DIRECTIONS FOR USE

saypha® MagIQ™

Caution: Federal (USA) law restricts this device to sale by or on the order of a licensed physician or properly licensed practitioner.

BEFORE USING PRODUCT, READ THE FOLLOWING INFORMATION THOROUGHLY.

1. DEVICE DESCRIPTION

saypha MagIQ is a sterile, biodegradable, non-pyrogenic, viscoelastic, clear, colorless, and homogeneous gel used as soft tissue filler. It consists of hyaluronic acid (HA), produced by Streptococcus species of bacteria, which is cross-linked with BDDE (1,4-butanediol diglycidyl ether). The medical device has a sodium hyaluronate concentration of 23 mg/mL in a phosphate buffered saline at physiological pH and contains 3 mg/mL lidocaine hydrochloride.

2. INTENDED USE/INDICATIONS

saypha MagIQ is indicated for injection into the mid to deep dermis for correction of moderate to severe facial wrinkles and folds (such as nasolabial folds) in adults over the age of 21.

3. CONTRAINDICATIONS

- saypha MagIQ is contraindicated for patients with severe allergies manifested by a history of anaphylaxis or history or presence of multiple severe allergies.
- saypha MagIQ contains trace amounts of Gram-positive bacterial proteins and is contraindicated for patients with a history of allergies to such material.
- saypha MagIQ contains lidocaine and is contraindicated for patients with a history of allergies to such material.
- saypha MagIQ is contraindicated for patients with bleeding disorders.

4. WARNINGS

- saypha MagIQ must not be injected into blood vessels. Introduction of the product into the vasculature may lead to embolization, occlusion of the vessels, ischemia, or infarction. Take extra care when injecting soft tissue fillers; for example, after insertion of the needle, and just before injection, the plunger rod can be withdrawn slightly to aspirate and verify the needle is not intravascular, inject the product slowly, and apply the least amount of pressure necessary. Negative aspiration cannot be relied upon to avoid vascular complications. Rare but serious adverse events associated with the intravascular injection of soft tissue fillers in the face and tissue compression have been reported and include occlusion of vessels, vasospasm, and vascular compromise, resulting in ischemia, temporary or permanent visual impairment, loss of vision, ophthalmoplegia, cerebral ischemia or cerebral hemorrhage leading to stroke, skin necrosis, and damage to underlying facial structures. Immediately stop the injection if a patient exhibits any of the following symptoms, including changes in vision, signs of stroke, pallor, or unusual pain during or shortly after the procedure. Patients should

receive prompt medical attention and, possibly, evaluation by an appropriate healthcare specialist should an intravascular injection occur (see Healthcare Professional Instructions).

- Product use at specific sites in which an active inflammatory process (skin eruptions such as sores, cysts, pimples, rashes, or hives) or infection is present should be deferred until the underlying process has been controlled.
- Inflammatory reaction, anaphylactic reaction, edema, implant migration, blisters, scarring, papules, and delayed onset of granulomas have been reported following the use of dermal fillers.
- Injection site reactions consist mainly of short-term inflammatory symptoms (e.g., swelling, redness, tenderness, or pain) starting early after treatment and generally resolve within 14 days. Refer to the ADVERSE EVENTS section for details.

5. PRECAUTIONS

- saypha MagIQ is packaged for single use. Do not re-sterilize. Do not use if package is open or damaged.
- To minimize the risk of potential complications, this product should only be used by healthcare professionals who have appropriate training, experience, and who are knowledgeable about the anatomy at and around the injection site.
- Healthcare professionals are encouraged to discuss all potential risks of soft tissue injection with their patients prior to treatment and ensure that patients are aware of signs and symptoms of potential complications.
- The safety and effectiveness for the treatment of anatomic regions other than facial wrinkles and folds (such as nasolabial folds) have not been established in controlled clinical studies.
- As with all transcutaneous procedures, soft tissue filler implantation carries a risk of infection. Standard precautions associated with injectable materials should be followed.
- saypha MagIQ should be used as supplied. Modification or use of the products outside the Directions for Use may adversely impact the sterility, homogeneity, and performance of the product.
- The safety for use during pregnancy, in breastfeeding females, or in patients under 21 years of age has not been established.
- The safety in patients with known susceptibility to keloid formation, hypertrophic scarring, and pigmentation disorders has not been studied.
- saypha MagIQ should be used with caution in patients with a history of autoimmune or connective tissue disease and/or who are receiving immune (-modulation) or immunosuppressive therapy, or with a history of severe allergies or anaphylactic shock. Treatment decisions need to be taken on a case-to-case basis. For patients presenting with an active or evolving autoimmune disease, the treatment is not recommended.
- Patients who are using substances that can prolong bleeding (such as aspirin, nonsteroidal anti-inflammatory drugs, and anticoagulants) may, as with any injection, experience increased bruising or bleeding at injection sites.
- The syringe is made of glass, handle with care (risk of laceration when broken).
- If laser treatment, chemical peeling, or any other procedure based on active dermal response is considered after treatment with saypha MagIQ, there is a possible risk of eliciting an

