.

7. Fages J, Marty A, Delga C, Condoret JS, Combes D, Frayssinet P. Use of supercritical CO_2 for bone delipidation. Biomaterials 1994; 15-9:650-6.

8. Fages J, Poirier B, Barbier Y, Frayssinet P, Joffret ML, Majewski W, Bonel G, Larzul D. Viral inactivation of human bone tissue using supercritical fluid extraction. Asaio J 1998; 44-4:289-93.

9. Frayssinet P, Rouquet N, Mathon D, Autefage A, Fages J. Histological integration of allogeneic cancellous bone tissue treated by supercritical CO2 implanted in sheep bones. Biomaterials 1998; 19-24:2247-53.

10. Garazzino S, Aprato A, Baietto L, D'Avolio A, Maiello A, De Rosa FG, Aloj D, Siccardi M, Biasibetti A, Masse A, Di Perri G. Glycopeptide bone penetration in patients with septic pseudoarthrosis of the tibia. Clin Pharmacokinet 2008;47-12:793-805.

11. Gonzalez Della Valle A, Bostrom M, Brause B, Harney C, Salvati EA. Effective bactericidal activity of tobramycin and vancomycin eluted from acrylic bone cement. Acta Orthop Scand 2001;72-3:237-40.

12. Gristina AG, Costerton JW. Bacterial adherence to biomaterials and tissue. The significance of its role in clinical sepsis. J Bone Joint Surg Am 1985;67-2:264-73.

13. Gristina AG, Jennings RA, Naylor PT, Myrvik QN, Webb LX. Comparative in vitro antibiotic resistance of surface-colonizing coagulase-negative staphylococci. Antimicrob Agents Chemother 1989;33-6:813-6.

14. Matzke GR, Zhanel GG, Guay DR. Clinical pharmacokinetics of vancomycin. Clin Pharmacokinet 1986;11-4:257-82.

15. Rose WE, Poppens PT. Impact of biofilm on the in vitro activity of vancomycin alone and in combination with tigecycline and rifampicin against Staphylococcus aureus. J Antimicrob Chemother 2009;63-3:485-8.

16. Smith K, Perez A, Ramage G, Gemmell CG, Lang S. Comparison of biofilm-associated cell survival following in vitro exposure of meticillin-resistant Staphylococcus aureus biofilms to the antibiotics clindamycin, daptomycin, linezolid, tigecycline and vancomycin. Int J Antimicrob Agents 2008.

17. Thoren K, Aspenberg P, Thorngren KG. Lipid extraction decreases the specific immunologic response to bone allografts in rabbits. Acta Orthop Scand 1993; 64-1:44-6.

18. Thoren K, Aspenberg P, Thorngren KG. Lipid extracted bank bone. Bone conductive and mechanical properties. Clin Orthop Relat Res 1995-311:232-46.

19. Thoren K, Aspenberg P. Increased bone ingrowth distance into lipid-extracted bank bone at 6 weeks. A titanium chamber study in allogeneic and syngeneic rats. Arch Orthop Trauma Surg 1995; 114-3:167-71.

20. Watanakunakorn C, Tisone JC. Synergism between vancomycin and gentamicin or tobramycin for methicillin-susceptible and methicillin-resistant Staphylococcus aureus strains. Antimicrob Agents Chemother 1982;22-5:903-5.

21. Winkler H, Janata O, Berger C, Wein W, Georgopoulos A. In vitro release of vancomycin and tobramycin from impregnated human and bovine bone grafts. J Antimicrob Chemother 2000;46-3:423-8.

22. Winkler H, Stoiber A, Kaudela K, Winter F, Menschik F. One stage uncemented revision of infected total hip replacement using cancellous allograft bone impregnated with antibiotics. J Bone Joint Surg Br 2008;90-B-12:1580-4.

EDITORIAL

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The European Cell and Tissue Bank (ECTB) acts in Austria under the synonym Österreichische Gewebebank gemeinnütziger Verein (ÖGGV) and is based in Bernadingasse 12, 4600 Wels, Austria.