CONTIPRO

# Summary of safety and clinical performance
# Sicalm HA®

**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 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.**

Issued by: Jana Poslušná

Signature:

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Reference number: SSCP-SIC-77

Document revision: 06

## 1. Device identification and general information

1.1. Device trade name:
Sicalm HA®

1.2. Manufacturer's name and address:
Contipro a.s., Dolní Dobrouč 401, Dolní Dobrouč 56101

1.3. Manufacturer's SRN (single registration number):
CZ-MF-000014702

1.4. Basic UDI-DI
859 51637 7700 N8

1.5. Medical device nomenclature description / text:
EMDN code Q010399 – Surgical dental devices – Other.

1.6. Class of device:
Class III, according to Annex VIII of MDR, rule 14

1.7. Year when the first certificate (CE) was issued covering the device: 2023

1.8. Authorised representative if applicable; name and the SRN:
N/A

1.9. NB's name (the NB that will validate the SSCP) and the NB's single identification number
Notified Body No. 2265
3EC International a.s.
Hraničná 18
821 05 Bratislava
Slovakia

## 2. Intended use of the device

2.1. Intended purpose

Sicalm HA is a sterile medical device designed for the mechanical protection and healing of traumatized tissue in oral cavity.

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

Indication: Sicalm HA is intended for the treatment of alveolar osteitis (also known as dry socket) and for wound care after dental surgical procedures.

Target population are adult patients (without age or weight limitations) after tooth extraction and after dental surgical procedures.

2.3. Contraindications and/or limitations

Do not combine with agents containing alcohol (e.g. Chlumsky solution, some mouthwashes). The efficacy of Sicalm HA may be lowered when combined with agents containing iodine, PVP-iodine or other oxidizing agents.

Currently, there are no known contraindications for the local administration of sodium hyaluronate. In hypersensitive individuals, the octenidine hydrochloride contained in the product may cause an allergic reaction. It is not recommended to use the Sicalm HA in the presence of an abscess or pus.

Limitation: There are no known limitations of the use of the product, or the substances contained in the product.

## 3. Device description

### 3.1. Description of the device

The product is in the form of a soft freeze-dried tampon that may be formed as required. The tampon is composed of freeze-dried sodium hyaluronate, octenidine and calcium chloride.

Mode of action

Sodium hyaluronate a linear, negatively-charged polysaccharide that is a natural compound of the body, therefore, it is a non-toxic substance and does not cause any allergic or adverse reactions. SH is present in virtually all human and animal tissues, mainly as the component of extracellular matrix (ECM). Sodium hyaluronate has unique physical-chemical properties and thanks to its biocompatibility, non-toxicity, biodegradability and ability to absorb water, SH is widely used as a hydrogel capable to regulate hydration and osmotic balance in tissues. SH is able to form a thin film on the surface of skin and mucosa, therefore it serves as a mechanic barrier.

Freeze-dried sodium hyaluronate forms a tampon with a porous sponge-like structure, providing large surface area for contact. In a wet environment,

the tampon structure quickly turns into a gel. In its dry state, the product adheres well to the treated tissue and, thanks to the calcium chloride, will stay in place of application. The gel delivers safe and natural physical conditions for the healing process. The gel also fills the wound and provides mechanical protection against traumatization.

Antimicrobial effectiveness

Octenidine dihydrochloride (N,N'-(1,10-decanediyldi-1[4h]-pyridinyl-4-ylidene) bis-(1-octanamine) dihydrochloride) is an antiseptic substance, preventing infection that could slow down the healing process. Octenidine has rapid onset of action, it is active against a wide spectrum of Gram-positive and Gram-negative bacteria, fungi and plaque-producing organisms even at low concentrations.

Pharmacokinetic studies with octenidine dihydrochloride indicate a low systemic exposure after cutaneous and mucosal application. The report No. EMA/CVMP/735219/2009 of European Medicine Agency confirms, that octenidine does not penetrate through the intact skin at all (assessed in porcine, bovine, equine, feline and canine skin) and its penetration through the skin with disrupted barriers is negligible (0.6 % in porcine skin and 2.7 % in bovine skin). In case of 14-day mucosal application (vaginal) in rabbits, no octenidine was detectable in serum.

Octenidine is poorly absorbed also by oral administration. The elimination of the substance is mainly in the faeces and no accumulation in the body was observed. Sporadically observed adverse effects (gaseous distension, emesis, salivation, anorexia) after oral administration of higher doses of octenidine to experimental animals are suggested to be a consequence of a change in gut flora induced by octenidine. Octenidine is neither absorbed by disrupted/non-

disrupted skin, nor via the/ mucousa membrane, nor after oral administration, therefore it causes no systemic effects and is non-toxic, even during long term use.