inflammatory reaction at the implant site. An inflammatory reaction is also possible if the product is administered before the skin has healed completely after such a procedure.
- Failure to comply with the needle attachment instructions (see section 8A) could result in needle disengagement and/or product leakage.
- saypha MagIQ is a clear, transparent gel without visible particulates. If the content of a syringe shows signs of separation and/or is not clear, do not use the syringe; notify 1-800-636-7546.

6. ADVERSE EVENTS (AE)

- Potential AEs (e.g., complications) associated with the use of the device, as well as for other devices in the same category, as reported in the clinical study, include tenderness, swelling, firmness (induration), lumps/bumps (mass), bruising, pain, redness, discoloration, and itching.
- The following reported AEs were received from post-market surveillance of the use of saypha MagIQ for treatment of nasolabial folds outside the United States and were not observed in the clinical study. These AEs are listed in order of prevalence: device dislocation, skin inflammation/irritation, hematoma, obstruction/occlusion, herpes simplex reactivation, hypersensitivity/allergic reaction, itching sensation, hemorrhage/bleeding, bruise/contusion, phlebitis, granuloma and necrosis.
- The following additional AEs were observed with similar viscoelastic implants and are considered as potential risks for this device: abscess, angioedema, bacterial infection, capsular contracture, dizziness, fever, fibrosis, hypoesthesia, malaise, medical device site induration, nausea, numbness, paresthesia, peeling, physical asymmetry, presyncope, rash, scleroderma, sebaceous hyperplasia, skin burning sensation, skin disorders, syncope/fainting, tactile disorder.

A. Clinical Evaluation of saypha MagIQ in Nasolabial Folds (NLFs)

Pivotal Study FILIDO US STUDY

In the pivotal, randomized, active-controlled clinical trial to evaluate safety and effectiveness of saypha MagIQ, 270 subjects were injected with saypha MagIQ in one NLF and another US-approved HA dermal filler plus lidocaine (Control) in the contralateral NLF. Touch-up treatment, if needed to achieve optimal correction, occurred approximately 2 weeks after the initial injection. Optional repeat treatment was offered at 36 or 48 weeks using only saypha MagIQ for both NLFs. At the end of each treatment session, subjects used a diary to record injection site reactions (ISRs) and AEs that occurred within 4 weeks after treatment. Subjects were instructed to rate each ISR listed on the diary as Mild, Moderate, Severe, or None.

Local injection-site reactions after the initial treatment were recorded in 95% of subjects with saypha MagIQ treated NLFs and 93% of subjects with Control treated NLFs (Table 1). The most common ISRs were firmness, swelling, and lumps/bumps. The vast majority of ISRs was mild or moderate in intensity. There were no significant differences in ISRs reported between saypha MagIQ and the control. ISRs after the touch-up treatment were similar to those after the initial treatment.

