SUMMARY OF SAFETY AND CLINICAL PERFORMANCE (for users/healthcare professionals)

"SODIUM HYALURONATE 2.4% AND SODIUM CHONDROITIN 1.6% - VISCO-SUPPLETIVE JOINT DEVICE"

With the following brand names:

CONDROSULF Intrarticolare

CONDROSULF Intrarticular

SINOGEL

ARTROCOAT

in accordance with Medical Device Regulation (EU) 2017/745 and MDCG 2019-9

Manufacturer

IBSA Farmaceutici Italia srl

Via Martiri di Cefalonia 2, 26900 Lodi, Italy

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****.*

SUMMARY

1. *Device identification and general information*

1.1. Device trade name(s)

"SODIUM HYALURONATE 2.4% AND SODIUM CHONDROITIN 1.6% - VISCO-SUPPLETIVE JOINT DEVICE" can be marketed with the following trade names:

- CONDROSULF INTRARTICOLARE
- CONDROSULF INTRARTICULAR
- SINOGEL
- ARTROCOAT

1.2. Manufacturer's name and address

The Manufacturer of this device is:
IBSA Farmaceutici Italia Srl
Via Martiri di Cefalonia 2, 26900 Lodi, Italy

1.3. Manufacturer's single registration number (SRN)

The Manufacturer's single registration number (SRN) is IT-MF-000008111.

1.4. Basic UDI-DI

The basic UDI, for this medical device, as reported in Declaration of Conformity, are the following:

- for the pre-filled syringe only is 803363895IA0024T
- for the kit is 803363895IAK00269

1.5. Medical device nomenclature description / text

The CND for "SODIUM HYALURONATE 2.4% AND SODIUM CHONDROITIN 1.6% - VISCO-SUPPLETIVE JOINT DEVICE" is P900402.

1.6. Class of device

"SODIUM HYALURONATE 2.4% AND SODIUM CHONDROITIN 1.6% - VISCO-SUPPLETIVE JOINT DEVICE" has been classified according to the rules 8 of Annex VIII of Regulation EU 2017/745 as Class III.

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

The first certificate has been issued in 2019.

At the Date of Application (DoA) of the MDR, 26th May 2021, the Medical Device "SODIUM HYALURONATE 2.4% AND SODIUM CHONDROITIN 1.6% - VISCO-SUPPLETIVE JOINT DEVICE" was covered by the following certificates:

- EC design-examination certificate n. EPG-0208-19, addendum n. 01-19 dated 21.03.2019
- Full Quality assurance system certificate n. QCT-0043-17, addendum n. 06-19 dated 21.03.2019

both issued by the Notified Body ISS (CE0373) in accordance with Directive 93/42/EEC prior to 25 May 2017 and valid until 04.06.2022.

As per MDR, Art. 120(3), starting from 26.05.2021 (DoA), the Device "SODIUM HYALURONATE 2.4% AND SODIUM CHONDROITIN 1.6% - VISCO-SUPPLETIVE JOINT DEVICE" is intended to be a Legacy Device, because is a Device lawfully placed on the market pursuant to Directive 93/42/EEC, which may continue to be placed on the market until 04.06.2022 (the end of the period indicated on the MDD-CE certificates).

1.8. Authorised representative if applicable; name and the SRN

N.A. – Not Applicable

1.9. NB's name (the NB that will validate the SSCP) and the NB's single identification number

Eurofins 0477

2. Intended use of the device

2.1. Intended purpose

"SODIUM HYALURONATE 2.4% AND SODIUM CHONDROITIN 1.6% - VISCO-SUPPLETIVE JOINT DEVICE" with its particular formula and its high concentration of glycosaminoglycans (GAG) belongs to the latest generation of intra-articular treatments and is specifically designed for viscosupplementation of large joints for which a large volume of solution with a high concentration of hyaluronic acid without high viscosity is recommended. Thanks to a specific and patented treatment of the solution, the hyaluronic acid and sodium chondroitin chains present in the device interact with each other giving the solution rheological properties such as to obtain viscosity values lower than those of only hyaluronic acid at the same concentration.

