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 SSCP is not intended to replace the Instructions for Use (IFU) as the main document to ensure the safe use of the device, nor is it intended to provide diagnostic or therapeutic suggestions to intended users or patients.
The following information is intended for users/healthcare professionals.

1. Device identification and general information

1.1. Trade name(s)

INNOTERE Paste-CPC
VELOX
CERASORB CPC

1.2. Manufacturer's name and address

INNOTERE GmbH
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1.3. Manufacturer's single registration number (SRN)

DE-MF-000006515

1.4. Basic UDI-DI

++EINNPCT3

1.5. European Medical Device Nomenclature (EMDN)

P900402 – Resorbable filling and reconstruction device

1.6. Class of device

Class III, according to Rule 8, number 3 of the EU Regulation 2017/745 (MDR), Annex VIII, chapter III.

1.7. Year of first certification (CE)

2014, year of first CE-mark under MDD 93/42/EEC

1.8. Authorized representative

N/A

1.9. Notified Body and single identification number

TÜV Rheinland LGA Products GmbH
No. 0197

2. Intended use of the device

2.1. Intended purpose

Paste-CPC is a synthetic, self-setting bone graft substitute for filling non-infected bone defects.

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

Paste-CPC is intended for filling non-infected and non-load-bearing bone defects or for filling bone defects that have been sufficiently stabilised by means of suitable measures.

Particular areas of application are:

- metaphyseal bone defect fractures, e.g. fractures of the tibia, radius and humerus
- bone defects following resection of benign tumours and cysts
- bone defects after removal or replacement of osteosynthetic implants
- support for the fixation of osteosynthetic implants (e.g. of bone screws)

Intended patient population: Adults

2.3. Contraindications and/or limitations

Paste-CPC is not to be used in the case of:
- acute or chronic infections at the implant site, e.g. osteomyelitis
- bone defects due to malignant tumours
- bone defects in the area of open epiphyseal joints
- known intolerance to any ingredient of Paste-CPC (see composition)

Paste-CPC is not be used in the following cases as there is no clinical experience so far:
- augmentations in the area of the spine
- cranioplasty
- pregnant or breastfeeding women
- children; with a known dose limitation of 3 ml Paste-CPC per surgery

Paste-CPC is to be used only after individual risk-benefit assessment in the case of:
- bone metabolism disorders
- endocrinopathies
- immunosuppressive therapy
- concurrent therapy with drugs that affect bone metabolism

3. Device description

3.1. Description of the device

Paste-CPC is a synthetic, self-setting, biocompatible, osteoconductive and bioresorbable bone graft substitute for filling non-infected and non-load-bearing bone defects. The material is applied from the syringe or with the cannula attached directly into the bone defect. The setting reaction starts upon contact with bodily fluid, leading to a microcrystalline, calcium-deficient hydroxyapatite and alpha-tricalcium phosphate. The product does not contain substances of animal origin, added preservatives, or pharmacologically active agents. It is sterilized by gamma radiation and replaced by endogenous bone by biological processes.

3.2. Product variants

The product family Paste-CPC comprises procedure packs consisting of an application system with syringe / applicator filled with Paste-CPC and cannula. These procedure packs are available in three product variants (PV) which vary in the application system (syringe / applicator) and the filling quantity with paste. The application system of PV1 (3 ml) and PV2 (1 ml) are conventional syringes with plungers, while the PV3 (14 ml) uses applicator combined with a spindle nut and spindle drive for the application of Paste-CPC.

For the multiple syringe packaging configurations of PV2, the number of cannulas is equal to the number of syringes in each package. The procedure packs have undergone a conformity assessment, UDI and CE marking. The product family Paste-CPC is marketed under three trade names, INNOTERE Paste-CPC, VELOX and CERASORB CPC.

The product family Paste-CPC includes the Medical Device Directive (MDD) legacy device and the device to be certified according to MDR 2017/745 (MDR device). The MDR device is the same product of the product previously CE marked under the MDD 93/42/EEC that is marketed by INNOTERE for the same intended use under the same trade names. The following table shows the currently available product variants for the legacy device and the planned ones for the MDR device.