Table 1. Injection Site Reactions After Initial Treatment by Maximum Severity

Injection site reaction	Maximum Severity							
	saypha MagIQ (N=255)* n (%)				Control (N=257)* n (%)			
	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total
Any ISR	91 (35.7)	117 (45.9)	35 (13.7)	243 (95.3)	91 (35.4)	115 (44.7)	32 (12.5)	238 (92.6)
Redness	115 (45.1)	48 (18.8)	9 (3.5)	172 (67.5)	108 (42.0)	47 (18.3)	3 (1.2)	158 (61.5)
Pain after injection	88 (34.5)	28 (11.0)	1 (0.4)	117 (45.9)	90 (35.0)	23 (8.9)	2 (0.8)	115 (44.7)
Tenderness to touch	131 (51.4)	44 (17.3)	3 (1.2)	178 (69.8)	123 (47.9)	45 (17.5)	7 (2.7)	175 (68.1)
Firmness	100 (39.2)	96 (37.6)	9 (3.5)	205 (80.4)	103 (40.1)	82 (31.9)	14 (5.4)	199 (77.4)
Swelling	121 (47.5)	64 (25.1)	8 (3.1)	193 (75.7)	115 (44.7)	66 (25.7)	7 (2.7)	188 (73.2)
Lumps/bumps	101 (39.6)	67 (26.3)	13 (5.1)	181 (71.0)	105 (40.9)	53 (20.6)	11 (4.3)	169 (65.8)
Bruising	101 (39.6)	53 (20.8)	17 (6.7)	171 (67.1)	80 (31.1)	58 (22.6)	15 (5.8)	153 (59.5)
Itching	60 (23.5)	7 (2.7)	6 (2.4)	73 (28.6)	56 (21.8)	3 (1.2)	4 (1.6)	63 (24.5)
Discoloration	47 (18.4)	9 (3.5)	7 (2.7)	63 (24.7)	41 (16.0)	10 (3.9)	3 (1.2)	54 (21.0)
Other	35 (13.7)	8 (3.1)	6 (2.4)	49 (19.2)	24 (9.3)	14 (5.4)	2 (0.8)	40 (15.6)

Abbreviation: ISR, injection site reaction; N, number of subjects in each treatment group of the safety analysis set who returned filled-in subject diaries after the initial treatment.

Note: Treatment, saypha MagIQ or Control, was based on the ISR side of face. In cases where severity was missing for an ISR, the ISR was considered to be severe.

* Subject number refers to subjects who returned diaries

Table 2 shows the duration of all ISRs after initial treatment. The maximum duration for any ISR reported was similar between treatments with saypha MagIQ and Control and most ISR lasted for less than 14 days. For subjects who subsequently received touch-up treatment at Week 2, the maximum duration of ISRs was generally lower than after initial treatment.

Table 2. Injection Site Reactions After Initial Treatment by Maximum Duration

Injection site reaction	Maximum Duration							
	saypha MagIQ (N=255)* n (%)				Control (N=257)* n (%)			
	1-3 Days	4-7 Days	8-14 Days	>14 Days	1-3 Days	4-7 Days	8-14 Days	>14 Days
Any ISR	41 (16.1)	53 (20.8)	90 (35.3)	59 (23.1)	52 (20.2)	53 (20.6)	88 (34.2)	45 (17.5)
Redness	116 (45.5)	36 (14.1)	14 (5.5)	6 (2.4)	102 (39.7)	31 (12.1)	18 (7.0)	7 (2.7)
Pain after injection	86 (33.7)	17 (6.7)	13 (5.1)	1 (0.4)	84 (32.7)	17 (6.6)	11 (4.3)	3 (1.2)
Tenderness to touch	87 (34.1)	36 (14.1)	43 (16.9)	12 (4.7)	91 (35.4)	38 (14.8)	34 (13.2)	12 (4.7)
Firmness	58 (22.7)	43 (16.9)	64 (25.1)	40 (15.7)	60 (23.3)	48 (18.7)	58 (22.6)	33 (12.8)
Swelling	93 (36.5)	50 (19.6)	34 (13.3)	16 (6.3)	100 (38.9)	48 (18.7)	24 (9.3)	16 (6.2)
Lumps/bumps	54 (21.2)	38 (14.9)	56 (22.0)	33 (12.9)	61 (23.7)	33 (12.8)	48 (18.7)	27 (10.5)
Bruising	67 (26.3)	53 (20.8)	41 (16.1)	10 (3.9)	50 (19.5)	48 (18.7)	46 (17.9)	9 (3.5)
Itching	47 (18.4)	11 (4.3)	13 (5.1)	2 (0.8)	37 (14.4)	8 (3.1)	14 (5.4)	4 (1.6)
Discoloration	43 (16.9)	10 (3.9)	8 (3.1)	2 (0.8)	34 (13.2)	8 (3.1)	7 (2.7)	5 (1.9)
Other	31 (12.2)	8 (3.1)	6 (2.4)	4 (1.6)	26 (10.1)	4 (1.6)	7 (2.7)	3 (1.2)

Abbreviation: ISR, injection site reaction; N, number of subjects in each treatment group of the safety analysis set who returned filled-in subject diaries after the initial treatment.