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

"SODIUM HYALURONATE 2.4% AND SODIUM CHONDROITIN 1.6% - VISCO-SUPPLETIVE JOINT DEVICE" is indicated for pain or reduced mobility due to degenerative affections, post-traumatic disorders or joint alterations. "SODIUM HYALURONATE 2.4% AND SODIUM CHONDROITIN 1.6% - VISCO-SUPPLETIVE JOINT DEVICE" is a device for integration of the synovial fluid, which allows restoring the physiological and rheological properties of arthritic joints. Restoring the viscoelastic properties of the synovial fluid, "SODIUM HYALURONATE 2.4% AND SODIUM CHONDROITIN 1.6% - VISCO-SUPPLETIVE JOINT DEVICE" reduces pain and restores joint mobility.
"SODIUM HYALURONATE 2.4% AND SODIUM CHONDROITIN 1.6% - VISCO-SUPPLETIVE JOINT DEVICE" is indicated for adults of both sexes and is to be administered by intra-articular injection by qualified personnel only.

2.3. Contraindications and/or limitations

"SODIUM HYALURONATE 2.4% AND SODIUM CHONDROITIN 1.6% - VISCO-SUPPLETIVE JOINT DEVICE" should not be injected in the presence of an infected or severely inflamed joint or if the patient has a skin affection or infection in the injection site area.

3. Device description

3.1. Description of the device

Osteoarthritis (OA) is a chronic degenerative disease characterized by progressive damage of joint cartilage, reduction of joint space, subchondral bone remodelling, formation of marginal joint osteophytes and synovitis. An optimal OA therapy is intra-articular injection of exogenous hyaluronic acid, which can relieve the symptoms thanks to restoration of the viscoelastic properties of the synovial fluid. Hyaluronic acid sodium salt is formed by repetitive chains of disaccharide units of N-acetylglucosamine and sodium glucuronate and is an essential component of the synovial fluid, where it acts as joint lubricant during shear stress and as shock absorber during compressive stress. "SODIUM HYALURONATE 2.4% AND SODIUM CHONDROITIN 1.6% - VISCO-SUPPLETIVE JOINT DEVICE" is composed of a buffered saline solution of highly purified hyaluronic acid with high molecular weight and sodium chondroitin of biotechnological origin. The hyaluronic acid used in the device is obtained by fermentation and has not undergone chemical modification processes. This results in excellent tolerability.

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

The product has not previous generation or variant.

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

The device is not intended to be used with any accessory.

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

The device is intended to be used with needles and it can be placed on the market as a single syringe or a system, according to art. 22 of the Regulation, that is in combination with other device (needle 21G x1 ½ ").

4. Risks and warnings

4.1. Residual risks and undesirable effects

According to Risk Assessment, it is possible to state that Residual Risks are intrinsic and cannot be further reduced and that the Overall Residual Risk can be considered as acceptable. For these reasons, "SODIUM HYALURONATE 2.4% and SODIUM CHONDROITIN 1.6% - VISCO-SUPPLETIVE JOINT DEVICE" Residual Risks are acceptable if compared with its Benefits hence the Benefit/Risk ratio can be considered as positive. According to Risk Assessment, however, the following side-effects and adverse events must be reported on IFU – Instructions for Use.

Side-effects:
Extra-articular seepage of "SODIUM HYALURONATE 2.4% and SODIUM CHONDROITIN 1.6% - VISCO-SUPPLETIVE JOINT DEVICE" may cause undesirable effects locally. During the use of "SODIUM HYALURONATE 2.4% and SODIUM CHONDROITIN 1.6% - VISCO-SUPPLETIVE JOINT DEVICE", symptoms such as pain, the sensation of heat, reddening or swelling may appear at the injection site. These secondary manifestations can be relieved by applying ice on the treated area. They generally disappear in a short period of time. Physicians/specialists must ensure that patients notify them of any undesired effects which occur after the treatment.
In case of incident, inform the Manufacturer or the Competent Authority.

