0.0 INTRODUCTION AND PURPOSE OF THE SUMMARY

To comply with article 32 of the European Regulation 745/2017, this document serves as a summary relating to the safety and clinical performance (SSCP) of the product mentioned below with the aim of making information on the safety and performance of the medical device publicly accessible.
The SSPC must be a source that contains important information for users (both professional users and information relevant to patients).
This document is drawn up for medical devices with risk class III or if it is an implantable device and subsequent must be validated by the notified body and published the European Database (Eudamed).
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.
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 following information is intended for users/healthcare professionals (doctors).
Following this information there is a summary intended for patients.

1.0 DEVICE IDENTIFICATION AND GENERAL INFORMATION

1.1 - Device trade name	**ALGENESS LD, ALGENESS HD, ALGENESS VL, ALGENESS DF**
1.2 - Manufacturer	GHIMAS S.p.A. Via Domenico Cimarosa, 85, 40033 – Casalecchio di Reno, BO, Italy
1.3 - SRN Manufacturer	IT-MF-000017070.
1.4 - Basic UDI-DI	ALGENESS LD: 803357637ALGENESS10YU ALGENESS HD: 803357637ALGENESS15Z6 ALGENESS VL: 803357637ALGENESS25Z9 ALGENESS DF: 803357637ALGENESS35ZC
1.5 - Nomenclature CND and Description	P900402 - REABSORBABLE PRODUCTS FOR FILLING AND REBUILDING
1.6 - Class of device	III – Rule 8 of Annex VIII of the Regulation EUE 2017/745.
1.7 - Year of the first certificate (CE)	2004
1.8 - NB's name and the NB's single identification number	Eurofins Product Testing Italy Srl – number 0477

2.0 INTENDED USE

2.1 - Intended purpose	Algeness is effective for the treatment of cases of dermal atrophy and connective tissue deficits. Algeness can also be used for deep filling of cutaneous tissue. Treatment with Algeness is part of reconstructive surgery which aims to correct congenital malformations or functions compromised by trauma, disease, accidents, burns, wounds, often accompanied by loss of substance. For Algeness, the clinical advantage is the reduction of the psychological impact, which can have pathological consequences, caused by the morphological alterations of the patient's body.

2.2 - Indications

Algeness is a slowly absorbed filler and is totally biocompatible.
The treatment must only be performed by competent doctors trained in the use of injection techniques.
Before using the product, the patient must be informed about the indications, contraindications and possible side effects that may occur with use.
Prior to use, mix the gel back and forth between the two syringes at least ten times (10) for improving consistency and better results.
Before the injection, it is necessary to carry out a thorough cleansing and complete disinfection of the implant site. It is recommended to maintain a correct asepsis of the treated area before, during and after the insertion of the implant as well as to ensure a proper environment.
It is recommended to position Algeness in the medium-deep subdermis under the site to be corrected or deeper, depending on the concentration of the agarose. The quantity to be injected is left to the judgment of the doctor.
Algeness should not be used in excess (overcorrection).
The correction can be performed with the usual techniques: linear threading technique, deep linear or fan technique. The injection must be carried out slowly for better positioning of the product in the desired areas with less trauma to the tissues.
The product is extruded by applying continuous and constant pressure on the plunger of the syringe while withdrawing the needle.
For an optimal correction, after implantation, always massage the treated area to make a homogeneous distribution of the injected material.
It is recommended to apply a cold compress to the treatment area to reduce any local undesirable reactions.
For proper maintenance of the result, remind the patient of the importance of a clinical follow-up a few months after treatment.
The patient must also be informed that the treatment can be suspended at any time at his request.
Inform the patient they must not to apply cosmetics to the implant site for the next twelve hours and not to expose themselves to direct heat for the next few days (for example: exposure to the sun or to UVA and UVB rays, use of hair dryers or of hair dryers, heat reverberated by fireplaces, saunas, etc.).
The device is intended for women and men with tissue alterations and who do not fall within the populations described in the contraindications paragraph.