Note: Treatment, saypha MagIQ or Control, was based on the ISR side of face.

* Subject number refers to subjects who returned diaries

ISRs as recorded by subjects after repeat treatment with saypha MagIQ are summarized by maximum severity in Table 3. Overall, 30 (85.7%) subjects reported ISRs after repeat treatment with saypha MagIQ of which 29 subjects had received initial treatment with saypha MagIQ and 28 subjects had received initial treatment with Control. The most common ISRs after repeat treatment were firmness, redness, and swelling. Most subjects reported ISRs with a maximum severity of mild or moderate.

Table 3. Injection Site Reactions After Repeat Treatment by Maximum Severity

	Maximum Severity							
Injection site reaction	**saypha MagIQ (N=35)* n (%)**				**saypha MagIQ (initial treatment with Control) (N=35)* n (%)**			
	Mild	**Moderate**	**Severe**	**Total**	**Mild**	**Moderate**	**Severe**	**Total**
Any ISR	10 (28.6)	15 (42.9)	4 (11.4)	29 (82.9)	14 (40.0)	11 (31.4)	3 (8.6)	28 (80.0)
Redness	14 (40.0)	5 (14.3)	2 (5.7)	21 (60.0)	15 (42.9)	4 (11.4)	1 (2.9)	20 (57.1)
Pain after injection	15 (42.9)	1 (2.9)	1 (2.9)	17 (48.6)	13 (37.1)	1 (2.9)	1 (2.9)	15 (42.9)
Tenderness to touch	9 (25.7)	6 (17.1)	2 (5.7)	17 (48.6)	9 (25.7)	5 (14.3)	2 (5.7)	16 (45.7)
Firmness	11 (31.4)	11 (31.4)	2 (5.7)	24 (68.6)	14 (40.0)	9 (25.7)	3 (8.6)	26 (74.3)
Swelling	14 (40.0)	4 (11.4)	1 (2.9)	19 (54.3)	13 (37.1)	4 (11.4)	1 (2.9)	18 (51.4)
Lumps/bumps	6 (17.1)	6 (17.1)	1 (2.9)	13 (37.1)	7 (20.0)	7 (20.0)	2 (5.7)	16 (45.7)
Bruising	7 (20.0)	8 (22.9)	2 (5.7)	17 (48.6)	9 (25.7)	5 (14.3)	1 (2.9)	15 (42.9)
Itching	4 (11.4)	0	2 (5.7)	6 (17.1)	4 (11.4)	1 (2.9)	1 (2.9)	6 (17.1)
Discoloration	2 (5.7)	4 (11.4)	1 (2.9)	7 (20.0)	5 (14.3)	3 (8.6)	0	8 (22.9)
Other	0	0	1 (2.9)	1 (2.9)	1 (2.9)	0	0	1 (2.9)

Abbreviation: ISR, injection site reaction; N, number of subjects in each treatment group of the safety analysis set who returned filled-in subject diaries after the repeat treatment.

Note: Treatment, saypha MagIQ or Control, was based on the ISR side of face. In cases where severity was missing for an ISR, the ISR was considered to be severe.

* Subject number refers to subjects who returned diaries

Table 4 shows the duration of all ISRs after repeat treatment with saypha MagIQ. The maximum duration for any ISR reported after repeat treatment with saypha MagIQ was similar between subjects who had initial treatments of saypha MagIQ or Control.

Table 4. Injection Site Reactions After Repeat Treatment with saypha MagIQ by Maximum Duration

	Maximum Duration							
Injection site reaction	**saypha MagIQ (N=35)* n (%)**				**saypha MagIQ (initial treatment with Control) (N=35)* n (%)**			
	1-3 Days	**4-7 Days**	**8-14 Days**	**>14 Days**	**1-3 Days**	**4-7 Days**	**8-14 Days**	**>14 Days**
Any ISR	9 (25.7)	4 (11.4)	5 (14.3)	11 (31.4)	8 (22.9)	5 (14.3)	6 (17.1)	9 (25.7)
Redness	12 (34.3)	4 (11.4)	2 (5.7)	3 (8.6)	14 (40.0)	3 (8.6)	2 (5.7)	1 (2.9)
Pain after injection	13 (37.1)	2 (5.7)	2 (5.7)	0	11 (31.4)	2 (5.7)	2 (5.7)	0
Tenderness to touch	6 (17.1)	3 (8.6)	5 (14.3)	3 (8.6)	6 (17.1)	4 (11.4)	3 (8.6)	3 (8.6)