No spontaneous adverse events have been cumulatively collected from 21Mar2019, i.e. the date of first CE Certification, till 31 December 2020, being the medical device not on the market at that time.
Contra-indications:
"SODIUM HYALURONATE 2.4% and SODIUM CHONDROITIN 1.6% - VISCO-SUPPLETIVE JOINT DEVICE" must not be injected in the presence of an infected or seriously inflamed joint or if the patient has a cutaneous disease or an infection in the area of the injection site.

4.2. Warnings and precautions

- The content of the prefilled syringe is sterile. The syringe is packed in a sealed blister pack.
- The outer surface of the syringe is not sterile.
- Do not use the device after the expiry date indicated on the package.
- Do not use the device if the packaging is open or damaged.
- The injection site must be on healthy skin.
- Do not use in pregnant or breast-feeding women.
- Do not use in patients with autoimmune diseases.
- Do not inject intravascularly. Do not inject outside the joint cavity, into the synovial tissue or into the articular capsule.
- Do not administer SINOGEL® in the presence of heavy intra-articular effusion.
- Do not resterilize. The device is intended for single use only.
- Do not reuse in order to prevent any risk of contamination.
- Store at ambient temperature below 25°C and away from heat sources. Do not freeze.
- Once opened, the device must immediately be used and discarded after use.
-SINOGEL® is indicated for adult patients.
- Keep out of the reach and sight of children.
- Do not use SINOGEL® in case of known hypersensitivity or allergies to the components of the product.
- After the intra-articular injection advise the patient to avoid any intense physical activity and to resume his or her normal activities only after several days.
- Protect from sunlight.
- Any air bubble present does not compromise the characteristics of the product.

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

No Field Safety Corrective Actions and Field Safety Notices have ever been required.

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

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

Several similar devices are available in the market but none of them can be considered fully equivalent with SINOGEL. Therefore, no clinical data related to equivalent device has been evaluated.

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

The following study has been performed on SINOGEL when still marketed under the Directive 93/42/EEC.

- *Papalia R., Salini V., Voglino N., Fortina M., Carta S., Sadile f., Costantino C.. Single-Dose Intra-Articular Administration of a Hybrid Cooperative Complex of Sodium Hyaluronate and Sodium Chondroitin in the Treatment of Symptomatic Hip Osteoarthritis: A Single-Arm, Open-Label, Pilot Study Reumatol Ther. 2020 Nov 27*

Intended use of the Medical device used in the investigation	The device was used in patients affected by symptomatic hip OA and moderate to severe pain.
Objectives of the study	This study evaluated the safety and efficacy of a single intra-articular injection of an innovative formulation of sodium hyaluronate 2.4% plus sodium chondroitin non-sulphated 1.6% of biotechnological origin (HA-SC) for the treatment of patients with radiographically confirmed symptomatic hip OA and moderate-to-severe pain.
Study design	This is a prospective, multi-center, open-label, pilot study.
Endpoints	The primary objective was to evaluate the safety of intra-articular SINOGEL in patients with symptomatic hip OA. The secondary objective was to evaluate the efficacy of the product in terms of pain and function of the affected hip joint. The primary safety endpoint was the number and type of ADE (i.e., AEs related to the medical device). Secondary safety endpoints included tolerability at the injection site, assessment of global tolerability by the patient and investigator, vital signs, and laboratory parameters. The efficacy endpoints were changes in visual analogue scale (VAS) pain from baseline to time points atday 7, 30, 60, 90 and 180, changes in Lequesne's algofunctional Index from baseline to any time points, and subject and investigator assessment of change in global status evaluating hip OA pain symptoms, according to a 5-point qualitative scale (4=very much improved, 3=slightly improved, 2=no change, 1=slightly worsened, 0=very much worsened). Consumption of concomitant analgesic treatments(number of subjects using paracetamol and number of used tablets) was recorded.
Inclusion/exclusion criteria	Eligible subjects were male or female patients aged ≥ 40 years attending the outpatient clinics at the participating Italian public hospitals with symptomatic primary hip OA radiographically confirmed within the previous 6 months and continuous moderate-to-severe OA pain despite the failure of or non-response to regular use of analgesics and/or NSAIDs or other conservative treatments. OA, and pain at the target hip ≥40 mm as measured on a VAS after a wash-out period from analgesics and/or NSAIDs of 5 times the drug half- life before the screening visit and confirmed at the baseline visit (visit 2).