2.3 - Contraindications

The use of Algeness is contraindicated in all cases other than those specified in the indications of the product, therefore, it must not be injected superficially at the level of the dermis or as a bolus.
Prior to the injection, assure that the patient does not experience particular hypersensitivity to any of the components in the product.
As with all fillers, the use of the product for the correction of particularly vascularized areas is not recommended, as it can increase the risk of compression and occlusion of the vessels and related phenomenology.
Algeness must not be injected in subjects with acute or chronic skin diseases in the areas to be corrected or in the immediate vicinity and, for precautionary reasons, in subjects with a history of anaphylactic reactions or severe allergies, in patients with severe organ or systemic diseases, including autoimmune disorders. The product is not intended for use on children, pregnant and or lactating women. It is recommended to avoid the combined use with other substances such as crosslinked fillers in the same treatment area.

3.0 DEVICE DESCRIPTION

3.1 - Description of the device

Algeness, is a medical device consisting of agarose, sterile water for injectable preparations, phosphate buffer, and, for the VL and DF type, non cross-linked hyaluronic acid.
Algeness, injected into the subdermal tissue, provides a viscoelastic supplement to the matrix. Agarose restores the lost tissue volume of both the adipose tissue and the connective stroma, ensuring biocompatibility with the extracellular matrix and the harmony of natural forms. Therefore Algeness is effective for the treatment of cases of dermal atrophy and connective tissue deficits. Algeness can also be used for deep filling of cutaneous tissue.
At the implantation site, Algeness is reabsorbed within 6-12 months.
Conserve the product at room temperature, between 6°C and 30°C. If necessary, the product may be stored in s refrigerator, the product must not be frozen.
Do not use Algeness after the expiry date shown on the package.

3.2 – Previous generation or variants

The four Algeness models on the market are distinguished by the concentration of agarose, in particular the higher the agarose content, the more the device must be injected deep under the dermis. Below are the indications for use by model:

Algeness LD (low density - subdermal) is indicated for repairs and superficial subdermal corrections surface repairs and subdermal corrections of hypotrophy or tissue lesions such as in the perioral area.

Algeness HD (medium density - subdermal) is indicated for repairs and superficial subdermal corrections due to hypotrophy or tissue lesions in the perioral area.

Algeness VL (medium / high density - deep subdermal) is indicated in the volumetric restoration for all forms of deep tissue hypotrophy with severe or modest loss of tone of the deep ligaments such as in the suborbital areas and in the anterior mandibular area.

Algeness DF (high density - deep subdermal) is indicated all forms of volumetric restorations for all forms of severe deep tissue hypotrophy with severe loss of volume and tone of the deep ligaments such as in the suborbital areas and in the anterior mandibular area.

3.3 - Description of any accessories

The product is sold in a syringe that is connected, via a Luer fitting, to a second empty syringe to facilitate mixing of the gel before use. Together with the double syringe, a fin is available to increase the contact surface and a hypodermic needle to be used in connection with the pre-filled syringe for injection. The needle is certified as a medical device by the supplier and is supplied sterile.

4.0 RISKS AND WARNINGS

4.1 - Residual risks & undesirable effects

The manufacturer has personal and documentary resources for risk analysis according to the harmonized standard ISO 14971 and ISO / TR 24971: through this method, no residual risks were recorded following the actions taken to mitigate those identified.
Following the implant, edematous reactions or skin redness, of a mild or moderate degree, may rarely occur, which resolve completely within a few days.
Even if the application of Algeness is not painful, the possibility of rare reports of transient pain due to the injection cannot be excluded, especially in particularly sensitive areas.
Despite this, the implant may involve risks of infection, if the product is injected into anatomical sites where inflammatory or infectious processes are present, or without carrying out proper cleaning and disinfection of the area to be corrected.