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

N/A

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

N/A

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

N/A

## 4. Risks and warnings

4.1. Residual risks and undesirable effects

Sodium hyaluronate cause no side effects and is generally well tolerated. Currently no side effects are known.

Following octenidine application, a warm sensation may infrequently be observed at the site of administration. In hypersensitive individuals, octenidine may cause an allergic reaction, which may manifest itself as a burning sensation, irritation and swelling at the site of application. In rare cases, nausea and change of taste (dysgeusia) may be observed.

Any side effects or unusual reactions must be discussed with a dentist.

4.2. Warnings and precautions

Intended for use in oral cavities. Do not use if the product packaging is damaged. Do not use after date of expiry. Expired product has to be disposed with hazardous waste. Do not use if the tampon is damp. Keep out of reach of children. Do not use for self-treatment. Apply under sterile conditions.

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

N/A

## 5. The summary of clinical evaluation

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

Assessing various products intended to treat alveolar osteitis and other wounds in oral cave with different design no equivalent device was found on the market that would give sufficient equivalency for clinical evaluation. Commercially available products differ in either construction, composition or the way of use (Taberner-Vallverdú, M, 2015).

- **Taberner-Vallverdú, M**.; Nazir, M.; Sánchez-Garcés, M.Á.; Gay-Escoda, C. Efficacy of different methods used for dry socket management: A systematic review. Med. Oral Patol. Oral Cir. Bucal. **2015**, 20, 633–639.

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

During the development of Sicalm HA, both bench and animal testing have confirmed safety and efficacy of the HA/octenidine combination. It has been shown that for successful support of healing, it is essential to use both components to achieve an advantage given by the product structure. The most suitable concentration octenidine was identified in order to reach the best results both in the support of extraction wound healing as well as infection management provided by the presence of the antiseptic component and not to cause any adverse reaction on the device.

Clinical investigation of the device showed significant decrease in inflammatory signs in the extraction wound (mainly pain) in wounds treated with investigational device. The subjective evaluation of positive effect was significant also in wound infection management as assessed by investigators. Very good efficacy of Sicalm HA was confirmed thanks to the properly selected device properties and mechanism of achievement of the device intended use.

Good tolerability to the product was confirmed in animal studies as well as in clinical investigation. During the clinical trial the average duration of exposure to the treatment was 4.8 days with minimum and maximum of 1 and 9 days respectively. Clinical investigation showed very good tolerability and safety of the investigated device with no detected adverse device effect. There was no serious adverse event reported.

From all these safety findings we can consider the use of Sicalm HA as generally safe without major risk to the patient or user.

The clinical evidence demonstrates conformity with relevant Essential Requirements.

The Risk/Benefit ratio is discussed in the Risk Management process. Data gathered from clinical investigation of the device showed no risk to the patient. Other expected risks were gathered from literature review of standard of care of alveolar osteitis. The main benefit of the device is to provide good environment for the healing of extraction wound and provide mechanical barrier/protection of extraction wounds. These are expected to provide listed benefits to the physician and patient. Residual risks connected to the device use can be prevented by proper use and storing of the device according to instructions for use listed in product leaflet. Device deficiencies were as well discussed during risk analysis and there is highly negligible chance to deficient product could be given to the final user. Device is not to be used in case the package of the product is damaged, as it is mentioned in the package leaflet.

Post-marketing surveillance system set by manufacturer is planning to gather more information from the device use in standard care and literature review as well as in PMCF trials. The main aim of the PMCF is to get information of alveolar osteitis prevention as well as to confirm good therapeutic effect on the alveolar osteitis treatment. From the obtained data from clinical investigation and this evaluation no risk was detected that need to be verified by PMCF trial. Nevertheless, as this is a new product and as the clinical investigation was performed on the small sample size (59 subjects) the first phase of the PMCF will include especially the bigger sample size and in other aspects will mostly copy the design of the first in man clinical trial. To copy mostly the standard use of the product the exclusion criterion of smoking is deleted from the PMCF plan (Suchanek, 2019).

- **Suchánek J**, Ivančaková R, Mottl R, Browne K, Pilneyová K, Pilbauerova N, Schmidt J, Kleplová T. Hyaluronic Acid-Based Medical Device for Treatment of Alveolar Osteitis—Clinical Study. International Journal of Environmental Research and Public Health. 16. 3698. 10.3390/ijerph16193698. **2019**

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

N/A

5.4. An overall summary of the clinical performance and safety

From results of clinical performance and all safety findings we can consider the use of Sicalm HA as generally safe without major risk to the patient or user.