	Exclusions from the study, which were related to circumstances considered likely to interfere with the study treatment or confound the evaluation of the affected joint were the follow: • Presence of concomitant rheumatic disease • Previous or planned surgery on the target hip • Intra-articular viscosupplementation in the hips B 6 months previously • Significant venous or lymphatic stasis • Body mass index (BMI) C 32 kg/m2 • Systemic or i.a. corticosteroid treatment of the target hip in the past 3 months • Treatment of any non-target joint with systemic or i.a. corticosteroids in the past 4 weeks Systemic NSAIDs or paracetamol (acetaminophen) within the past 48 h • Opioids/narcotic analgesics in the past 7 days • Chronic use of topical or systemic analgesics, NSAIDs, or narcotics • Start of therapy or change of dosage of any SySADOA in the last 3 months • History of alcohol or drug abuse • Allergy or hypersensitivity to hyaluronic acid or paracetamol • Clinically significant or unstable medical condition that might compromise successful participation in another clinical trial within the preceding 90 days • Pregnant or breast-feeding women or lack of adequate contraception
Number of enrolled patients	48 subjects were enrolled with the first subject enrolled on the 1st of August 2017 and the last subject completing the study on the April 4, 2019.
Study population	The average age of the subjects was 61.2 years and more males (N = 29) than females (N = 19) were enrolled. All subjects were Caucasian, and the majority had bilateral hip OA, with the target hip balanced similarly between the left and right side. The diagnosis of hip OA was radiographically confirmed in all subjects, 94% of whom had Kellgren–Lawrence grade 2 or 3 radiographic hip OA. The mean time since diagnosis of hip OA was 44.9 (range, 0.7–220.6) months

Summary of the study methods	The investigational medical device was a sterile 3 ml unit-dose syringe containing high molecular weight sodium hyaluronate 2.4% and sodium chondroitin non-sulphated 1.6% of biotechnical origin for intra-articular administration. Each syringe provided 72 mg of sodium hyaluronate and 48 mg of sodium chondroitin. A standard ultrasound-guided procedure was used with the aim of ensuring the correct placement of the intra-articular injection and minimizing the risk of adverse effects due to incorrect positioning of the needle. . Using an antero-superior approach, a 22-gauge spinal needle was advanced through the biopsy guide into the anterior capsular recess, at the level of the femoral head, using real-time imaging guidance software. Subjects underwent a screening visit (visit 1) between 1 and 10 days before treatment with the intra-articular injection of SINOGEL at the baseline/ treatment visit (visit 2, day 0). Follow-up visits were performed after 7 days from treatment (visit 3, post-treatment follow-up), and after 30 (visit 4), 60 (visit 5), 90 (visit 6), and 180 days (visit 7, final visit).