4.2 – Warnings and precautions

Algeness must not be injected into blood vessels, as it could cause the onset of occlusion, local tissue necrosis or emboli.
Product is for single use only. Sterilized product.
Product must not be re-sterilized.
If the stickers on the inner package, which indicate the sterility of the product are NOT red, DO NOT use the product. In case of any irregularities with the packaging, isolate the non-compliant packaging and dispose of as special waste. Never use the product if it has not been stored correctly or if it has been frozen.
The unused material left in the syringe must be eliminated (disposed of) after treatment to avoid any risk of cross-infection due to use on other patients.
The doctor and / or the patient must report any serious incidents occurring in relation to the device to the manufacturer Ghimas and to the competent authority of the Member States where the user and / or patient is established.
FOR PROFESSIONAL USE ONLY.
DO NOT USE the product after the expiry date shown on the package.
As with all percutaneous procedures, the implant can entail risks of infection if the product is injected into anatomical areas where inflammatory or infectious processes are present, or without proper cleansing and disinfection of the area to be corrected.
In patients with bleeding and / or coagulation disorders or during treatments with anticoagulants, the product should be used with caution, as the injection may frequently cause local bleeding or bruising.

4.3 – Other relevant aspects of safety

The medical device Algeness, since their first marketing date, have never been subject to any field safety corrective action (FSCA) or field safety notification (FSN).

5.0 CLINICAL EVALUATION and Post market clinical follow-up (PMCF)

(Summary of clinical evaluation in accordance with Annex XIV of Reg. 2017/745)

5.1 - Summary of clinical data from conducted investigations of the device before the CE-marking

A recent and important study, concluded by Dott. Scuderi in 2019, made it possible to summarize the effects after the use of the Algeness VL medical device. In particular, the study demonstrates the safety and performance of the medical device implanted in the site concerned as it has been compared to a filler based on hyaluronic acid (HA), currently the most used and present on the market. It was also possible to record the investigators' opinions on the handling and management of the product used, product tolerability, assess the duration of the fillers and obtain opinions on patient satisfaction.

In this study, with a protocol authorized by the independent ethics committee (IEC), both products were used on each patient (68 total), thus excluding individual susceptibility.
In conclusion, the study demonstrated the following results:

- Algeness is completely absorbed in about 8 months.
- There are no differences concerning the safety aspects of the two fillers
- No serious or unexpected adverse effects were reported.

5.2 - Summary of clinical data from other sources

The clinical data deriving from surveys through PMCF activities and the referenced scientific literature support the performance and safety of the medical device, in fact, the use of Algeness as a device for the regeneration of tissue atrophies and the restoration of the natural structure of the dermal tissue. , it is safe and suitable for that destination. The clinical benefits that emerged from the collected questionnaires, clinical investigations and scientific articles demonstrate objectively and professionally.
These data, but above all the failure to indicate specific product problems collected in the field, confirm the excellent tolerability and efficacy of the device in the non-surgical correction of soft tissues, among other things, with the absence of unwanted effects. As there are no residual risks and / or aspects to be explored in terms of performance or safety, it is not necessary to start other studies to determine the safety and performance of the medical device as there are neither problems related to use, nor safety problems or elements. performance-related that need to be investigated.
The clinical benefits identified therefore concern the restoration of the normal tissue morphology, its volumes and symmetries, and therefore that makes the damaged tissue natural.
Dr. Scuderi's study focused on the safety of the device and on the results regarding the restoration of normal morphology, not strictly related to this clinical evaluation but, the data collected through the “case report”, show how all the treated lesions were cured and therefore the depth, compared to the preliminary visit, it has significantly decreased and almost zeroed. The general condition of clinical cases has significantly improved, as indicated by the improvement index indicated, and the psychological health of the patients has been confirmed, which could have been compromised with the continuation of atrophies and anatomical deformities.
The risks associated with the implantation of the device were found and confirmed to be minimal as its integration with the host tissue occurs in a natural way and consistent with its nature, filling empty spaces and restoring atrophy.
There were no serious adverse reactions, undesirable and previously unidentified effects or inflammatory reactions triggered by the immune system. Therefore, all the identified risks were assessed in the risk analysis document, mitigated, and therefore kept under control.

