SUMMARY of SAFETY and CLINICAL PERFORMANCE
SSCP

OPACITY+®

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SUMMARY of SAFETY and CLINICAL PERFORMANCE (SSCP) for HEALTH CARE PROFESSIONNALS
OPACITY+®

Foreword

This Summary of Safety and Clinical Performance (SSCP) is intended to provide public access to an updated summary of main aspects of the safety and clinical performance of the device.

The SSCP is not intended to replace the Instructions For Use as the main document to ensure the safe use of the device, nor intended to provide diagnostic or therapeutic suggestions to intended users or patients

The following information is mainly intended to users (health care professionals such as surgeons). A summary intended for patients can be found at the end.

1. Device Identification and general information

1.1. Device Trade Name(s): **OPACITY+®**

The medical device has also the following private labels:
OSSEOFIX+ (ALPHATEC) / EXOFIX (TEKNIMED) / OSTEOFLEX LV (ZAVATION) / THERMALFIX (IZI MEDICAL PRODUCTS LLC) / Synth-X SL (HC biologics) / Merit Fastrak VP (Merit Medical Systems, Inc) / LV 45 (TEKNIMED) / 12,5 CEM (TEKNIMED) / ZR+ (TEKNIMED) / BLACK C (TEKNIMED) / SAFE CEM (TEKNIMED) / OPT15 (TEKNIMED) / PMM+ (TEKNIMED).

1.2. Manufacturer name and address(es):

TEKNIMED S.A.S.		
Headquarters 8, rue du Corps Franc-Pommiès 65500 Vic en Bigorre France	*Production and facilities* 11-12, rue d'Apollo - ZI de Montredon 31240 L'Union France	*Supply Chain site (labelling)* ZI de la Herray 65500 Vic en Bigorre France

1.3. Manufacturer's SRN (Single Registration Number): **FR-MF-000001224**

1.4. Basic UDI-DI: **376017704B05D2**

1.5. Medical device nomenclature description / EMDN nomenclature: **P900403** - Non-resorbable filling and reconstruction devices

1.6. Class of device: According to EU MDR 2017/745, Annex VIII, Rule 8, OPACITY+® is a **class III** device

1.7. Year when the first certificate (CE) was issued covering the device: **2016**

The medical device has been introduced for the first time in the following countries:

Country	Year of introduction
Europe	2006
Serbia	2013
Taïwan	2014
Israël	2015
India	2016
Ukraine	2016
Uruguay	2016
Macedonia	2017
Costa Rica	2017
Mexico	2018
Brazil	2018
Indonesia	2018

Thailand	2018
Argentina	2019
Malaysia	2019
Vietnam	2019
Lebanon	2020
United Arab Emirates	2020
Bosnia	2020
Colombia	2022
Montenegro	2022

1.8. Authorised representative if applicable; name and SRN: **NA as the manufacturer is located in the EU**.

1.9. NB's name (the NB that will validate the SSCP) and single identification number: **BSI Netherlands (CE 2797)**

2. Intended use of the device

2.1. Intended purpose

OPACITY+® bone cement is intended for use in palliative percutaneous cementoplasty procedures such as vertebroplasty or kyphoplasty.

2.2. Indication(s) and target population(s)

OPACITY+® bone cement is indicated for the fixation of painful vertebral compression fractures.

OPACITY+® bone cement is intended to be used in adult patients suffering from painful vertebral compression fractures resulting from osteoporosis, benign or malignant lesions, or of traumatic origin.

2.3. Contraindications or restriction for use

- Procedures other than those stated in the INDICATIONS section.
- Coagulation disorders, or severe cardiopulmonary disease;
- Unstable vertebral fractures;
- Compromise of the vertebral body or of the pedicle' walls;
- Hypersensitivity or allergy to one of the constituents of the product;
- Patients clearly improving on more conservative treatment;
- Prophylactic use in spinal metastatic or osteoporotic patients with no evidence of vertebral fracture.
- Due to non-sufficient available clinical evidence, the bone cement is contraindicated in paediatric patients and in pregnant or breast-feeding women.

3. Device description

3.1. Description of the device

OPACITY+® is a bone cement intended to be used in human beings, for the palliative stabilisation of pathological fractures of the vertebral body, using percutaneous cementoplasty procedures such as vertebroplasty and kyphoplasty.



This low viscosity bone cement is made of two sterile components: Poly-methyl-methacrylate polymers (powder) and

monomers (liquid) which must be mixed at the time of use.

Composition	% (w/w)
POWDER – 27.2g	
PMMA (Polymethylmethacrylate)	49.5
Benzoyl peroxide (BPO)	0.5
Zirconium oxide (ZrO2)	45.0
Hydroxyapatite	5.0
LIQUID – 9.2g	
MMA (Methylmethacrylate)	99.0
N, N dimethyl-p-toluidine (DMPT)	1.0
Hydroquinone	20ppm

The powder component is mainly composed of polymethylmethacrylate polymers and of Zirconium dioxide and hydroxyapatite, added as radiopaque agents. It also additionally contains benzoyl peroxide as an initiator to start polymerisation
The liquid component is mainly composed of methylmethacrylate monomers. N, N dimethyl-p-toluidine is the activator necessary to promote acceleration of polymerisation reaction when powder and liquid are mixed and the obtention of an acceptable setting time and maximum polymerisation temperature in the operating theatre. In order to prevent a premature polymerisation of the monomer during storage due to heat or excessive exposure to light, a stabiliser or inhibitor, hydroquinone, is added to the liquid in small quantities.