Summary of results	In summary, the treatment was generally well tolerated.. The most common ADEs by preferred term were injection site pain and arthralgia localized in the treated area. There was one serious AE (SAE) reported in one subject not related to treatment. The intensity of AEs was mild and moderate. None of the subjects discontinued the study due to AEs. The global evaluation of tolerability was rated as excellent or good for 36 subjects (75.0%), fair by eight (16.7%), and poor by four (8.3%). Corresponding values reported by the investigators were excellent or good in 37 subjects (77.1%), fair in seven (14.6%), and poor in four (8.3%). There was a rapid and significant decrease in hip pain after a single intra-articular injection of HA-SC. VAS pain score decreased from baseline to visit 3 (day 7), with the effects sustained during 6 months of follow-up. The mean Lequesne's algofunctional Index for hip OA total score after the single injection of HA-SC decreased from a mean of 10.4 at baseline at 6 months. The decrease was marked and remained significant at all evaluated time points. The subjects' assessment of global improvement showed an assessment of 'Very much improved' or 'Slightly improved' in the majority of subjects at any time point throughout the study. Consistent with the assessments of the subjects, the investigators reported 'Very much improved' or 'Slightly improved' for the majority of subjects at any time point.
Limitations	This was a small open-label, single-arm pilot study, and there was therefore no control group. However, extensive monitoring for AEs and ADEs was undertaken over the duration of the study up to the final visit at day 180, and the use of a number of validated clinical parameters and the kinetics of the performance effects observed on pain and function suggest that a tangible treatment effect was present.

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

No other clinical data from other sources is available.

5.4. An overall summary of the clinical performance and safety

SINOGEL is a device designed for the integration of the synovial fluid, that allows the re-establishment of the physiological and rheological properties of joints affected by arthrosis. It intended for pains or reduced joints mobility due to degenerative diseases, post-traumatic diseases or joint alterations. It is indicated to be injected into large joints, in which a large volume of solution, with high HA concentration, is advisable. The sodium hyaluronate used in the formulation is obtained through a fermentative process and sodium chondroitin has a biotechnological origin. Therefore, SINOGEL results to have excellent biocompatibility and its injection into the synovial cavity counteract the OA-induced deficit of HA and can alleviate symptoms of OA or joint disorders (degenerative or post-traumatic ones), thanks to the restoration of a proper viscoelastic properties of synovial fluid.

The clinical study conducted by Papalia et al. (see the paragraph above) on SINOGEL, confirmed that the treatment was considered safe, the adverse events were mostly mild and transient in terms of intensity and duration. The efficacy of the device was also demonstrated when used in patients affected by hip osteoarthritis, reporting a rapid and significant decrease in hip pain with a single shot of the product (3 ml), sustained up to 6 months. The use of rescue paracetamol was lower and decreased over time.

Other several studies have been conducted on similar devices supporting the safety and the performance of intra-articular injections of HA in patients affected by osteoarthritis. Several data are available with similar product since viscosupplemtenation is a widely treatment for OA, with a good tolerability and it is able to alleviate symptoms of OA, thanks to the restoration of viscoelastic properties of synovial fluid.

In conclusion, on the basis of the data obtained from the literature and clinical study performed with the device, it is possible to conclude that the use of SINOGEL is effective to reduce pain and improve joint mobility in patients with OA. SINOGEL is overall safe and a good tolerability. Therefore, it is believed that the benefits deriving from the use of SINOGEL outweigh the risks. All possible adverse events derived from the use have been analysed from the Manufacturer, and all possible complications and precautions are detailed in the leaflet.

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

During the Post Market Clinical Follow up activities, the Manufacturer will collect additional clinical data thorough a survey with questionnaires, that will be submitted to the professional users in order to collect their experience after the use of the device. The survey aims to collect efficacy data, in relation to the clinical performance endpoints provided for the product, defined in coherence with the anatomical areas of interest and with the treatment plan (n. cycles), in relation to the indications of the product. Questions aimed to collect and monitor the safety of the device through the incidence of expected adverse events, and to confirm the absence of events not yet identified.

Moreover, the Manufacturer plans for the next year to finalize one clinical investigation to confirm performance and safety of the medical device SINOGEL for the treatment of symptomatic knee OA.When this study is completed, the paragraph 5.2 will be updated.

6. *Possible diagnostic or therapeutic alternatives*

Osteoarthritis (OA) is a progressive, degenerative disease of the synovial joints causing joint pain and functional impairment with different degrees of disease severity that requires long-term management with various treatment options over the course of the disease.