5.3 - Summary of the clinical performance and safety

The behavior of the filler inside the host tissue, with regard to safety and biocompatibility, has been carefully studied by some authors who, following the injection of filler with 1.5% agarose, concluded that, after six months the filler is well attached to the hypodermis, a physiological increase in collagen fibers has been noted and the tissue is still well vascularized without any signs of granulomas or fibrosis.
The same check, carried out one year after the date of injection, made it possible to state that the filler has been completely absorbed and that there is a thickening of the collagen at the level of the dermis-hypodermis. The connective tissue and its structure are similar to what emerged from the tissue biopsy before implantation, so there were no alterations.

In fact, the analyzed data confirm the adequate performance and safety of the product:

- Natural and biodegradable: the product is not rejected following its injection because, being based on agarose, it is naturally accepted by the cells formed at the treatment site. This advantage is also confirmed by the few adverse reactions that have occurred both in the literature search and in reports from clients.
- Restructuring: following the treatment, the restorative effect is immediately evident and does not cause swelling in the following days because it is not a

	hydrophilic substance that activates water molecules, unlike the more common hyaluronic acid-based fillers. • Gradually reabsorbed: the natural composition of the gel allows its complete degradation in longer times as the agarose is not directly attacked by an enzyme, but is subjected to the macrophage action and subsequently attacked by the galactosinases with detachment of the molecules that make up the polymer. • Homogeneous and soft gel, consisting of a three-dimensional network with rigid meshes capable of retaining molecules and organic liquids in dynamic equilibrium with its resorption, easy to extrude through a light pressure of the thumb on the syringe plunger and through smaller caliber needles (27-30 Gauge). • Modest or no pain during implantation. • Ideal implant in the medium and deep dermis, with variable orientation of the flute beak, depending on the anatomical region treated and the characteristics of the imperfection. • Low post-implantation edema, dose dependent, in rare cases with amplifications lasting 24-48 hours. In conclusion, all the biocompatibility tests carried out on the reference DM Algeness were valid for the current standard of the EN ISO 10993 series. The absence of acute and subacute / subchronic toxicity effects, irritation, sensitization, genotoxic and reproductive potential, mutagenic potential and short and long term systemic toxicity effects after intramuscular implantation, allows to confirm the biocompatibility of DM Algeness.
5.4 - Ongoing or planned post-market clinical follow-up	In the clinical field, to support the use of the product after many years on the market and to confirm what emerged from the preclinical studies and the clinical study of Dr. Scuderi, regarding the safety of the device, post-marketing activities were started in which, from the questionnaires drawn up by users professionals, information has emerged that supports the safety and tolerability of the product because it immediately achieves clinical benefit and therefore restores the morphology of the damaged tissue without activating the immune system and therefore without adverse effects. No risks and serious side effects emerged from the injection of the product; therefore, the medical device was found to be safe with a benefit - risk ratio to the advantage of the applicability and use of Algeness. In addition, a clinical study will be initiated with the aim of increasing feedback on the performance of the Algeness medical device and continuing to demonstrate its effectiveness in restoring tissue following tissue atrophy and other connective tissue deficits resulting from trauma and / or other pathologies.

6.0 POSSIBLE THERAPEUTIC ALTERNATIVES

There are really many fillers available for clinical use today and each one has specific advantages and disadvantages. Even if the final choice is up to the patient, the filler sector is a field where it is more than ever necessary to consult with a doctor who is experienced in the use of various materials, in order to obtain all possible clarifications to their doubts and thus face in full awareness of the treatment. The use of fillers, in particular temporary fillers, allows to achieve the best results in terms of naturalness and restoration of the fabric.
The best-known alternative of Algeness is the hyaluronic acid-based filler, being a temporary implant, it requires repeating the treatment periodically and therefore does not completely restore the morphological defect or asymmetry. However, this feature will have the benefit of protecting the patient from changes in the patient's mind or in the case of corrections that have not been perfectly executed (it will be enough not to repeat the infiltration to return to the original situation in a short time).
If, on the other hand, a very marked increase in size is desired, subject to the willingness to accept compromises in terms of naturalness and natural restoration of the fabric, the choice may fall on solutions such as methacrylate-based fillers, lipofilling or implants. The same solutions should be considered if you want a treatment with definitive effects.