Injection site reaction	Maximum Duration							
	saypha MagIQ (N=35)* n (%)				saypha MagIQ (initial treatment with Control) (N=35)* n (%)			
	1-3 Days	4-7 Days	8-14 Days	>14 Days	1-3 Days	4-7 Days	8-14 Days	>14 Days
Firmness	7 (20.0)	6 (17.1)	2 (5.7)	9 (25.7)	8 (22.9)	7 (20.0)	3 (8.6)	8 (22.9)
Swelling	12 (34.3)	4 (11.4)	2 (5.7)	1 (2.9)	11 (31.4)	4 (11.4)	2 (5.7)	1 (2.9)
Lumps/bumps	5 (14.3)	2 (5.7)	3 (8.6)	3 (8.6)	6 (17.1)	4 (11.4)	3 (8.6)	3 (8.6)
Bruising	5 (14.3)	9 (25.7)	1 (2.9)	2 (5.7)	5 (14.3)	6 (17.1)	2 (5.7)	2 (5.7)
Itching	3 (8.6)	2 (5.7)	1 (2.9)	0	3 (8.6)	2 (5.7)	1 (2.9)	0
Discoloration	5 (14.3)	1 (2.9)	0	1 (2.9)	6 (17.1)	0	0	2 (5.7)
Other	1 (2.9)	0	0	0	1 (2.9)	0	0	0

Abbreviation: ISR, injection site reaction; N, number of subjects in each treatment group of the safety analysis set who returned filled-in subject diaries after the repeat treatment.

Note: Treatment, saypha MagIQ or Control, was based on the ISR side of face.

* Subject number refers to subjects who returned diaries

The maximum duration reported for ISRs overall were as follows: firmness (38 days), swelling (38 days), lumps/bumps (38 days), tenderness to touch (31 days), redness (29 days), bruising (33 days), pain (18 days), itching (29 days), discoloration (30 days), other (29 days).

AEs were also reported by the evaluating Investigator at follow-up visits. Treatment-emergent adverse device effects (TEADEs) after initial/touch-up treatment were reported for 9.6% of subjects in the saypha MagIQ and 8.9% of subjects in the Control group (5). The most frequent TEADEs with both saypha MagIQ and Control were headache, contusion, and swelling. Other frequent TEADEs were eyelid margin crusting, discomfort, and local reactions like injection site erythema. Most TEADEs were mild in intensity.

No TEADEs were reported after repeat treatment.

Table 5. Treatment-Emergent Adverse Device Effects by Preferred Term (Reported in >2 Subjects in Total Group) After Initial/Touch-up Treatment

Preferred Term	saypha MagIQ (N=270) n (%)	Control (N=270) n (%)	Total (N=270) n (%)
TEADEs	26 (9.6)	24 (8.9)	27 (10.0)
Headache	6 (2.2)	6 (2.2)	6 (2.2)
Contusion	4 (1.5)	4 (1.5)	4 (1.5)
Swelling	4 (1.5)	2 (0.7)	4 (1.5)
Eyelid margin crusting	3 (1.1)	3 (1.1)	3 (1.1)
Discomfort	3 (1.1)	3 (1.1)	3 (1.1)
Injection site erythema	3 (1.1)	1 (0.4)	3 (1.1)
Feeding disorder	2 (0.7)	2 (0.7)	2 (0.7)
Pruritus	2 (0.7)	1 (0.4)	2 (0.7)
Erythema	1 (0.4)	2 (0.7)	2 (0.7)

TEADE, treatment-emergent device effect.

Note: Treatment, saypha MagIQ or Control, was based on the AE side of face; if AE side was not applicable, it was considered that the AE happened to both sides of the face.

The maximum duration reported for these TEAEs were as follows: headache (2 days), contusion (14 days), swelling (14 days), eyelid margin crusting (10 days), discomfort (14 days), redness (5 days), feeding disorder (6 days) and itching (38 days). One case of mild erythema was reported starting 91 days after initial treatment and was ongoing at the end of the study without intervention taken. A mild papule was reported for a single patient 44 days after initial treatment and went away on its own after 211 days.