Several guidelines for the management of OA are available developed by clinical experts such as, for example, the *European Society For Clinical And Economic Aspects Of Osteoporosis, Osteoarthritis And Musculoskeletal Diseases (ESCEO),* the *American College of Rheumatology (ACR) e the Osteoarthritis Research Society International (OARSI),* the *European Alliance of Associations for Rheumatology (EULAR),* the *Arthroscopy Association of Canada (AAC).* The most used pharmacological and non-pharmacological agents are proposed with different strengths of recommendations across the different societies' guidelines. In general, the guidelines for the management of OA suggest that patients should be educated regarding nonpharmacological interventions including lifestyle, weight loss (for those who are overweight), and exercises that do not involve high-impact activities especially in patients with mild to moderate OA. However, there are not clearly defined parameters for the nature, frequency and duration and physical therapies programs to assign for patients with OA.

Currently no pharmacologic interventions exist that can decrease the progression of the disease or reverse existing damage. Pharmacological treatments are usually started when the OA becomes symptomatic since pain is the main cause of reduced everyday activities. The wide range of available agents includes oral, topical and intra-articular treatments able to provide an improvement in the patient's quality of life, either alone or more often combined with other non-surgical approaches.

Oral interventions include Acetaminophen, Nonsteroidal anti-inflammatory drugs (NSAIDs), opioid analgesics and Slow Acting Drugs for OA (SYSADOAs). Of note, when these treatments are prescribed, it is important to consider the patients status, comorbidities and treatments related side effects. It is recommended to avoid the use of acetaminophen and NSAIDs for a long time since they could lead liver damage, or other adverse events, such as stomach irritation, nausea, vomiting and dizziness etc. Similarly, since the potential abuse could be associated with important gastrointestinal and cognitive adverse events, opioids like tramadol should be an option only for patients who have not responded to acetaminophen or NSAID therapy or cannot tolerate them because of adverse effects.

Another important pharmacological treatment option for osteoarthritis is represented by the Slow Acting Drugs for OA (SYSADOA), that includes oral glucosamine sulphate and related compounds, such as chondroitin sulphate (CS). In particular, chondroitin sulphate is a glycosaminoglycan, an important structural constituent of the extra-cellular matrix of the cartilage, which contribute to give the cartilage its mechanical and elastic properties. Therefore, the administration of exogenous CS contributes to the maintenance of the articular cartilage, thus limiting the erosive action of the disease. CS has proven to be a valuable therapeutic tool for the symptomatic treatment of OA, but it has also structure modifying properties acting on cartilage structure (SMOAD). There are some differences among the International Recommendations regarding the use of SYSADOAs, however, recent meta-analyses indicate the

potential benefits related to their use in patients with knee OA. In fact, it has been shown that prescription-grade CS is more effective in reducing pain in knee OA than nutraceutical grade or over-the-counter (OTC) chondroitin preparations. Additionally, the safety profile of prescription-grade CS is good and the use of pharmaceutical-grade CS it is also recommend by the ESCEO guidelines, as first-line long-term therapy in symptomatic knee OA as both single therapy and in combination with acetaminophen.

Topical NSAIDs (i.e diclofenac) offer a favourable risk benefit profile and may be safely used in combination with other treatment strategies for optimal management of OA.

Nowadays, among the non- surgical strategies, intra-articular therapies are commonly use for the reduction of the symptoms of this disease. One of them, consists in the intra-articular administration of corticosteroids, that are used to treat osteoarthritis patients affected by moderate-severe joint pain who are not responding to oral anti-inflammatory or analgesic drugs. Injection of corticosteroids alleviate pain for few weeks but the number of injections each year is generally limited, because the medication can worsen joint damage over time and can cause other side effects.

Platelet- Rich Plasma (PRP) is another injectable option of treatment, that provides a concentrate of autologous growth factors that can be used to enhance tissue regeneration, and lead to reduce inflammatory distress. Side effects are uncommon, but the biological effects depend on differences between some of the key characteristics, including platelet concentration, anticoagulant and coagulation activation agent type, presence of inflammatory white blood cells, and activation level.