Clinical benefits: Product accelerates the healing process and reduces the level of pain. Clinical investigation of the device showed significant decrease in inflammatory signs in the extraction wound (mainly pain) in wounds treated with investigational device. The subjective evaluation of positive effect was significant also in wound infection management as assessed by investigators.

5.5. Ongoing or planned post-market clinical follow-up

| | |
|---|---|
| Title | **Multi-centre, open-label PMCF study with Sicalm HA in adult patients suffered from alveolitis sicca** |
| Investigational Product | Sicalm HA |
| Number of Sites | 10-20 sites in Czech Republic<br>(clinical sites specialized on dental surgery will be selected from private practices, regional hospitals and university hospitals in Czech Republic) |
| Intended Use | Sicalm HA is a sterile medical device designed for the mechanical protection and healing of traumatized tissue in oral cavity. |
| Design | Multi-centre, open-label PMCF study. |
| Primary Objectives | To provide further data on safety of the device in terms of a clinical results as well as efficacy and thus usefullness of the drug component |
| Study Duration | The estimated trial duration is 36 months.<br>The recruitment period is about to start approx. Q2 2025. |
| Sample Size | 100 – 200 patients |
| Population | Adult patients suffered from alveolitis sicca |
| Inclusion/Exclusion Criteria | Inclusion Criteria<br>- Patient suffered from alveolitis sicca after tooth extraction<br>- Patient willing and able to provide the written consent<br>Exclusion Criteria<br>- Age < 18 years<br>- Pregnant or lactating woman<br>- Patient in terminal stage of living<br>- Patient with known hypersensitivity or allergy to any of |

| | |
|---|---|
| | substances contained in Medical Device<br>- Patient participating in other interventional clinical study |
| Investigational Product Design | The product is a Class III Medical Device incorporating medicinal substances (antiseptic-octenidine, sodium hyaluronate). The device is a tampon for dentistry use. Sponge structure is made by sodium hyaluronate polysacharide stabilised by calcium chloride. |
| Investigational Product Administration | Device is administered directly into the extraction wound after washing by 3% solution of hydrogen peroxide or water stream.<br>The frequency of administration is up to once per day. Duration of the treatment will be up to 7 administrations. Treatment with the investigational device is terminated either after fadaway of pain, no effect in pain reduction after first three days of treatment or after 7 administrations of study device. |
| Control product | No |
| Efficacy Measurements | Primary Endpoint<br>- Fadeaway of inflammation symptoms in the extraction wound.<br>Secondary Endpoints<br>- Control of infection (subjective evaluation of investigator)<br>- Investigator satisfaction with the device use<br>- |
| Safety Criteria for Evaluation | Each patient will be routinely assessed for any signs of potential adverse events in terms of pain, allergic reactions or infection within the wound.<br>Based on previous clinical experience, there are no expected adverse device effects in the use of this device. |
| Statistical considerations | The analysis will include collected and derived continuous and categorical variables. Descriptive statistics will be provided for each of the criteria. A descriptive analysis of major protocol violations will be prepared for each subject. |

### 5.6. Statement of conformity

The medical device Sicalm HA meets the requirements of the EU Regulation 2017/745 on medical devices and is in accordance with all general safety and performance requirements and listed in Annex I of this Regulation.

## 6. Possible diagnostic or therapeutic alternatives

The standard treatment protocols consist of cleaning the wound and pain management often associated with the management of infection. Systemic antibiotics are usually avoided.

Alvogyl is the only more widely used product in the treatment of the alveolar osteitis. (Suchanek, 2019) nevertheless there is none state of the art standard of care that would be used and recommended as generally efficient in the treatment of alveolar osteitis.

Existing approaches to the treatment of dry socket do not have any recommended treatment standards, and doctors are testing different approaches to the treatment of the disease in case of its development. From the gained information through literature and market research it can be said that according to the available sources, the application of chlorhexidine-based preparations is probably the most therapeutic standard in the Czech Republic nowadays for the prevention of alveolar osteitis, although it is still not the most common approach comparing the local intraalveolar treatment, systemic antibiotic.


- **Suchánek J**, Ivančaková R, Mottl R, Browne K, Pilneyová K, Pilbauerova N, Schmidt J, Kleplová T. Hyaluronic Acid-Based Medical Device for Treatment of Alveolar Osteitis—Clinical Study. International Journal of Environmental Research and Public Health. 16. 3698. 10.3390/ijerph16193698. **2019**


## 7. Suggested profile and training for users

The product is to be used by dentists.