No clinically meaningful differences in the safety profiles of saypha MagIQ and Control were found during the study.

Supportive Study FINO

The open-label, post-market EU study aimed to identify possible residual risks of saypha MagIQ for the correction of moderate to severe NLFs. A total of 60 subjects were treated.

The results confirmed the safety profile of the pivotal study. A total of 47% of subjects reported AEs, most frequently injection site reactions: injection site hematoma in 26.7% of subjects, injection site pain in 20% of subjects, and injection site swelling in 3.3% of subjects. The injection site related AEs were considered TEADEs. All TEADEs were mild or moderate in intensity.

B. Post Market Surveillance

saypha MagIQ has been marketed outside the United States since 2016 under different brand names.

The following AEs were received from post market surveillance for this device outside of the United States and were not observed in the clinical studies. These include reports received globally from all sources including scientific journals and voluntary reports. All AEs obtained through post market surveillance are listed in order of number of reports received: device dislocation, skin inflammation/irritation, herpes simplex reactivation, hypersensitivity/allergic reaction, hemorrhage/bleeding, phlebitis, granuloma, necrosis.

In many cases the symptoms resolved without any treatment. Reported treatments included (in alphabetical order): antibiotics, antihistamines, anti-viral treatment, corticosteroids, hyaluronidase, NSAID. Outcomes for these reported events ranged from resolved to ongoing at the time of last contact.

The following additional AEs were observed with similar viscoelastic implants and are considered as potential risks for this device: abscess, angioedema, bacterial infection, capsular contracture, dizziness, fever, fibrosis, hypoesthesia, malaise, nausea, numbness, paresthesia, peeling, physical asymmetry, presyncope, rash, scleroderma, sebaceous hyperplasia, skin burning sensation, skin disorders, syncope/fainting, tactile disorder.

Adverse reactions should be reported to 1-800-636-7546.

7. CLINICAL STUDIES

A. Pivotal Study for saypha MagIQ

a. Pivotal Study Design

A multicenter, randomized, within-subject controlled (split-face), double-blind pivotal clinical study was conducted to evaluate the safety and effectiveness of saypha MagIQ versus the active Control for the treatment of moderate to severe NLFs. A total of 270 subjects were randomized and underwent treatment with saypha MagIQ in one NLF and Control in the other NLF. An optional touch-up treatment was performed approximately 2 weeks after the initial injection to achieve optimal correction.

The follow-up period consisted of safety and effectiveness follow-up visits after treatment at 2, 12, 24, 36, 48 weeks and beyond. Subjects were eligible for a repeat treatment with saypha MagIQ at 36 weeks or beyond, with follow-up for 3 months after treatment.

b. Study Endpoints

The primary effectiveness measure was the blinded evaluating investigator's assessment of NLF severity at Week 24. A responder was defined as a subject with at least a 1-point improvement on the Nasolabial Folds Severity Rating Scale (NLF-SRS) since baseline.

Additional analyses included blinded photographic reviewer and treating investigator's live NLF severity assessments as well as subject evaluations of aesthetic response using the Global Aesthetics Improvement Scale (GAIS) and FACE-Q ratings of Subject Satisfaction with Outcome and Improvement over Baseline.

c. Subject Demographics

A total of 270 subjects were randomized and treated. Of these subjects, 174 received touch-up treatment and 48 received repeat treatment. The median injection volume of saypha MagIQ required to achieve optimal correction was 1.0 mL at initial treatment and 0.4 mL at touch-up treatment. The repeat treatment was performed with saypha MagIQ on both nasolabial folds and the median injection volume required to achieve optimal correction was 0.7 mL per NLF.

Subject demographics and pre-treatment characteristics of the saypha MagIQ and controls groups are presented in Table 6.