Article number	Product name
111VX2	INNOTERE Paste-CPC 3 ml
211IP1	INNOTERE Paste-CPC 1 ml
231IP1	INNOTERE Paste-CPC 3x1 ml
311IP2	INNOTERE Paste-CPC 6 ml
311IP1	INNOTERE Paste-CPC 12 ml
111VXE	VELOX 3 ml

Article number	Product name
211VX1	VELOX 1 ml
231VX1	VELOX 3x1 ml
311VX2	VELOX 6 ml
311VX1	VELOX 12 ml
3019150	CERASORB CPC 1 ml
9100000002	CERASORB CPC 6 ml
9100000003	CERASORB CPC 12 ml

3.3. Description of accessories
N/A.

3.4. Other devices used in combination with Paste-CPC
Paste-CPC can be used to support the fixation of osteosynthetic implants, e.g. for augmentation of bone screws. In this context, Paste-CPC can be used in the drill channel to augment osteoporotic bone or applied through cannulated screws.

4. Risks and warnings
4.1. Residual risks and undesirable side effects
Product- and treatment-related side effects include: Swelling, seroma and hematoma formation, fever, allergic reaction, pain, fracture of the implant, wound healing disorders, rejection reaction, infection, delayed or non-union (pseudoarthrosis).

4.2. Warnings and precautions
The use of Paste-CPC is restricted to professionals familiar with the handling of bone graft substitutes, the relevant surgical techniques and the treatment of bone defects.

Paste-CPC is intended for single use on a single person.

Paste-CPC may only be applied after sufficient debridement in a well-vascularized, infection-free bone bed. In addition, correct reduction and stabilization of the fracture must be ensured. Direct contact between Paste-CPC and the surrounding bone is only ensured if the bone defect is completely filled.

When using Paste-CPC, leakage of the bone substitute material into adjacent soft tissue or blood vessels must be avoided. In order to prevent embolism, it must be ensured that no bone substitute material enters open venous or arterial accesses, especially when applied under pressure in defects that are enclosed on all sides.

In the case of heavily bleeding bone defects, the bleeding must first be under control before Paste-CPC is applied. Otherwise there is a risk that the bone substitute will be forced out again by the bleeding pressure.

Due to its mechanical properties, Paste-CPC can support the stabilization of bone defects. However, the actual stabilization must be ensured by other measures.

Paste-CPC must not be mixed with aqueous solutions prior to application, including those of autologous or allogeneic origin (e.g. blood), as this may alter the material properties of Paste-CPC.
Paste-CPC is slowly resorbed in the course of natural bone metabolism and replaced by the body's own bone. Depending on the implantation conditions and the metabolic activity at the implant site, Paste-CPC can also remain permanently in the body as a bone-integrated material.

Treatment of postoperative infections may be complicated by the presence of an implanted foreign body and may require removal of the bone graft substitute. Revision surgery may be required due to undesirable side effects of the surgical procedure.

Particularly in immunocompromised patients (e.g. rheumatics, diabetics) and addicts, it should be noted that there may be an increased risk of infection and implant failure. Such patients must be informed by the medical staff about the possible dangers before the operation.

For the component polyoxyl-35-castor oil contained in Paste-CPC, very rare cases of allergic reactions and anaphylactic shock have been described in the literature. The aforementioned dosage restriction is derived from this.

Paste-CPC contains 24 mg of potassium per millilitre in the form of K_2HPO_4. In patients with severely impaired renal function, adrenal insufficiency or liver cirrhosis, lower amounts of additionally absorbed potassium may increase the risk of hyperkalaemia or exacerbate existing hyperkalaemia. This also applies to patients with decreased renal potassium excretion induced by drug administration (e.g., heparin, ACE inhibitors, potassium-sparing diuretics, spironolactone, nonsteroidal anti-inflammatory drugs, cyclosporine A). Since potassium is released from Paste-CPC only successively and the amount contained corresponds to only a fraction of the amount ingested daily with food, only a low risk is to be assumed even in the case of severely impaired kidney function.

4.3. Other safety relevant aspects
There were no field safety corrective actions (FSCA) in 2023.

5. Summary of clinical evaluation and post-market clinical follow-up (PMCF)
5.1. Summary of clinical data
INNOTERE has obtained one investor-initiated study involving Paste-CPC. The retrospective case series evaluating the use of INNOTERE Paste-CPC for bone defect filling after complex tibial head fractures with severe closed soft tissue lesions demonstrated promising results. For complex tibial plateau fractures, the achievement of a bone healing rate of more than 80% is considered a clinical success. In this study, stable bone consolidation was achieved in 85.7% of cases after 6 month and there were no biomaterial-associated side effects. FRI was experienced in tibial head fractures with severe C3 soft tissue lesions. Quality of life assessment revealed satisfying overall health states and quality of life in patients with this complex injury.

