Ellanse™
Reveal the Inner you

Regenerate Beauty through Collagen Stimulation
Facial ageing is a multifactorial process that affects different layers.

**Bone Resorption & Remodelling**
- Significant loss of facial bone with age
- Leads to biometric volume loss
- Noticeable changes in the other layers of overlying soft tissue and skin

**Muscle Tone & Atrophy**
- Facial muscles become more tensed and atrophic
- Contribute to facial sagging and droopiness
- Fat pads displacement

**Fat Loss & Redistribution**
- Fat pads loss and/or migration under muscular action leading to deep creases and contour defects
- Accumulation of fat in some areas (e.g. under the lower eyelid, jaw, mouth) leading to the impression of permanent puffiness
DERMAL AGEING & COLLAGEN LOSS

As the ageing skin loses its structural proteins (collagen and elastin), it becomes more lax and begins to sag, which contributes to a tired and aged look.

COLLAGEN MODIFICATIONS WITH AGEING

- Decrease in the level of collagen
- Changes in histological characteristics (collagen fibres distribution)
- Changes in ultrastructure (collagen network disorganisation)
- Fragmentation of fibrils, fibroblast can no longer bind

COLLAGEN IN YOUTHFUL SKIN

Collagen
Provides infrastructure for elastin and hyaluronic acid

Elastin
Helps the skin retain its elasticity

Hyaluronic Acid
Water binds to hyaluronic acid, keeping the skin moist

Well structured collagen network

COLLAGEN IN AGEING SKIN

Decreased Collagen

Decreased Elastin

Decreased Hyaluronic Acid

Collagen network disorganisation
ELLANSE™: A TAILOR-MADE BIORESORBABLE COLLAGEN STIMULATOR

COMPOSITION

- Totally smooth polycaprolactone (PCL) microspheres 25-50 μm
- PBS*-based carboxymethylcellulose (CMC) gel-carrier

PCL & CMC

- Excellent safety profile and largely used in bioresorbable implants (sutures and orthopaedic implants dermal fillers, oral and maxillo-facial surgery) for several decades worldwide
- Used in numerous European (CE-certified) and US Food and Drug Administration (FDA) approved commercial bioresorbable products in cosmetic and pharmaceutical industries

STAT™ TECHNOLOGY: A unique manufacturing process with several benefits

Sustained Performance, Tunable Longevity and Total Bioresorbability

THESE 3 FEATURES GIVE ELLANSÉ™ UNIQUE ADVANTAGES

- Maintained correction over total duration of effect through one single injection
- Different levels of action depending on patients’ needs
- Fully resorbable treatment with a predictable, controlled and tunable bioresorption and a high safety profile

PBS: Phosphate Buffered Saline
ELLANSÉ™ is an injectable implant, indicated for subdermal implantation in the face for the lasting correction of wrinkles and other facial ageing signs or conditions.

- Medical Device Class III®
- CE mark obtained in 2009
- Distributed in more than 80 countries

ELLANSÉ™ comes in ready-to-use syringes:
- 2 x 1 ml syringes of ELLANSÉ™ with 4 x 27G 3/4" needles
- 2 x 0.5 ml syringes of ELLANSÉ™ with 4 x 27G 3/4" needles

ELLANSÉ™ is available in 2 options -S and -M, that differ only in their duration of action. All the other product characteristics are identical for the entire product range.
MECHANISM OF ACTION

2-in-1 action
Immediate filling
- CMC gel provides the immediate filling & wrinkle correction

Long-lasting volumisation through collagen stimulation
- PCL microspheres stimulate neocollagenesis

1. Before treatment
2. When ELLANSÉ™ is injected subcutaneously CMC gel provides immediate results
3. CMC gel is resorbed and PCL microspheres remain
4. PCL microspheres stimulate fibroblasts to produce new collagen
5. Overtime PCL microspheres are bioresorbed
6. Smooth and natural correction maintained throughout total duration of effect

CMC: Carboxymethylcellulose; PCL: Polycaprolactone
PREDICTABLE AND CONTROLLED TOTAL BIORESORBABILITY\textsuperscript{10-13}

Thanks to state-of-the art STAT\textsuperscript{TM} Technology:

- Initial length of the PCL chains is the uniquely distinguishing characteristic of ELLANSÉ\textsuperscript{TM}.
- Varying the length of the PCL chains is the basis of the different levels of longevity options which differ from 1 to 2 years* that you can adapt to your patient needs and expectations.
- Fully resorbable product via hydrolysis.

MICROSHERES SIZE: 25-50 \textmu{}m for the whole range

ELLANSÉ\textsuperscript{TM} provides an effect of different durations from 1 to 2 years*.

* Expected longevity \textit{in-vivo} based on extrapolation of clinical data from –S and –M and accepted PCL degradation behaviour.

PCL: Polycaprolactone
AREAS OF TREATMENT: ELLANSÉ™ RANGE

Sustained volumising capacity through collagen stimulation for natural and long-lasting results from 1 to 2 years*, ideal for volume restoration and contour definition.

TREATMENT AREAS WHERE ELLANSÉ™-S and -M

- Temples and Brow Area
- Malar Augmentation Cheek
- Cheek
- Nasolabial Folds
- Jaw Line
- Nose Reshaping
- Marionette Lines
- Chin Definition

NB: Glabella, lips, tear trough and eyelids are not recommended for the use of ELLANSÉ™

Depth of Injection

ELLANSÉ™ is indicated for sub-dermal injections. For further injection techniques please refer to the ELLANSÉ™ Injection Technique Guidelines (available upon request). Due to its cohesiveness, ELLANSÉ™ is easy to shape and mold, enabling higher precision in the shaping and definition of treated areas.