When the powder and the liquid are mixed in the operating room, a medium viscosity mixture is first obtained. The BPO (benzoyl peroxide) from the powder and N, N-dimethyl-p-toluidine DMPT from the liquid react to generate free radicals by means of a redox reaction. The free radicals react with the monomeric liquid, causing an increase of viscosity and the hardening of the cement into a solid matrix.
Injection must be performed during the viscous phase, before the final hardening of the cement which must take place inside the treated bone or cavity.

OPACITY+® bone cement expected lifetime is 10 years. At the end of this expected lifetime, the cement is not intended to be removed and does not need any maintenance, unless a medical complication would require a surgery.

The product (powder and liquid) is supplied sterile.
It is a single use product.

3.2. Reference to previous generation(s) or variants if such exist, and a description of the differences

OPACITY+® is not issued from any previous generation and has no variant.

3.3. Description of any accessories which are intended to be used in combination with the device

OPACITY+® bone cement is intended to be used with the following accessories (sold separately by Teknimed):

- EASYKIT® M mixing and injection system – Reference: T060415 – Classification: I sterile
- S5M mixing and injection system – Reference: T060407 – Classification: I sterile

3.4. Description of any other device or products which are intended to be used in combination with the device

No other devices or products are intended to be used in combination with OPACITY+®.

4. Risks and warnings

4.1. Residual risks and undesirable side effects

- Leakage of spinal bone cement beyond the intended site of implantation. They are frequent: rates up to 56% have been reported in the literature[1], and in a clinical study with OPACITY+® (Cf. section 5.3 below). These leakages are almost always asymptomatic. Yet, in some cases, when the cement penetrates into the vascular system, leakages can result in embolism of the lung and/or heart or other clinical sequelae (rates up to 1.5% have been reported in the literature[2], none concerning OPACITY+®).
- Adverse reactions affecting the cardiovascular system (also known as Bone Cement Implantation Syndrome), including chest pain, tachycardia, signs of severe respiratory distress, and death have also been reported in the literature, with a rate of 0.43%[3]. They are supposedly due to MMA monomer release in the blood during polymerisation, and/or to excessive exothermic reaction, and/or to too much pressure applied during cement injection. For this reason, patients should be monitored carefully for any change in blood pressure during and immediately following the application of bone cement. The anaesthetist should be told during the operation when the bone cement is implanted.
- Some isolated cases of perioperative fractures have also been reported, such as: Fracture of ribs, of posterior element or of pedicle in patients suffering from diffuse osteopenia or osteoporosis, in particular during thoracic vertebroplasty procedures, due to the high pressure exerted downwards while the needle is being inserted (incidence <1%)[4]; Fracture or collapse of a vertebra adjacent to the one injected due to an osteoporotic disease (up to 23% in the literature[4], 1 case (2.2%) in a clinical study with OPACITY+®).
- Other isolated complications reported in clinical studies with OPACITY+® are: 1 case of paravertebral hematoma (0.8%) and 1 case of pain due to injection of the cement (0.8%).

Other side effects include:
- Allergy to one of the bone cement constituents (rate up to 1.4% reported in the literature[5]);
- Exposure of the health care operators to monomer fumes[6].

Any serious incident occurring in relation to the OPACITY+® bone cement must be reported without delay to the manufacturer and the competent local authority where the user and/or the patient is established.

4.2. Warnings and Precautions

Read instructions for use carefully prior use and follow preparation and handling instructions of the cement and its injection system carefully.
Ignoring the instructions for use may lead to potential undesirable effects.
For an optimum use of the cement, it is essential to perform a thorough pre-operative review of the patient before the intervention in order to confirm the indication and plan the surgical technique. The healthcare professional must be familiar with cement properties and handling characteristics, and experienced in cement injection procedures. It is advisable to respect the recommended preparation and application times.
Pre-clinical testing has been performed on one unit of cement, so it is recommended to use no more than one unit of cement per patient.

Conservation
- It is strictly forbidden to re-sterilise the product. This product is supplied sterile unless package has been opened or damaged.

[1] Alhashash M. et al. *Effects of Polymethylmethacrylate Cement Viscosity and Bone Porosity on Cement Leakage and New Vertebral Fractures After Percutaneous Vertebroplasty: A Prospective Study*. Glob Spine J. 2019;9(7):754–60.

[2] Hinde K. et al. *Mortality Outcomes of Vertebral Augmentation (Vertebroplasty and/or Balloon Kyphoplasty) for Osteoporotic Vertebral Compression Fractures: A Systematic Review and Meta-Analysis*. Radiology. 2020;295(1):96–103.

[3] Krueger A. et al. *Management of pulmonary cement embolism after percutaneous vertebroplasty and kyphoplasty: a systematic review of the literature*. Eur Spine J. 2009;18(9):1257–65

[4] Luo K. et al. *Poly(methyl methacrylate) bone cement composited with mineralized collagen for osteoporotic vertebral compression fractures in extremely old patients*. Regen Biomater. 2019;7(1):29–34.

[5] Goon A. et al. *Screening for acrylate/methacrylate allergy in the baseline series: our experience in Sweden and Singapore*. Contact Dermatitis 2008: 59: 307–313.