5.2. Summary of clinical data before the CE-marking
N/A

5.3. Summary of clinical data from SOTA
Despite the profound clinical and economic impact, the management of bone defects remains controversial which is in part related to the size of the defect and how to determine whether the defect is critical sized. What constitutes a ''critical-sized defect'' varies with the anatomic location of the defect as well as the state of the soft tissues surrounding it. Bone defects that do not heal spontaneously can develop into atrophic non-unions because of the nature of the fracture, with impaired vascularity and soft tissue injury.

Calcium phosphate cement (CPC) is obtained by mixing one or several reactive calcium phosphate powders with an aqueous solution to form a paste that hardens in situ within a reasonable period of time (minutes). Numerous CPC formulations have been proposed over the years; according to end products of the CPC reaction they are classified in brushite or apatite such as hydroxyapatite or calcium-deficient hydroxyapatite. The setting of CPC is based on a dissolution-precipitation mechanism, which is induced by mixing calcium phosphate powders with a liquid phase. The precipitated crystals interlock to form a hard mass. The advantages of CPC are no exothermic reaction and setting without shrinkage. In addition, its composition is similar to the mineral phase of bone, rendering excellent bone biocompatibility.

Conventional CPC are prepared just before implantation since setting starts from the moment that the powder comes in contact with water. Pre-mixed (= ready-to-use) products are available on the market only as non-setting calcium phosphate preparations.

Alternative treatment options in bone replacement include the use of autologous bone grafts (autograft); bone grafts of other human individuals (allograft) or animal origin (xenograft), synthetic bone grafts substitutes (BGS), or a combination of any of these options. Major disadvantages of autografts are persistent pain at the harvest site, limited availability and for allografts and xenografts the residual risks of infection or disease transmission.

The majority of clinical outcomes with CaP grafts in bone replacement confirm the excellent biocompatibility, minimal side effects, good bone substitute integration and confirm the material

properties supporting the bone healing, remodelling and regeneration process; the low allergy potential. Functional outcome was improved in many cases but not correlated to bone integration. For a limited amount of bone loss, whenever there is good contact between the BGS and the surrounding bone tissue and/or a stabilization can be realised, CaP graft represents an effective and safe treatment of bone defects and fractures with good functional recovery and no inflammatory reactions.

According to the literature safety data confirms the low rate of complications due to the CPC properties. Undesirable side-effects include swelling at the operation site, pain, bleeding, local inflammation and numbness that are associated with surgery rather than the cement material Major complications such as non-union requiring revision, infection and foreign-body reaction were rare in the majority of studies.

Injectable CPC are increasingly applied in minimal invasive surgery due to the material properties. They are widely used as injectable bone void fillers/bone graft substitutes, in which they are injected into the osseous defects (e.g. treatment of complicated bone cysts in children) or bone defects secondary to traumatic injury to the bone (e.g. augmentation of the fixation of displaced intra-articular calcaneal fractures). CaP based BGS are used both in adults and in children but the majority of cases are reported in adults with favourable outcomes. There is few clinical data available for children and no data for pregnant and lactating women to draw conclusions.

5.4. Overall summary of the clinical performance and safety

The clinical benefit of Paste-CPC is its ability to fill, reconstruct and/or fuse bone defects to promote bone regeneration.

Paste-CPC belongs to the resorbable bone substitute materials due to its composition. There is clinical evidence of the resorption capacity of Paste-CPC in the form of case studies. In addition, this aspect is currently being investigated in an ongoing pilot study (DRKS-ID DRKS00025444).

Undesirable side effects associated with Paste-CPC include general surgical or anesthesia-related symptoms (e.g., pain, hematoma, seroma, swelling, fever, local inflammatory reactions), infections, wound healing disorders, allergic reactions, rejection reactions, and delayed or non-union (pseudarthrosis). No device related risks are known for the use of Paste-CPC. The precautions and warnings in the instructions for use must be followed.

As of the present, no undesirable side effects directly attributed to Paste-CPC have been reported. However, it is worth noting that in the literature, rare instances of allergic reactions and anaphylactic shock have been associated with the organic component of Paste-CPC, Polyoxyl-35-castor oil. Therefore, a dose limitation has been established as a safety precaution when using Paste-CPC.

Paste-CPC is recommended for the use in adults. To date, no studies involving children, pregnant individuals, or lactating women have been conducted. As a precautionary measure, the use of Paste-CPC in children and in individuals who are pregnant or breastfeeding is not recommended.

Based on the clinical data, it can be confirmed that the benefits of Paste-CPC outweigh the potential risks when used as intended. The benefit-risk ratio of Paste-CPC is considered acceptable, confirming its benefits in clinical use."