7.0 SUGGESTED PROFILE AND TRAINING FOR USERS

The device should only be used by professional users, doctors, who know and are skilled in injection techniques. The injection must be performed in a controlled medical environment in accordance with health regulations. Therefore, it is recommended to maintain a correct asepsis of the treated area before, during and after the insertion of the implant as well as to ensure a suitable environment.

8.0 REFERENCE TO ANY HARMONISED STANDARDS AND CS APPLIED

The medical device is manufactured inside a clean room with controlled contamination and is subsequently sterilized by Gamma rays; for these aspects, the product follows the common ISO standards relating to the processes of sterilization, cleanroom validation and evaluation and clinical investigations.
In particular, the reference standards are the following:

UNI CEI EN ISO 13485:2016+ A11:2021 "Medical devices - Quality management systems - Requirements for regulatory purposes" (acknowledges EN ISO 13485: 2016 + AC: 2018)
EN ISO 14971:2019 + A11:2021 Medical devices - Application of risk management to medical device
EN ISO 15223-1:2021 Medical devices - Symbols to be used in medical device labels, labeling and information to be provided - Part 1: General requirements
IS**O 10993-1:2021** Biological evaluation of medical devices Evaluation and testing within a risk management process
ISO 10993-2:2006 Biological evaluation of medical devices Part 2: Animal welfare requirements
ISO 10993-3:2014 Biological evaluation of medical devices Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity
ISO 10993-5:2009 Biological evaluation of medical devices Part 5: Tests for in vitro cytotoxicity
ISO 10993-6:2016 Biological evaluation of medical devices Part 6: Tests for local effects after implantation
ISO 10993-10:2013 Biological evaluation of medical devices Part 10: Tests for irritation and skin sensitization
ISO 10993-11:2018 Biological evaluation of medical devices Part 11: Tests for systemic toxicity
ISO 10993-12:2012 Biological evaluation of medical devices Part 12: Sample preparation and reference materials
ISO 10993-16:2018 Biological evaluation of medical devices Part 16: Toxicokinetic study design for degradation products and leachables
ISO 10993-17:2009 Biological evaluation of medical devices Part 17: Establishment of allowable limits for leachable substances
ISO 10993-18:2009 Biological evaluation of medical devices Part 18: Chemical characterization of materials
ISO 10993-23: 2021 Biological evaluation of medical devices Part 23: Tests for irritation
ISO/TS 10993-19:2006 Biological evaluation of medical devices Part 19: Physico-chemical, morphological and topographical characterization of materials
ISO/TR 15499:2016 Biological evaluation of medical devices — Guidance on the conduct of biological evaluation within a risk management process
EN 62366:2008 Medical devices - Application of engineering of use characteristics to medical devices
UNI EN ISO 11137-1: 2020 Sterilization of healthcare products - Radiation - Part 1: Requirements for the development, validation and systematic control of the sterilization process for medical devices.
UNI EN ISO 11137-2:2015 Sterilization of healthcare products - Radiation - Part 2: Definition of the sterilizing dose
UNI EN ISO 11737-1:2018 + A1:2021 Sterilization of medical devices - Microbiological methods - Part 1: Determination of a population of microorganisms on products
UNI EN ISO 11737-2:2021 Sterilization of medical devices - Microbiological methods - Part 2: Sterility tests performed during the definition, validation and maintenance of a sterilization proces
UNI EN ISO 11607-1:2020 Packaging for terminally sterilized medical devices - Part 1: Requirements for materials, sterile barrier systems and packaging systems
UNI EN ISO 11607-2:2020 Terminally Sterilized Medical Device Packaging - Part 2: Validation Requirements for Format, Seal and Assembly Processes
UNI EN ISO 14644-14:2016 Clean rooms and associated controlled environments - Part 14: Evaluation of the fitness for use of an equipment by determining the concentration of particles in the airport
UNI EN ISO 14644-2:2016 Cleanrooms and Associated Controlled Environments - Part 2: Monitoring to provide evidence of cleanroom performance in terms of air cleanliness in terms of particle concentration.