Table 6. Subject Demographics

Characteristic	Attribute	Overall (N=270) n (%)
Age (years)	Median	55
	Range	30 – 86
Gender	Female	264 (97.8%)
	Male	6 (2.2%)
Ethnicity	White	226 (83.7%)
	Black or African American	29 (10.7%)

Characteristic	Attribute	Overall (N=270) n (%)
	American Indian or Alaska Native	10 (3.7%)
	Asian	2 (0.7%)
	Native Hawaiian or Other Pacific Islander	1 (0.4%)
	Other	2 (0.7%)
Fitzpatrick Skin Type	I	12 (4.4%)
	II	78 (28.9%)
	III	81 (30.0%)
	IV	63 (23.3%)
	V	21 (7.8%)
	VI	15 (5.6%)

Note: N = Number of subjects in the analysis population. n (%) = Number and percentage of subjects among N.

d. Effectiveness Results

The primary effectiveness endpoint in this study was met and non-inferiority of saypha MagIQ relative to Control in terms of NLF responder rates shown at 24 weeks after treatment start for the full analysis set (FAS) (Table 7) and the per-protocol set (PPS) (Table 8). Similar proportions of NLF-SRS responders showing at least a clinically significant 1-point improvement were found in the two treatment groups (82.2%/83.5% of subjects with saypha MagIQ vs 81.9%/83.5% of subjects with Control).

Table 7. NLF-SRS Response Rate at Week 24 - Independent Blinded Evaluating Investigator (FAS)

NLF-SRS Change From Baseline	saypha MagIQ (N=270) n (%)	Control (N=270) n (%)	Difference of Proportions (%) (95% CI)[a]	p-value[b]
Responder[c]	222 (82.2)	221 (81.9)	0.37 (-2.96, 3.70)	<0.0001
Non-Responder (incl. Missing)	48 (17.8)	49 (18.1)	-	-
Missing[d]	23 (8.5)	23 (8.5)	-	-

Abbreviations: FAS, full analysis set; NLF-SRS, nasolabial folds-severity rating scale.
[a] Difference in proportion of responders saypha MagIQ – Control with respective 95% CI.
[b] McNemar type test.
[c] Responder was defined as a subject with at least 1 grade improvement from Baseline in NLF-SRS.
[d] Missing values at Week 24 were imputed as non-responder.

Table 8. NLF-SRS Response Rate at Week 24 - Independent Blinded Evaluating Investigator (PPS)

NLF-SRS Change From Baseline	saypha MagIQ (N=224) n (%)	Control (N=224) n (%)	Difference of Proportions (%) (95% CI)[a]	p-value[b]
Responder[c]	187 (83.5)	187 (83.5)	-0.00 (-3.71, 3.71)	<0.0001
Non-Responder (incl. Missing)	37 (16.5)	37 (16.5)	-	-
Missing[d]	15 (6.7)	15 (6.7)	-	-

Abbreviations: PPS, per-protocol analysis set; NLF-SRS, nasolabial folds-severity rating scale.
[a] Difference in proportion of responders saypha MagIQ – Control with respective 95% CI.
[b] McNemar type test.
[c] Responder was defined as a subject with at least 1 grade improvement from Baseline in NLF-SRS.
[d] Missing values at Week 24 were imputed as non-responder.

The proportion of NLF-SRS responders as rated by the independent blinded evaluating investigator in the FAS was slightly higher after initial treatment with saypha MagIQ compared with Control at Week 12 (93.4% vs 91.1%), Week 36 (80.6% vs 78.8%) and Week 48 (76.9 vs 70.4%) (Table 9). In the PPS, the proportion of NLF-SRS responders after initial treatment with saypha MagIQ compared with Control was as follows: Week 12 (93.0% vs 91.5%), Week 36 (80.4% vs 78.3%) and Week 48 (76.8 vs 70.2%) (Table 10), consistent with the results obtained in the FAS.

Table 9. NLF-SRS Response Rate Over Time - Blinded Evaluating Investigator (FAS)

Timepoint	NLF-SRS Change From Baseline	saypha MagIQ (N=270) n (%)	Control (N=270) n (%)	Difference of Proportions (%)[c]
week 12 (n[d] = 257)	Responder[a]	240 (93.4)	234 (91.1)	2.33
	Non-Responder (excl. Missing)	17 (6.6)	23 (8.9)	-
	Missing[b]	13	13	-
week 36 (n[d] = 170)	Responder[a]	137 (80.6)	134 (78.8)	1.76
	Non-Responder (excl. Missing)	33 (19.4)	36 (21.2)	-
	Missing[b]	100	100	-
week 48 (n[d] = 186)	Responder[a]	143 (76.9)	131 (70.4)	6.45
	Non-Responder (excl. Missing)	43 (23.1)	55 (29.6)	-
	Missing[b]	84	84	-

Abbreviations: FAS, full analysis set; NLF-SRS, nasolabial folds-severity rating scale.
[a] 'Responder' is defined as a subject with at least one grade improvement from Baseline in NLF-SRS.
[b] Subjects who do not have NLF-SRS assessment at baseline and/or at respective post-baseline visit are not considered in this analysis.
[c] Difference in proportion of responders saypha MagIQ – Control.
[d] n = Number of participants with available data at the specified time point.
The percentage is based on the subjects with results available at baseline and at respective post-baseline visit in each treatment group of Full Analysis Set.