[6] The American Conference of Governmental Industrial Hygienists recommends an 8-hr time-weighted average of 50 ppm (205 mg/m^3) and a short-term exposure limit of 100 ppm. Cited in: Ungers L. et al. *Control of Methyl Methacrylate During the Preparation of Orthopedic Bone Cements*. Journal of Occupational and Environmental Hygiene. 2007; 4: 272–280.

- This device is packaged and sterilised for single use only. Do not reuse, reprocess or resterilise. Reuse, reprocessing, or resterilisation may compromise the structural integrity of the device and/or lead to device failure which may result in patient injury or illness. Also, reprocessing or resterilisation of single use devices may create a risk of contamination and/or cause patient infection or cross-infection, including, but not limited to, the transmission of infectious disease(s) from one patient to another.
- Before use, check the packaging carefully to ensure that it has not been opened nor damaged in a way that could affect its sterility.
- Do not use this product after the expiration date mentioned on the package.

Before use
- Do not implant products with defects.
- When removing the product from its packaging, be sure to follow asepsis rules.
- If packaging is unintentionally opened before use or damaged, do not use the product.
- Always check the condition of the liquid before carrying out the procedure. Do not use the liquid component if it shows any sign of thickening or premature polymerization. These conditions indicate that the product has not been stored correctly.

Cement preparation
- For controlled and optimal use of the cement, the doses are to be stored at the recommended temperature of OPACITY+°C for a minimum of 24 hours before use.
- The duration of the cement working phases depends on the temperature of the room and those of the components, but also on the degree of relative humidity of the operating room. A high temperature reduces waiting, injection and hardening time. A low temperature extends these times.
- Prechilling of bone cement and accessories for at least 24 hours is recommended if a lower viscosity or a prolonged handling time is required. Mixing time is the same as for non-prechilled cement, however application time and hardening time are prolonged.
- The application phases of OPACITY+® cement have been determined using injection systems recommended by the manufacturer. They may vary when different systems are used. The recommended mixing time should be followed in order to prevent polymerization from progressing to such an extent that the cement is no longer fluid enough to allow easy transfer into the injection system and proper filling of the bone cavities.
- Additives (such as liquid antibiotics) are not to be mixed with the bone cement, as this will alter cement properties.
- The manufacturer does not recommend any surgical technique in particular; it is the responsibility of the healthcare professional to determine the appropriateness of the OPACITY+® cement and specific technique for each patient.

Personnel safety
- The liquid component is a powerful lipid solvent. Do not allow the liquid to come into contact with rubber or latex gloves. Should contact occur, the gloves might dissolve and tissue damage may occur. Wearing a second pair of gloves may diminish the possibility of hypersensitivity reactions.
- The liquid monomer is highly volatile and flammable.
- Make sure the operating room is properly ventilated to eliminate monomer fumes as much as possible.
- Make sure electrocautery devices are not used near freshly implanted bone cements as that could cause the ignition of monomer fumes.
- Caution should be exercised to prevent excessive exposure to the concentrated fumes of the monomer, which may cause drowsiness, irritate the respiratory tract, eyes and even the liver.
- Do not allow personnel wearing contact lenses to be near or be involved in mixing of the bone cement.

Monitoring during application
- During application of the bone cement, radiological control is essential so that the healthcare professional can follow the progress of the filling and stop the procedure if the slightest leakage of cement is detected.
- Use appropriate imaging techniques to verify correct needle placement, absence of damage to surrounding structures, and appropriate location of the injected cement. Use imaging, such as bi-planar fluoroscopy or CT guidance, to assess the

ability of the vertebra or the lesion to contain the injected bone cement.
- Avoid over-pressurizing the bone cement, as this may cause the bone cement to leak beyond the site of its intended application. Cement leakage may cause tissue damage, and nerve or circulatory problems. Excessive pressure can also be applied to the injection device, which could cause it to break.
- Leakages may also occur upon injection if the needle is in a vein or if there are undetected micro-fractures.
- The final polymerization stage occurs in situ and is an exothermic reaction with considerable liberation of heat. According to ISO 5833 standard, the temperature can reach up to 95°C. The heat produced in situ during polymerisation can lead in rare cases to modification of structure of the bone. Maintain the patient's position until the polymerization process has been completed, so as to obtain proper stabilisation.

Patient monitoring
- Adverse reactions affecting the cardiovascular system have been attributed to release of methylmethacrylate monomer into the circulatory system. Data indicate that the monomer undergoes rapid hydrolysis into methacrylic acid, and that a significant fraction of the circulating methacrylate is present in the form of free acid rather than methyl ester. Correlation between changes in circulating concentrations of methyl methacrylate / methacrylic acid and changes in blood pressure has not been established.
- Methyl methacrylate may cause hypersensitivity among high-risk persons, which can result in an anaphylactic reaction.

4.3. Other relevant aspect of safety, including a summary of any field safety corrective action (FSCA) if applicable

No field safety corrective actions have been issued for OPACITY+®.

5. Summary of clinical evaluation and relevant information on post-market clinical follow-up (PMCF)

5.1. Summary of clinical data related to equivalent device, if applicable

Not applicable. No devices are claimed equivalent.

5.2. Summary of clinical data from conducted investigations of the device before the CE-marking, if applicable

Not applicable. No clinical investigations have been conducted before the CE-marking.