9.0 DATE AND SIGNATURE OF RESPONSIBLE FOR DRAFTING

Dott. Alberto Poletti –
RAQ e Responsible Person of MDR

10.0 REVISION HISTORY

SSCP revision number	Date issued	Change description	Revision validated by the Notified Body
00	20.12.2022	First issue	☒**Yes** ☐**No** (only applicable for class IIa or some IIb implantable devices)

A summary of the safety and clinical performance of the device, intended for patients, is given below.

Summary of safety and clinical performance (SSCP) for patients

Revision: 00
Date issued: 20.12.2022

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. IDENTIFICAZIONE DEL DISPOSITIVO MEDICO

Device trade name	**ALGENESS LD, ALGENESS HD, ALGENESS VL, ALGENESS DF**
Manufacturer	GHIMAS S.p.A. Via Domenico Cimarosa, 85, 40033 – Casalecchio di Reno, BO, Italy
Basic UDI-DI	ALGENESS LD: 803357637ALGENESS10YU ALGENESS HD: 803357637ALGENESS15Z6 ALGENESS VL: 803357637ALGENESS25Z9 ALGENESS DF: 803357637ALGENESS35ZC
Year of the first certificate (CE)	2004

2. INTENDED USE

Intended purpose	Algeness is effective for the treatment of cases of dermal atrophy and connective tissue deficits. Algeness can also be used for deep filling of cutaneous tissue. Treatment with Algeness is part of reconstructive surgery which aims to correct congenital malformations or functions compromised by trauma, disease, accidents, burns, wounds, often accompanied by loss of substance. For Algeness, the clinical advantage is the reduction of the psychological impact, which can have pathological consequences, caused by the morphological alterations of the patient's body.
Indications	The treatment must only be performed by competent doctors trained in the use of injection techniques. The patient must also be informed that the treatment can be suspended at any time at his request. Inform the patient they must not to apply cosmetics to the implant site for the next twelve hours and not to expose themselves to direct heat for the next few days (for example: exposure to the sun or to UVA and UVB rays, use of hair dryers or of hair dryers, heat reverberated by fireplaces, saunas, etc.)
Contraindications	The use of Algeness is contraindicated in all cases other than those specified in the indications of the product, therefore, it must not be injected superficially at the level of the dermis or as a bolus. Prior to the injection, assure that the patient does not experience particular hypersensitivity to any of the components in the product. As with all fillers, the use of the product for the correction of particularly vascularized areas is not recommended, as it can increase the risk of compression and occlusion of the vessels and related phenomenology. Algeness must not be injected in subjects with acute or chronic skin diseases in the areas to be corrected or in the immediate vicinity and, for precautionary reasons, in subjects with a history of anaphylactic reactions or severe allergies, in patients with severe organ or systemic diseases, including autoimmune disorders. The product is not intended for use on children, pregnant and or lactating women. It is recommended to avoid the combined use with other substances such as crosslinked fillers in the same treatment area.

Pazienti target	Women and men with morphological alterations of the tissue and who do not fall within the populations described in the contraindications paragraph.

3. DEVICE DESCRIPTION

Description of the device	**Algeness**, is a medical device consisting of agarose, sterile water for injectable preparations, phosphate buffer, and, for the VL and DF type, non cross-linked hyaluronic acid. Algeness, injected into the subdermal tissue, provides a viscoelastic supplement to the matrix. Agarose restores the lost tissue volume of both the adipose tissue and the connective stroma, ensuring biocompatibility with the extracellular matrix and the harmony of natural forms. Therefore Algeness is effective for the treatment of cases of dermal atrophy and connective tissue deficits. Algeness can also be used for deep filling of cutaneous tissue. At the implantation site, Algeness is reabsorbed within 6-12 months.
Description of any accessories	The product is sold in a syringe that is connected, via a Luer fitting, to a second empty syringe to facilitate mixing of the gel before use. Together with the double syringe, a fin is available to increase the contact surface and a hypodermic needle to be used in connection with the pre-filled syringe for injection. The needle is certified as a medical device by the supplier and is supplied sterile.