5.5. Ongoing PMCF

Currently, INNOTERE is observing two investor-initiated studies involving Paste-CPC.

One pilot study is referenced in the german clinical trial register under DRKS-ID DRKS00025444. Substantial defect humeral head fractures are often difficult to treat. Surgical management includes percutaneous anatomic reduction and stable fixation to ensure early mobilization and minimal surgical trauma. To increase stability, the void created after anatomic reduction is usually filled with an autologous or synthetic bone graft substitute. Because bone grafts provide limited stability, synthetic bone substitutes such as calcium phosphate cements have been evaluated and shown to result in more stable anatomic reduction compared with autologous grafts. In this prospective pilot study, 15 patients are treated with the bone graft substitute INNOTERE Paste-CPC, which is filled into the respective bone cavity using a decompression cannula (Arthrex Company). The decompression cannula allows comfortable reduction of depressed fractures with a minimally invasive procedure. The Arthrex PEEKPower humeral fracture plate is used for fixation. Within the first 48 hours after

surgical treatment, a CT scan of the affected humeral head is performed. The raw data set from this examination is then sequenced using specially adapted software and the exact amount of calcium phosphate cement is determined. In a second CT scan of the same region after 9 months, this procedure can be used to determine the amount of calcium phosphate cement that has degraded and been replaced by endogenous bone during this period.

The second investor-initiated study is a comparison of resorbable vs. non-resorbable cement for augmentation of proximal humerus fractures. Proximal humerus fracture (PHF) is a common fracture (5%) that is challenging to treat, especially in the elderly with osteopotic bone. Despite its frequency, there are no clear guidelines or evidence-based treatment recommendations for PHF. Cement augmentation of humeral head screws is a concept to reduce the complications such as cutting out in angular stable plate osteosynthesis. To date, non-absorbable PMMA cement has been predominantly used for screw augmentation in PHF. PMMA cements lead to local heating of the bone due to an exothermic setting reaction with the risk of bone tissue damage or hazards to the surrounding tissue. Resorbable calcium phosphate cements could be an alternative, provided their mechanical properties are adequate. In a preliminary biomechanical study, it was shown that there is no significant difference in primary stability between PMMA cement and the resorbable calcium phosphate cement of INNOTERE in osteoporotic bone. This Prospective, randomized clinical observational study investigates bone healing and clinical outcomes after screw augmentation with a PMMA cement and the resorbable calcium phosphate cement INNOTERE Paste-CPC.

6. Possible diagnostic or therapeutic alternatives

Managing bone defects involves complex considerations, including critical defect size, location, patient health, and underlying conditions. In some cases, even non-critical defects may warrant the careful evaluation of bone cement use. There are various bone substitute materials and bone cement available, each with specific pros and cons. These materials fall into three main categories: autologous bone, allografts, and synthetic materials.

- Autologous bone, considered the gold standard due to osteogenic, osteoinductive, and osteoconductive properties. However, it comes with drawbacks such as harvesting morbidity, persistent pain at the graft site, and limited availability.
- Allografts offer osteoconductive properties but carry potential infection risks, including viral transmission.
- Synthetic materials (alloplasts) are available in various forms, including ready-to-use and two-component mixing kits, enabling precise defect filling and providing user-friendly options for surgeons. They encompass osteoconductive, resorbable bone cements based on calcium phosphate, and polymethylmethacrylate (PMMA), which generate heat during the curing process and are non-resorbable.

The use of any bone graft substitute or cement is not an option for non-critical defect sizes that will heal naturally without medical intervention.

7. Suggested profile and training for users

Paste-CPC is intended for use by healthcare specialists trained in the treatment of bone defects. Device-specific training is not required for its use.

8. Reference to any harmonized standards and common specifications applied

There are no common specifications applicable for the product family Paste-CPC.

DIN EN 556-1:2024, DIN EN ISO 10993-3:2015, DIN EN ISO 10993-5:2009, DIN EN ISO 10993-9:2022, DIN EN ISO 10993-10:2023, DIN EN ISO 10993-11:2018, DIN EN ISO 10993-12:2021, DIN EN ISO 10993-14:2009, DIN EN ISO 10993-17: 2024, DIN EN ISO 10993-23:2021, DIN EN ISO 11137-1:2020, DIN EN ISO 11737-1:2021, DIN EN ISO 11737-2:2020, DIN EN ISO 13485:2021, DIN EN ISO 14602:2012, DIN EN ISO 14971:2022, DIN EN ISO 15223-1: 2022