5.3. Summary of clinical data from other sources, if applicable

a) Performance and safety of OPACITY+® were evaluated through a PMCF study performed in 2009.

Population: 126 patients (55 men and 71 women) with a mean age of 66.2 years. All patients (100%, n=126) presented simple or multiple vertebral compression fracture (VCF), most of them due to osteoporosis (52%, n=65) or malignant lesions (primitive or secondary tumours) (n=54, 43%) and only 3 (2.4%) to a trauma. A total of 169 vertebrae were treated.

Surgical procedure: Most procedures were performed by transpedicular access (n=159, 94.6%). Other procedures were unilateral extra-pedicular (n=7, 4.2%) or posterolateral access (n=2, 1.2%).

Clinical outcomes: *Pain*: A clear alleviation of pain was reported by all patients. At baseline, pain was described as 'disabling' (n=21, 16.7%), 'severe' (n=69, 54.8%), 'moderate' (n=29, 23%), 'mild' (n=5, 4%) or 'none' (n=2, 1.5%). At 6- month follow-up, 3.2% (n=4) of patients evaluated their pain as 'moderate', 1.6% (n=2) as 'mild', and 95.2% (n=120) as 'none'. Outcomes were identical at 12-month FU.

Function: Restoration of function was reported by all patients. Before the surgery, patients evaluated their daily life function as 'disabled' (n=11, 8.7%), with 'severe' impact (n=38, 30.2%), 'moderate' impact (n=55, 43.6%), 'mild' impact (n=19, 15.1%) or 'normal' (n=3, 2.4%). At 6-month follow-up, the function clearly improved with respectively 86.5% (n=109) and 94.4% (n=119) of patients reporting 'normal' function. Outcomes were identical at 12-month FU.

Safety: No perioperative complications were reported. Out of the 169 procedures, leakages were reported in 92 (54.4%) treated vertebrae, all without sequelae. Two other complications, unrelated to the cement, were reported: 1 patient with pain due to injection of the cement; 1 paravertebral hematoma.

Conclusion: This clinical study demonstrated the performance and safety of use of OPACITY+® bone cement vertebroplasty procedures for patients suffering from VCF.

b) Analysis of publications in the scientific literature with OPACITY+®.

Outcomes from a series of patients who beneficiated from a kyphoplasty procedure using a balloon of PET, expanded inside

the vertebral body by the injection of cement (OPACITY+®) was published in 2009[77] (vesselplasty). 29 patients (mean 69 ±12 years, range, 36–85) were enrolled in the study, for a total of 37 procedures. The cause of vertebral collapse was osteoporosis in 27 (73%) of the treated vertebrae. Other causes of VCF were high-impact trauma in five VCFs (13.5%), myeloma in 3 (8%), and metastatic fracture in 2 (5.4%). Transpedicular approach was used in 35 (94.6%) of the cases and parapedicular in 2 (5.4%).

There was no evidence of clinical complications and only one technical complication (2.7%): a small intradiscal leakage in a case of vertebral endplate displaced fracture with marked vertebral height loss, without clinical repercussion.

The pre-treatment pain score was 8.72 ±1.25, whereas the post-treatment pain score was 3.38 ± 2.35. The pre-treatment mobility score was 2.31 ±1.94, whereas the post-treatment score was 0.59 ± 1.05 ($p < 0.001$). 93% (n=27) of patients had an improved mobility score, with a decrease of 1.7 ± 1.6 points (range, 0–4 points). Patients with a malignant cause of VCF (myeloma or metastasis) experienced worse clinical outcome with less improvement in pain score and no improvement in mobility and medication requirement than patients with a benign cause of VCF ($p < 0.05$).

Authors conclude that vesselplasty offers statistically significant benefits in improvements of pain, mobility, and the need for analgesia in patients with symptomatic VCFs, thus providing a safe alternative in the treatment of these fractures.

5.4. Overall summary of the clinical performance and safety

OPACITY+® bone cement is a product issued from a well-known technology which has been used in interventional radiology and neurosurgery for many years. It allows successful consolidation of fractured vertebrae, leading subsequently to clinical benefits for the patients such as pain alleviation and improved quality of life. Claims for performance and safety of OPACITY+® have been verified and confirmed against outcomes from published series in scientific literature, and from Post-Market Clinical Follow-up (PMCF) studies, as described above.

5.5. On-going or planned post-market clinical follow-up

Teknimed has implemented and is currently conducting a post-market clinical follow-up to confirm clinical performance, and safety outcomes for all its Spine bone cements products, including OPACITY+®. A first interim analysis of the cohort of patients with OPACITY+® has been performed in October 2022. Summary of main outcomes is presented below.

Title: Safety and Clinical Performance Assessment of Bone Cements and Injection Systems used in Spine Surgery - A Post-Market Clinical Follow-Up

Population: 45 patients (32 women and 13 men) were already included at the date of this interim analysis, with a mean age at time of surgery of 72.7 years ±10.1). A majority of them (76%, n=34) suffered from osteoporotic vertebral compression fractures, and 4 patients (9%) suffered from benign and 3 (7%) from malignant symptomatic lesions, equally located in thoracic (47%) or lumbar (53%) area.

Surgical procedures: All procedures were vertebroplasties. Investigators assessed the filling phase as 'easy' and the device handling/usability as 'good' in 100% of the procedures. Leakages were observed in 5 (11%) patients, with no consequences. No other perioperative complications were reported.