4. RISKS AND WARNINGS

Contact your healthcare professional if you believe that you are experiencing sideeffects 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.

Potential risk management	GHIMAS SPA as a manufacturer of medical devices, which it places on the market in its own name, maintains an active process for identifying the dangers associated with its devices, to estimate and evaluate the consequent risks, control the risks themselves and monitor the effectiveness of this process. The data is collected through the Post Market Surveillance plan, which Ghimas updates annually, through which information deriving from different sources and analyzed within the report is summarized.
Residual risks & undesirable effects	Ghimas has personal and documentary resources for risk analysis according to the harmonized standard recognized worldwide: through this method, no residual risks were recorded following the actions taken to mitigate those identified. Following the implantation, edematous reactions (bruises) or skin redness, of a mild or moderate degree, may rarely occur, which resolve completely within a few days. Even if the application of Algeness is not painful, the possibility of rare reports of transient pain due to the injection cannot be excluded, especially in particularly sensitive areas. Despite this, the implant may involve risks of infection, if the product is injected into anatomical sites where inflammatory or infectious processes are present, or without carrying out proper cleaning and disinfection of the area to be corrected.
Warnings	Algeness must not be injected into blood vessels, because it could cause the onset of occlusion, local tissue necrosis or embolism. The patient must report any serious incident in relation to the device to the manufacturer Ghimas and to the competent authority of the Member State where the patient is established. The patient must be given the implant card which contains the essential data to identify the implanted device. The patient must keep the implant card safely. FOR PROFESSIONAL USE ONLY.
Precautions and indications	As with all percutaneous procedures, the implant may involve risks of infection, if the product is injected into anatomical sites where inflammatory or infectious processes are present, or without proper cleansing and disinfection of the area to be corrected. In patients with bleeding and / or coagulation disorders or during treatments with anticoagulants, the product should be used with caution, as the injection can more frequently cause local hemorrhages or hematomas.

5. CLINICAL EVALUATION and Post market clinical follow-up (PMCF)

Clinical background

The field of fillers, substances for injective use used to restore and correct damage deriving from dermal atrophy but also for the corrective treatment aimed at restoring normal morphology, rehydrating and supporting the tissues, it is always in constant ferment and evolution.

One of the most interesting characteristics of this filler (compared to the other absorbable ones) seems to have been the duration, certainly more than 6 months even in the last review of the case series published in 2018 and also from what emerged in the multicentre study of 2019. in fact, that the longer duration is attributable to the different ways of resorption. Agarose, compared to fillers based on collagen or hyaluronic acid, is not directly attacked by the corresponding enzyme (the human body does not possess agarase) but is degraded after a macrophage attack and subsequently subjected to the action of galactosidases with detachment of the molecules that make up the polymer (D-galactose and 3,6-anhydro-L-galactose) and subsequent degradation of these through the pentose cycle.

Based on the observations and clinical experiences after years of using the fillers from the ALGENESS line, some authors (from 2005,2006 and 2008) reiterated the characterizing properties of the agarose gel in the first published works.

All the biocompatibility tests carried out on the reference Algeness confirm what is described in the published articles. The absence of acute and subacute / subchronic toxicity effects, irritation, sensitization, genotoxic and reproductive potential, mutagenic potential and short and long term systemic toxicity effects after intramuscular implantation, allows to confirm the biocompatibility of Algeness.