## 8. Reference to any harmonised standards and CS applied

**a) Applied standards:**

*Table 2: Applied standards*

| | |
|---|---|
| | Biological evaluation of medical devices |
| EN ISO 10993-1:2020 | Part 1: Evaluation and testing within a risk management process |
| EN ISO 10993-3:2014 | Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity |
| EN ISO 10993-5:2009 | Part 5: Tests for in vitro cytotoxicity |
| EN ISO 10993-7:2008 | Part 7: Ethylene oxide sterilization residuals |
| EN ISO 10993-10:2023 | Part 10: Tests for skin sensitization |
| EN ISO 10993-11:2018 | Part 11: Tests for systemic toxicity |
| EN ISO 10993-16:2017 | Part 16: Toxicokinetic study design for degradation products and leachables |
| EN ISO 10993-18:2020 | Part 18: Chemical characterization of materials |
| EN ISO 10993-23:2021 | Part 23: Tests for irritation |
| EN ISO 14155:2020 | Clinical investigations of medical devices for human subjects – Good clinical practice |
| EN 556-1:2024 | Sterilization of medical devices. Requirements for medical devices to be designated "STERILE". Part 1: Requirements for terminally sterilized medical devices |
| EN ISO 11135:2014 | Sterilization of healthcare products – EtO Sterilization – Requirements for the development, validation and routine of a sterilization process for medical devices |
| EN ISO 14971:2020 | Medical devices – Application of risk management to medical devices |
| EN 62366-1:2015 | Medical devices - Part 1: Application of usability engineering to medical devices |

| | |
|---|---|
| EN ISO 14644-1:2015 | Cleanrooms and associated controlled environments |
| EN ISO 14644-2:2015 | Part 1: Classification of air cleanliness by particle concentration |
| EN ISO 14644-3:2019 | |
| EN ISO 14644-4:2001 | Part 2: Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration |
| EN ISO 14644-5:2004 | |
| EN ISO 14644-7:2004 | Part 3: Test methods |
| EN ISO 14644-8:2022 | Part 4: Design, construction and start-up |
| EN ISO 14644-9:2022 | Part 5: Operations |
| | Part 7: Separative devices (clean air hoods, gloveboxes, isolators and mini-environments) |
| | Part 8: Assessment of air cleanliness by chemical concentration (ACC) |
| | Part 9: Classification of surface cleanliness by particle concentration |
| EN ISO 14644-10:2022 | Part 10: Assessment of surface cleanliness by chemical contamination |
| EN ISO 14698-1:2003 | Cleanrooms and associated controlled environments – Biocontamination control |
| EN ISO 14698-2:2003 | |
| EN ISO 13485:2016+A11:2021 | Medical devices – Quality management systems – Requirements for regulatory purposes |
| EN ISO 20417:2021 | Medical devices – Information to be supplied by the manufacturer |
| EN ISO15223-1:2021 | Medical devices -- Symbols to be used with information to be supplied by the manufacturer - Part 1: General requirements |
| EN ISO 11607-1:2020+A11:2022 | Packaging for terminally sterilized medical devices |
| | Part 1: Requirements for materials, sterile barrier systems and packaging systems |
| EN ISO 11607-2:2020+A11:2022 | |
| | Part 2: Validation requirements for forming, sealing and assembly processes |

**b) Legislative standards for medical devices in the Czech Republic**

1. Act. No. 375/2022 Sb., medical devices and in vitro medical devices act
2. Act. No. 90/2016 Sb., conformity assessment of specified products being delivered to the market
3. Act No. 505/1990 Sb., metrology
4. Act No. 477/2001 Sb., packaging
5. Act No. 541/2020 Sb., waste

**c) Legislative standards and guidelines for medical devices in EU**

1. Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices
2. European Pharmacopeia current version

## 9. Revision history

| SSCP revision number | Date issued | Change description | Revision validated by the Notified Body |
|---|---|---|---|
| Rev 01 | 27/07/2021 | Initial version | |
| Rev 02 | 12/01/2023 | Update of applied standards; revision of intended use during the conformity assessment procedure. | |
| Rev 03 | 27/03/2023 | Unification of terms | |
| Rev 04 | 19/05/2023 | Update of side effects description | |
| Rev 05 | 25/09/2023 | Point 1.1. and 1.7 update | |
| Rev 06 | 05/02/2025 | PMCF study design plan chap. 5.5, applied standards update chap. 8, | validated by NB, language: English |
| | | | |