Clinical outcomes. *Pain*: Cementoplasty procedures provided a clear alleviation of pain for all patients. At short-term FU (1.2 ±0.72 months), mean pain level decreased from a level of 8.0 ±1.65 at baseline to a level of 5.6 ±2.25 at FU, on a 10-point scale.

Function: The global Oswestry Disability Index (ODI) score decreased slightly from a mean value of 53.7 % at baseline to a mean value of 48.7% at follow-up.

Satisfaction: At FU, 89% of patients declared to be satisfied of their surgery.

Safety: 1 serious adverse event was reported which consisted in an adjacent vertebra compression fracture (L2) in a patient previously operated on L4 vertebra. A new vertebroplasty procedure was performed on L2 vertebra. This adverse event was qualified as "not related" to the device and "not related" to the procedure. 1 non-serious AE: an asymptomatic non-threatening small adjacent plateau fracture (proved by CT scan). No action was taken. This adverse event was qualified as "possibly related" to the device and "possibly" related to the procedure. These 2 adverse events were resolved without sequelae.

Conclusion: This short-term outcome analysis demonstrates that OPACITY+® is a safe device relevant to be used in procedures requiring spinal cementoplasty with a bone cement. Larger cohort and longer-term follow-up should allow to confirm its efficacy in vertebroplasty procedure.

[7] Flors L. et al. *Vesselplasty: A New Technical Approach to Treat Symptomatic Vertebral Compression Fractures*. AJR 2009; 193:218–226

6. Possible diagnostic or therapeutic alternatives

People with severe pain from vertebral compression fractures are traditionally treated with nonsurgical treatment including a reduction in activities, medications, and bracing. The first aim of conservative therapy is to control the pain. Therefore, medications such as bisphosphonate (alendronate and zoledronic acid), acetaminophen, and nonsteroidal anti-inflammatory drugs (NSAIDs) are often recommended in relieving pain. Muscle relaxing drugs for nerve/bone pain are often prescribed. Importantly, opioids should only be used for very short periods of time (1-2 weeks) for acute pain. Moreover, braces are also used to reduce pain as the rigid style of the back brace limits spine-related motion at the level of the fractured vertebra and thus allows bone healing.

7. Suggested profile and training for users

Implantation of TEKNIMED products should only be performed in an adapted environment and by health care professionals (radiologists, surgeons) having a sound knowledge and full mastery in preparation techniques specific to the product. Preparation techniques may be acquired from qualified distributors. The operator is responsible for any complications or harmful consequences which might result from an erroneous indication or operative technique, an improper use of the equipment and/or a failure to comply with the safety rules provided in the instructions for use. Neither the manufacturer nor the authorized representative can be held responsible for these complications.

8. Reference to any harmonized standards and CS applied

Standard reference	Standard revision	Standard title	Applicability
> General standards			
EN ISO 13485	2016/A11: 2021	Medical devices -- Quality management systems -- Requirements for regulatory purposes	Fully whenever applicable
EN ISO 14630	2012	Non-active surgical implants -- General requirements	Fully whenever applicable
EN ISO 14971	2019 / A11: 2021	Medical devices -- Application of risk management to medical devices	Fully whenever applicable
EN ISO 14155	2020	Clinical investigation of medical devices for human subjects — Good clinical practice	Fully whenever applicable
EN 62366	2015 / A1:2020	Medical devices – Application of usability engineering to medical devices	Fully whenever applicable
XP S99-223	2020	Medical Device – Benefit / Risk management	Fully whenever applicable
> Product standards			
ISO 5833	2002	Implants for surgery — Acrylic resin cements	Fully whenever applicable
ISO 13779-3	2018 / A1: 2021	Implants for surgery — Hydroxyapatite — Part 3: Chemical analysis and characterization of crystallinity and phase purity	Fully whenever applicable
ISO 13779-6	2015	implants for surgery — Hydroxyapatite — Part 6: Powders	Fully whenever applicable
ASTM F2118	2014	Standard test method for constant amplitude of force-controlled fatigue testing of acrylic bone cement materials	Fully whenever applicable
ISO 2859-1	1999/A1: 2011	Sampling procedures for inspection by attributes — Part 1: Sampling schemes indexed by acceptance quality limit (AQL) for lot-by-lot inspection	Fully whenever applicable
> Biocompatibility standards			

EN ISO 10993-1	2020	Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process	Fully whenever applicable
EN ISO 10993-2	2006	Biological evaluation of medical devices — Part 2: Animal welfare requirements	Fully whenever applicable
EN ISO 10993-5	2009	Biological evaluation of medical devices — Part 5: Tests for in vitro cytotoxicity	Fully whenever applicable
EN ISO 10993-10	2021	Biological evaluation of medical devices — Part 10: Tests for irritation and skin sensitization	Fully whenever applicable
EN ISO 10993-11	2018	Biological evaluation of medical devices — Part 11: Tests for systemic toxicity	Fully whenever applicable
EN ISO 10993-12	2021	Biological evaluation of medical devices — Part 12: Sample preparation and reference materials	Fully whenever applicable
EN ISO 10993-17	2009	Biological evaluation of medical devices — Part 17: Establishment of allowable limits for leachable substances	Fully whenever applicable
EN ISO 10993-18	2020 / A1: 2022	Biological evaluation of medical devices — Part 18: Chemical characterization of materials	Fully whenever applicable
EN ISO 10993-23	2021	Biological evaluation of medical devices — Part 23: tests for irritation	Fully whenever applicable