However, among the intra-articular treatment, hyaluronic acid injection is the most commonly non-surgical therapy used for OA. After several decades of use, it is usually recognised as a safe treatment for OA, restoring the viscoelastic behaviour of synovial fluid in terms of joint lubrication, shock absorption, and reducing mechanical stress on the joint. Viscosupplementation acts by replacing or reinforcing the rheological and protective properties of the synovial fluid, decreasing pain and improving joint functionality. The most commonly adverse events reported due to the use of intra-articular injection of HA are mild, transient local reactions such as pian, inflammation, swelling and pain at the injection site is rare and short-lived.

In severe case of the OA disease, the arthroplasty is performed to replace the damage surface of the bones with prostheses. This approach is considered for the later stage, restricted to patients with more severely affected functional status since risks of serious medical and post-surgical complications often occurred and this option of treatment is not often suitable for all patients and all joints.

In this context, IBSA Farmaceutici has developed SINOGEL that belongs to the last generation of intra-articular treatments and is specifically designed for the viscosupplementation of the large joints, for which a large volume of solution, with high HA concentration without a huge viscosity, is advisable. The hyaluronic acid chains and the sodium chondroitin chains contained in the device, interact each other providing to the solution rheological characteristics such as to obtain the viscosity values lower than the ones of the only hyaluronic acid at the same concentration.

7. Suggested profile and training for users

IBSA Institut Biochimique SA, the Head Quarter of IBSA Farmaceutici Italia srl, manufacturer of SINOGEL, organizes regularly educational courses and training sessions dedicated to IBSA Affiliates/Distributors and to physicians of different countries. These courses are aimed at training them on the correct infiltration practice and on the use of the ultrasound (US) technique that is propaedeutic to the utilization of intra-articular devices.

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

HARMONISED STANDARD	
• EN ISO 10993-9:2021	Biological evaluation of medical devices - Part 9: Framework for identification and quantification of potential degradation products (ISO 10993-9:2009)
• EN ISO 10993-12:2021	Biological evaluation of medical devices - Part 12: Sample preparation and reference materials (ISO 10993-12:2012)
• EN ISO 11737-1:2018/A1:2021	Sterilization of health care products - Microbiological methods - Part 1: Determination of a population of microorganisms on products (ISO 11737-1:2018)
• EN ISO 13485:2016	Medical devices - Quality management systems - Requirements for regulatory purposes (ISO 13485:2016)
• EN ISO 15223-1:2021	Medical devices - Symbols to be used with medical device labels, labelling and information to be supplied - Part 1: General requirements (ISO 15223-1:2016, Corrected version 2017-03)

NON HARMONISED STANDARD	
Use of following non harmonised standard is necessary to comply with relevant GSPR because, for the time being, in absence of harmonized standards, they represent the state of the art to meet the relevant requirement.	
• EN 285:2015+A1:2021	Sterilization - Steam sterilizers - Large sterilizers
• IEC 62366-1:2015+AMD1:2020	Medical devices Application of usability engineering to medical devices
• IEC/TR 62366-2:2016	Medical devices Guidance on the application of usability engineering to medical devices
• EN ISO 10993-1:2020	Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process (ISO 10993-1:2018, including corrected version 2018-11)