Clinical evidence for the CE-marking

A recent and important study, concluded in 2019, made it possible to summarize the effects after the use of the Algeness VL medical device. In particular, the study in conjunction with case report data, demonstrates the safety and performance of the medical device implanted in the site concerned as it has been compared to a filler based on hyaluronic acid (HA), currently the most used and present on the market. It was also possible to record the investigators' opinions on the handling and management of the product used, product tolerability, assess the duration of the fillers and obtain opinions on patient satisfaction.
In this study, with a protocol authorized by the independent ethics committee (IEC), both products were used on each patient (68 total), thus excluding individual susceptibility.
In conclusion, the study demonstrated the following results:

- Algeness is completely absorbed in about 8 months.
- There are not differences concerning the safety aspects of the two fillers
- No serious or unexpected adverse effects were reported

Summary of safety

The behavior of the filler inside the host tissue, with regard to safety and biocompatibility, has been carefully studied by some authors who, following the injection of filler with 1.5% agarose, concluded that, after six months the filler is well attached to the hypodermis, a physiological increase in collagen fibers has been noted and the tissue is still well vascularized without any signs of granulomas or fibrosis.
The same check, carried out one year after the date of injection, made it possible to state that the filler has been completely absorbed and that there is a thickening of the collagen at the level of the dermis-hypodermis. The connective tissue and its structure are similar to what emerged from the tissue biopsy before implantation, so there were no alterations.

The absence of acute and subacute / subchronic toxicity effects, irritation, sensitization, genotoxic and reproductive potential, mutagenic potential and short and long term systemic toxicity effects after intramuscular implantation, allows to confirm the biocompatibility of DM Algeness.

Finally, in the clinical field, to support the use of the product after many years on the market and to confirm what emerged from the preclinical studies and the clinical study of Dr. Scuderi, post-marketing activities were started in which, from the questionnaires drawn up by users professionals, information has emerged that supports the safety and tolerability of the product because it immediately achieves clinical benefit and therefore

restores the damaged tissue without activating the immune system and therefore without adverse effects. No risks and serious side effects emerged from the injection of the product, therefore, the medical device was found to be safe with a benefit - risk ratio to the advantage of the applicability and use of Algeness.

6. ALTERNATIVE POSSIBLE THERAPEUTIC ALTERNATIVES

When considering alternative treatments, it is recommended to contact your healthcare professional who can take into account your individual situation.

There are really many fillers available for clinical use today and each one has specific advantages and disadvantages. Even if the final choice is up to the patient, the filler sector is a field where it is more than ever necessary to consult with a doctor who is experienced in the use of various materials, in order to obtain all possible clarifications to their doubts and thus face in full awareness of the treatment. The use of fillers, in particular temporary fillers, allows to achieve the best results in terms of naturalness and restoration of the fabric.
The best-known alternative of Algeness is the hyaluronic acid-based filler, being a temporary implant, it requires repeating the treatment periodically and therefore does not completely restore the defect or asymmetry. However, this feature will have the benefit of protecting the patient from changes in the patient's mind or in the case of corrections that have not been perfectly executed (it will be enough not to repeat the infiltration to return to the original situation in a short time).
If, on the other hand, a very marked increase in size is desired, subject to the willingness to accept compromises in terms of naturalness and natural restoration of the fabric, the choice may fall on solutions such as methacrylate-based fillers, lipofilling or implants. The same solutions should be considered if you want a treatment with definitive effects.

7. SUGGESTED PROFILE AND TRAINING FOR USERS

The device should only be used by professional users, doctors, who know and are skilled in injection techniques. The injection must be performed in a controlled medical environment in accordance with health regulations. Therefore, it is recommended to maintain a correct asepsis of the treated area before, during and after the insertion of the implant as well as to ensure a suitable environment.

8. DATE AND SIGNATURE OF RESPONSIBLE FOR DRAFTING

Dott. Alberto Poletti –
RAQ e Responsible Person of MDR

9. REVISION HISTORY

SSCP revision number	Date issued	Change description	Revision validated by the Notified Body
00	20.12.2022	First issue	☒ **Yes** ☐ **No** (only applicable for class IIa or some IIb implantable devices)