> Labelling and packaging standards

EN ISO 14698-1	2003	Cleanrooms and associated controlled environments — Biocontamination control — Part 1: General principles and methods	Fully whenever applicable
EN 556-1	2001 / AC: 2006	Sterilization of medical devices. Requirements for medical devices to be designated "STERILE". Part 1: requirements for terminally sterilized medical devices	Fully whenever applicable
EN 556-2	2015	Sterilization of medical devices — Requirements for medical devices to be designated ''STERILE'' — Part 2: Requirements for aseptically processed medical devices	Fully whenever applicable
EN 868-5	2018	Packaging for terminally sterilized medical devices — Part 5: Sealable pouches and reels of porous materials and plastic film construction — Requirements and test methods	Fully whenever applicable
EN 868-7	2017	Packaging for terminally sterilized medical devices — Part 7: Adhesive coated paper for low temperature sterilization processes — Requirements and test methods	Fully whenever applicable
EN ISO 11607-1	2020	Packaging for terminally sterilized medical devices — Part 1: Requirements for materials, sterile barrier systems and packaging systems — Amendmt 1	Fully whenever applicable
EN ISO 11607-2	2020	Packaging for terminally sterilized medical devices — Part 2: Validation requirements for forming, sealing and assembly processes — Amendmt 1	Fully whenever applicable
EN ISO 15223-1	2021	Medical devices. Symbols to be used with medical device labels, labelling and information to be supplied. General requirements	Fully whenever applicable
EN ISO 20417	2021/CORR : 2021-12	Medical devices — Information to be provided by the manufacturer	Fully whenever applicable
ASTM D 4169	2022	Standard Practice for Performance Testing of Shipping Containers and Systems	Fully whenever applicable
ASTM D 4332	2022	Standard Practice for Conditioning Containers, Packages, or Packaging Components for Testing	Fully whenever applicable
ASTM D 4728	2017	Standard Test Method for Random Vibration Testing of Shipping Containers	Fully whenever applicable
ASTM D 5276	2019	Standard Test Method for Drop Test of Loaded Containers by Free Fall	Fully whenever applicable
ASTM D 999	2008	Standard Test Methods for Vibration Testing of Shipping Containers	Fully whenever applicable
ASTM F 1929	2015	Standard Test Method for Detecting Seal Leaks in Porous Medical Packaging by Dye Penetration	Fully whenever applicable
ASTM F 88	2021	Standard test method for seal strength of flexible barrier materials	Fully whenever applicable

ASTM F1886 / F1886M	2016	Standard Test Method for Determining Integrity of Seals for Flexible Packaging by Visual Inspection 1	Fully whenever applicable
ASTM D 6653 / D 6653 M	2021	Standard Test Methods for Determining the Effects of High Altitude on Packaging Systems by Vacuum Method	Fully whenever applicable
ASTM D642	2020	Standard Test Method for Determining Compressive Resistance of Shipping Containers, Components, and Unit Loads 1	Fully whenever applicable
> Microbiology standards			
EN ISO 11737-1	2018/A1: 2021	Sterilization of medical devices — Microbiological methods — Part 1: Determination of a population of microorganisms on products	Fully whenever applicable
EN ISO 11737-2	2020	Sterilization of medical devices — Microbiological methods — Part 2: Tests of sterility performed in the definition, validation and maintenance of a sterilization process	Fully whenever applicable
EN ISO 11138-1	2017	Sterilization of health care products — Biological indicators - Part 1: General requirements	Fully whenever applicable
EN ISO 11138-2	2017	Sterilization of health care products — Biological indicators — Part 2: Biological indicators for ethylene oxide sterilization processes	Fully whenever applicable
ANSI / AAMI ST72	2019	Bacterial endotoxins — Test methods, routine monitoring, and alternatives to batch testing	Fully whenever applicable
> Gamma sterilisation standards			
EN ISO 11137-1	2015 / A2: 2019	Sterilization of health care products — Radiation — Part 1: Requirements for development, validation and routine control of a sterilization process for medical devices	Fully whenever applicable
EN ISO 11137-2	2015 / A1: 2022	Sterilization of health care products — Radiation — Part 2: Establishing the sterilization dose	Fully whenever applicable
> Ethylene oxide sterilisation standards			
EN ISO 11135-1	2014 / A1: 2019	Sterilization of health care products — Ethylene oxide — Part 1: Requirements for development, validation and routine control of a sterilization process for medical devices	Fully whenever applicable
EN ISO 10993-7	2008 / A1: 2022	Biological evaluation of medical devices — Part 7: Ethylene oxide sterilization residuals	Fully whenever applicable
> Aseptic processing standards			
EN ISO 13408-1	2015	Aseptic processing of health care products — Part 1: General requirements	Fully whenever applicable
EN ISO 13408-2	2018	Aseptic processing of health care products — Part 2: Filtration	Fully whenever applicable

9. Revision history

Revision number	Date issued	Change description	Revision validated by the Notified Body
1.0	OCT 2022	Creation	☐ Yes, language: English ☑ No
1.1	MAY 2023	- § 1.5.: Correction of the EMDN code - § 4.1.: Quantification of 'Other side effects'	☐ Yes, language: English ☑ No
1.2	AUG 2023	- § 4.1.: Additional quantification of side effects (Clinical review BSI) - § 4.2: mention to use no more than 1 unit of cement per patient (Technical review BSI)	☑ Yes, language: English ☐ No

A summary of the safety and clinical performance of the device, intended for patients, is provided on next page.