* Expected longevity in-vivo based on extrapolation of clinical data from –S and –M and accepted PCL degradation behaviour.

PCL: Polycaprolactone
In rabbit tissue

ELLANSÉ™-M: 9 months post injection (rabbit)
Haematoxylin & Eosin staining shows:
Microspheres still round and intact during bioresorption process
Collagen fibres are stained red

ELLANSÉ™-M: 9 months post injection (rabbit)
Picro Sirius Red (PSR) Polarised light shows:
Red (arrows): collagen type I
Green (arrowheads): collagen type III
Confirmation of neocollagenesis

ELLANSÉ™-M: 21 months post injection (rabbit)
Picro Sirius Staining, Polarised light shows:
Red colour confirming predominant presence of collagen type I
Type I collagen confirms stable environment and long-term efficacy

In human tissue

13 months after ELLANSÉ™-M injection, PCL microspheres were surrounded with collagen deposition and a mild fibroblastic and histiocytic tissue response. Stainings were Haematoxylin & Eosin (A and B) and Martin-s Trichrome (C and D)

PCL: Polycaprolactone
PROVEN EFFICACY & SAFETY

High efficacy of ELLANSÉ™ - S and ELLANSÉ™ - M in nasolabial folds treatment with high safety over a 2 years period

Investigator Evaluated Aesthetic Global Improvement Scale GAIS

Comparative clinical study of ELLANSÉ™ vs a NASHA hyaluronic acid for treatment of nasolabial folds

ELLANSÉ™ offers clear advantages over the NASHA based dermal filler, both in terms of durability and efficiency
HIGH SAFETY PROFILE OF ELLANSÉ™

SAFE PRODUCT COMPONENTS WITH A LONG SAFETY HISTORY

Perfectly Smooth  Totally Spherical Microparticles  High Quality Scaffold

The unique smooth and spherical shape of ELLANSÉ™ microspheres:
- Is the basis for optimal biocompatibility as rough surfaces and irregular shaped microspheres have the propensity to induce adverse events, such as nodules, and result in decreased collagen deposition
- Provide a safe, long-lasting and high quality tissue scaffold

SHORT-TERM SAFETY: Pre-Clinical Data
- Total biocompatibility demonstrated via tests according to the ISO-10993 biocompatibility standard
- 2-weeks implantation data clearly show the particles well-embedded in a healthy tissue environment and demonstrate excellent local tolerance

LONG-TERM SAFETY: Scientific Evidence and Literature
- Long-term and total bioresorption of ELLANSÉ™ components through the normal metabolic pathways well documented
- PCL microspheres bioresorption demonstrated via radio-labeled bioresorption studies

IN-VITRO
- In-house in-vitro resorption study of ELLANSÉ™ Range PCL microspheres consistent with published literature data

HIGH PATIENT SATISFACTION

ELLANSÉ™ -S & -M: Satisfaction using Visual Analogue Scale (VAS)

<table>
<thead>
<tr>
<th>Patient Satisfaction</th>
<th>ELLANSÉ™- S 12 Months</th>
<th>ELLANSÉ™- M 24 Months</th>
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<tr>
<td>Satisfaction</td>
<td>74%</td>
<td>81.7%</td>
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At 24 months post-injection:
- 75% of patients like to repeat ELLANSÉ™ - S treatment
- 78% of patients like to repeat ELLANSÉ™ - M treatment

PCL: Polycaprolactone
ELLANSÉ™ ABILITY TO REGENERATE BEAUTY

ELLANSÉ™ -S  ✅ Nasolabial Folds

Before Treatment  After 12 Months

Before Treatment  After 12 Months

Before Treatment  After 24 Months

Courtesy of Marion Moers-Carpi, MD, Germany
ELLANSÉ™ -M  Nose Reshaping

Before Treatment  After 3 Weeks

Courtesy of Dr. Fab Equizi, Liverpool, UK

ELLANSÉ™ -M  Nasolabial Folds, Cheeks and Marionette Lines

Before Treatment  After 2 Months

Courtesy of Alida Harb, MD, Riyadh, Saudi-Arabia

ELLANSÉ™ -M  Cheeks and Submalar Augmentation

Before Treatment  After Treatment

Courtesy of Ayham Al-Ayoubi, MD, London, UK
REFERENCES


10. CE mark-Technical dossier (Whitepaper W113.05).


SINCLAIR is a pharmaceutical company with a renowned strong skin expertise:

- Provides best in class treatments in aesthetics to further support physicians in their practice thanks to unique treatments to answer all patient needs at all ages through minimally invasive procedures.
- Is dedicated to offering safe and effective solutions to achieve optimal results with limited downtime.
- SINCLAIR treatments respect skin’s own natural processes and contribute to maintain the skin in good condition and to rejuvenate the face at all ages.

SINCLAIR COMMITMENT

**BEST IN CLASS PRODUCTS**

Unique products portfolio based on physician and patient needs

**EXCELLENCE IN TRAINING**

High quality training program based on physician practice and expectations

**CREATION OF VALUE**

Create added value in your daily practice

Optimise aesthetics outcome to increase your patients satisfaction
Easy to inject
Immediate correction
Sustained volumising capacity through collagen stimulation
Maintained correction over total duration of effect

Easy to hold
Long-lasting effect from 1 to 2 years*
Natural results from patients own collagen stimulation
High level of patient satisfaction

* Expected longevity in-vivo based on extrapolation of clinical data from –S and –M and accepted Polycaprolactone (PCL) degradation behaviour.