• EN ISO 10993-2:2006	Biological evaluation of medical devices - Part 2: Animal welfare requirements (ISO 10993-2:2006)
• EN ISO 10993-3:2014	Biological evaluation of medical devices - Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity (ISO 10993-3:2014)
• EN ISO 10993-5:2009	Biological evaluation of medical devices - Part 5: Tests for in vitro cytotoxicity (ISO 10993-5:2009)
• EN ISO 10993-6:2016	Biological evaluation of medical devices - Part 6: Tests for local effects after implantation (ISO 10993-6:2016)
• EN ISO 10993-10:2013	Biological evaluation of medical devices - Part 10: Tests for irritation and skin sensitization (ISO 10993-10:2010)
• EN ISO 10993-11:2018	Biological evaluation of medical devices - Part 11: Tests for systemic toxicity (ISO 10993-11:2017)
• EN ISO 10993-17:2009	Biological evaluation of medical devices - Part 17: Establishment of allowable limits for leachable substances (ISO 10993-17:2002)
• EN ISO 10993-18:2020	Biological evaluation of medical devices - Part 18: Chemical characterization of medical device materials within a risk management process (ISO 10993-18:2020)
• EN ISO 14155:2020	Clinical investigation of medical devices for human subjects - Good clinical practice (ISO 14155:2020)
• EN ISO 14971:2019+A11:2021	Medical devices - Application of risk management to medical devices (ISO 14971:2019)
• EN ISO 17665-1:2006	Sterilization of health care products - Moist heat - Part 1: Requirements for the development, validation and routine control of a sterilization process for medical devices (ISO 17665-1:2006)
• EN ISO 11138-1:2017	Sterilization of health care products - Biological indicators - Part 1: General requirements (ISO 11138-1:2017)
• EN ISO 11138-4:2017	Sterilization of health care products - Biological indicators - Part 4: Biological indicators for dry heat sterilization processes (ISO 11138-4:2017)
• EN ISO 11737-2:2020	Sterilization of health care products - Microbiological methods - Part 2: Tests of sterility performed in the

	definition, validation and maintenance of a sterilization process (ISO 11737-2:2019)
• EN ISO 14644-1:2015	Cleanrooms and associated controlled environments - Part 1: Classification of air cleanliness by particle concentration (ISO 14644-1:2015)
• EN ISO 14644-2:2015	Cleanrooms and associated controlled environments - Part 2: Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration (ISO 14644-2:2015)
• EN ISO 14644-3:2019	Cleanrooms and associated controlled environments - Part 3: Test methods (ISO 14644-3:2019)
• ISO 11040-8:2016	Prefilled syringes Requirements and test methods for finished prefilled syringes
• EN 556-1:2001	Sterilization of medical devices - Requirements for medical devices to be designated "STERILE" - Part 1: Requirements for terminally sterilized medical devices
• EN ISO 14630:2012	Non-active surgical implants - General requirements (ISO 14630:2012)
• ISO 2859-1:1999	Sampling procedures for inspection by attributes Sampling schemes indexed by acceptance quality limit (AQL) for lot-by-lot inspection

MDCG	
• MDCG 2021-11	Guidance in Implant card – Device types
• MDCG 2019-8 v2	Guidance document implant card on the application of Article 18 Regulation (EU) 2017/745 on medical device
• MDCG 2021-19	Guidance note integration of the UDI within an organisation’s quality management system
• MDCG 2018-1	Guidance on basic UDI-DI and changes to UDI-DI
• MDCG 2019-1	MDCG guiding principles for issuing entities rules on basic UDI-DI
• MDCG 2019-2	Guidance on application of UDI rules to device-part of products referred to in art. 1(8), 1(9) and 1(10) of Regulation 745/2017

• MDCG 2018-4	Definitions/descriptions and formats of the UDI core elements for systems or procedure packs
• MDCG 2018-3	Guidance on UDI for systems and procedure packs
• MDCG 2019-9	Summary of safety and clinical performance
• MDCG 2020-6	Guidance on sufficient clinical evidence for legacy devices
• MDCG 2020-7	Guidance on PMCF plan template
• MDCG 2020-8	Guidance on PMCF evaluation report template
• MDCG 2020-10/2 • MDCG 2020-10/1	Guidance on safety reporting in clinical investigations Appendix: Clinical investigation summary safety report form
• MDCG 2020-13	Clinical evaluation assessment report template
• MDCG 2020-5	Guidance on clinical evaluation – equivalence
• MDCG 2021-8	Clinical investigation application/notification documents

9. Revision history

Revision	Validated by the NB	Date	Description of main changes	Languages
Rev. 0	Not yet/ongoing	02/2022	First issue of SSCP according to the Technical File	English (Validated by the NB)
Rev. 1	Validated	04/2022	Revision due to the Non Conformity	English (Validated by the NB)