SUMMARY of SAFETY and CLINICAL PERFORMANCE (SSCP) for PATIENTS - English Version
OPACITY+®

This Summary of Safety and Clinical Performance (SSCP) is intended to provide public access to an updated summary of the main aspects of the safety and clinical performance of the device. The information presented below is intended for patients or lay persons. A more extensive summary of its safety and clinical performance prepared for healthcare professionals is found in the first part of this document.
The SSCP is not intended to give general advice on the treatment of a medical condition. Please contact your healthcare professional in case you have questions about your medical condition or about the use of the device in your situation. This SSCP is not intended to replace an implant card or the Instructions For Use to provide information on the safe use of the device.

1. Device Identification and general information

1.1. Device Trade Name: **OPACITY+®**

The medical device has also the following private labels:
OSSEOFIX+ (ALPHATEC) / EXOFIX (TEKNIMED) / OSTEOFLEX LV (ZAVATION) / THERMALFIX (IZI MEDICAL PRODUCTS LLC) / Synth-X SL (HC biologics) / Merit Fastrak VP (Merit Medical Systems, Inc) / LV 45 (TEKNIMED) / 12,5 CEM (TEKNIMED) / ZR+ (TEKNIMED) / BLACK C (TEKNIMED) / SAFE CEM (TEKNIMED) / OPT15 (TEKNIMED) / PMM+ (TEKNIMED).

1.2. Manufacturer name and address(es):

TEKNIMED S.A.S.		
Headquarters 8, rue du Corps Franc-Pommiès 65500 Vic en Bigorre France	*Production and facilities* 11-12, rue d'Apollo - ZI de Montredon 31240 L'Union France	*Distribution site (labelling)* ZI de la Herray 65500 Vic en Bigorre France

1.3. Basic UDI-DI: **376017704B05D2**

1.4. Year when the device was first CE-marked: **2006**

2. Intended use of the device

2.1. Intended purpose

OPACITY+® is a bone cement. It can be used in to stabilize a vertebra (palliative percutaneous cementoplasty procedures such as vertebroplasty or kyphoplasty).

2.2. Indication(s) and intended patient groups

OPACITY+® bone cement is used to treat vertebral fractures (fixation of painful vertebral compression fractures).
Target population: Adult patients with fractures of vertebra due to bone loss (osteoporosis), lesions (benign or malignant), trauma.

2.3. Contraindications

- Procedures other than those stated in the INDICATIONS section
- Disorder related to blood clot formation (coagulation);
- Severe conditions that affect heart and lungs (cardiopulmonary disease);
- Fracture of vertebra which are not stable;
- Damaged vertebra (compromise of the vertebral body or of the pedicle walls);
- Intolerance to constituents of the product (hypersensitivity or allergy);
- Patients clearly improving on treatment not using Opacity+;
- Use in prevention (prophylactic) in patients having spine disorders without fracture (metastatic or osteoporotic patients with no evidence of vertebral fracture);
- Not enough data are available on some categories of patients. Opacity+® cannot be used in children. Opacity+® cannot be

used in breast-feeding or pregnant women.

3. Device description

3.1. Description of the device

OPACITY+® is an acrylic bone cement. It can be injected directly into the damaged bone through the skin (percutaneous use). It is used to stabilise damaged bones (vertebra for example). The result is an effective and rapid pain relief for the patient.



This bone cement is made of two sterile components: a powder and a liquid. They need to be mixed at the time of use.

Composition	% (w/w)
POWDER – 27.2G	
PMMA (Polymethylmethacrylate)	49.5
Benzoyl peroxide (BPO)	0.5
Zirconium oxide (ZrO_2)	45.0
Hydroxyapatite	5.0
LIQUID – 9.2g	
MMA (Methylmethacrylate)	99.0
N, N dimethyl-p-toluidine (DMPT)	0.71.0
Hydroquinone	20ppm

The powder is made of polymers (polymethylmethacrylate - PMMA). It also contains an additive to start the hardening reaction (Benzoyl peroxide - BPO). Two other products are added to appear dark on X-ray images (Zirconium dioxide – ZrO2 and hydroxyapatite - HAP).

The liquid is made of monomers (methyl-methacrylate - MMA). An additive is added to start the hardening reaction (N, N dimethyl-p-toluidine - DMPT). It helps to control the reaction and the generated heat. A last additive (hydroquinone) is used in very small quantity. It avoids any premature hardening reaction during storage.
During surgery, powder and liquid are mixed. A liquid mixture is obtained. It becomes harder and harder over time. It finally becomes fully solid at the end of the reaction. Injection must be done when liquid. The final hardening phase occurs inside the bone.

OPACITY+® expected lifetime is 10 years. At the end of this expected lifetime, the cement does not need to be removed and does not need any maintenance. The cement can remain in place all lifelong, unless a medical complication would require a new surgery.

The product (powder and liquid) is supplied sterile. It is a single use product.

4. Risks and warnings

Contact your healthcare professional if you believe that you are experiencing side-effects related to the device or its use or if you are concerned about risks. This document is not intended to replace a consultation with your healthcare professional if needed.

4.1. Remaining risks and undesirable effects

- Leakage of bone cement outside the treated bone. They are frequent: rates up to 56% have been reported in the literature, and in a clinical study with OPACITY+® (Cf. section 5.2 below). These leakages are almost always asymptomatic. Yet, in some cases, when the cement penetrates into the vascular system, leakages can result in embolism of the lung and/or heart or other clinical sequelae (rates up to 1.5% have been reported in the literature, none concerning OPACITY+®)
- Unexpected or unintended effect to blood circulatory system (cardiovascular system) (also known as Bone Cement Implantation Syndrome) with a rate of 0.43% reported in the literature. It includes chest pain, a heart rate that is too fast (tachycardia), signs of severe respiratory distress, and death. They may be due to the hardening reaction (MMA monomer release in the blood during polymerisation, and/or to excessive exothermic reaction, and/or to too much pressure applied during cement injection). For this reason, blood pressure should be monitored after implantation. The anaesthetist should be told when the bone cement is implanted.
- Some patients suffered from fracture around the time of surgery. Fracture of ribs, of posterior element or of pedicle in patients suffering from diffuse osteopenia or osteoporosis, in particular during thoracic vertebroplasty procedures, due to the high pressure exerted downwards while the needle is being inserted (less than 1% of cases); Fracture or collapse of a vertebra adjacent to the one injected due to an osteoporotic disease (up to 23% in the literature, 1 case (2.2%) in a clinical study with OPACITY+®).
- Some incidents were reported after surgery in a clinical study with OPACITY+: 1 case of paravertebral hematoma (0.8%) and 1 case of pain due to injection of the cement (0.8%).

Other side effects include:

- Allergy to one of the bone cement constituents (rate up to 1.4% reported in the literature);
- Exposure of the health care operators to monomer fumes.

Any serious incident occurring in relation to the device must be reported without delay to TEKNIMED and the competent local authority where the user and/or the patient is established.

4.2. Warnings and Precautions

No warning and precautions for patients. This device is only used by healthcare professionals. Patients with intolerance to bone cement components should mention it to their surgeon.

4.3. Summary of any field safety corrective action (FSCA) if applicable

None. No FSCA have been issued since the release of OPACITY+® on the market.

5. Summary of clinical evaluation and post-market clinical follow-up

5.1. Clinical background

OPACITY+® bone cement comes from a safe technology. It has been used in surgery for many years. It treats fractured vertebrae. Patients have pain alleviation. Patients have improved quality of life. Performance and safety have been shown by clinical studies.

5.2. Clinical evidence for CE marking

A clinical study has been done in 2009 in France. It evaluated performance and safety.

Patients were treated in spine (126 patients with simple or multiple vertebral compression fracture (VCF), most of them due to osteoporosis or malignant lesions (primitive or secondary tumours) or trauma). A total of 169 vertebrae were treated.

A clear pain alleviation was reported by all patients. A clear restoration of function for all patients was observed. No issues (complications) during surgery (perioperative) were reported. Leakages were reported in 92 (54.4%) treated vertebrae. All had no sequelae. Two other issues (complications) were reported. They were unrelated to the cement. 1 patient had pain (due to injection of the cement). 1 patient had a hematoma (paravertebral hematoma).

This study showed the performance and safety of the bone cement (used in vertebroplasty procedures for patients suffering from VCF).

A published scientific article studied Opacity+®. Bone cement is used in spine (kyphoplasty procedure using a balloon of

PET, expanded inside the vertebral body by the injection of cement). There was no evidence of clinical issues (complications). Only one technical issue (complications) occurred (a small intradiscal leakage in a case of vertebral endplate displaced fracture with marked vertebral height loss, without clinical repercussion).
Authors conclude on significant benefits for patient (improvements of pain, mobility, and the need for analgesia in patients with symptomatic VCFs, thus providing a safe alternative in the treatment of these fractures).
A clinical study is on-going (45 patients included up to now). All patients were treated in spine (vertebroplasty). Leakages were observed without consequences. No other issue during surgery were reported.

5.3 Safety

Teknimed is always doing clinical studies and surveys (scientific literature reviews, international safety database reviews and clinical follow-up studies). They document and evaluate the benefits and risks of the product.
Main risks during spine surgery have been identified: leakage outside of the bone, unexpected or unintended effect to blood circulatory system, fracture (ribs, posterior parts of the vertebra, or pedicles).
Main risks during surgery outside of spine are identified: leakage outside of the bone, infection after the surgery, new fracture (secondary fracture), and transient nerve injury.

6. Possible diagnostic or therapeutic alternatives

Patients who don't want to be treated with OPACITY+® have alternatives. They can reduce their activities. They can use medications. They can use bracing. The first aim of these alternatives is to control the pain. Different medications are often recommended in relieving pain (bisphosphonate (alendronate and zoledronic acid), acetaminophen, and nonsteroidal anti-inflammatory drugs (NSAIDs), as well as muscle relaxing drugs for nerve/bone pain). It is important to use opioids only for very short periods of time (1-2 weeks). Braces are used to limit motion of the spine. It allows bone to heal.

7. Suggested profile and training for users

Product should only be used in clinics or hospitals. It should be used by qualified health care professionals (radiologists, surgeons). They need to be expert in surgery using bone cements.