Table 10. NLF-SRS Response Rate Over Time - Blinded Evaluating Investigator (PPS)

Timepoint	NLF-SRS Change From Baseline	saypha MagIQ (N=224) n (%)	Control (N=224) n (%)	Difference of Proportions (%)[c]
week 12 (n[d] = 213)	Responder[a]	198 (93.0)	195 (91.5)	1.41
	Non-Responder (excl. Missing)	15 (7.0)	18 (8.5)	-
	Missing[b]	11	11	-
week 36 (n[d] = 143)	Responder[a]	115 (80.4)	112 (78.3)	2.10
	Non-Responder (excl. Missing)	28 (19.6)	31 (21.7)	-
	Missing[b]	81	81	-
week 48 (n[d] = 151)	Responder[a]	116 (76.8)	106 (70.2)	6.62
	Non-Responder (excl. Missing)	35 (23.2)	45 (29.8)	-
	Missing[b]	73	73	-

Abbreviations: PPS, per-protocol analysis set; NLF-SRS, nasolabial folds-severity rating scale.
[a] 'Responder' is defined as a subject with at least one grade improvement from Baseline in NLF-SRS.

[b] Subjects who do not have NLF-SRS assessment at baseline and/or at respective post-baseline visit are not considered in this analysis.
[c] Difference in proportion of responders saypha MagIQ – Control.
[d] n = Number of participants with available data at the specified time point.
The percentage is based on the subjects with results available at baseline and at respective post-baseline visit in each treatment group of Per-Protocol Set.

A summary of actual values on the NLF-SRS and changes from Baseline over time is presented as assessed by the independent blinded photographic reviewers in Table 11.

Table 11. Summary of NLF-SRS Actual Values and Changes from Baseline Over Time - Independent Blinded Photographic Reviewer

NLF-SRS Change From Baseline	n	saypha MagIQ		Control	
		NLF-SRS mean	change from baseline mean	NLF-SRS mean	change from baseline mean
baseline	270	2.3	-	2.4	-
week 12	258	1.2	-1.1	1.3	-1.1
week 24	247	1.3	-1.0	1.5	-0.9
week 36	192	1.3	-1.0	1.5	-0.9
week 48	191	1.3	-1.0	1.5	-0.9

Aesthetic improvement based on the GAIS at Week 24 was confirmed by 92% of subjects in each group (Table 12).

Table 12. GAIS Response Rate at Week 24 - Subject

GAIS	saypha MagIQ (N=270) n (%)	Control (N=270) n (%)	Difference of Proportions (%)[a]
Responder[b]	229 (91.6)	228 (91.6)	0.03
Non-Responder	21 (8.4)	21 (8.4)	
Missing[c]	20	21	

[a] Difference in proportion of responders saypha MagIQ – Control.
[b] 'Responder' is defined as a subject with grading of 'improved', 'much improved' or 'very much improved' on the GAIS assessment.
[c] Subjects who do not have GAIS assessment at Week 24 are not considered in this analysis.

Subject satisfaction with aesthetic outcome according to the Rasch-transformed FACE-Q score was comparable for both treatments at Week 24 (70 for saypha MagIQ Lidocaine and 68 for Control). The subjects reported improvement over baseline at Week 24 was also comparable for the saypha MagIQ and Control treated NLFs (41 vs 39).

B. Supportive Study for saypha MagIQ

a. Study Design

The prospective, open-label, post-market clinical follow-up study was conducted in Europe and assessed clinical performance and safety of saypha MagIQ for the correction of moderate to severe NLFs.

After initial treatment, follow-up visits were performed at 2, 4, 24, and 36 weeks. A touch-up treatment could be administered at the Week 2 visit.

b. Study Endpoints

Primary effectiveness endpoints were the average change versus Baseline (Day 0) in the NLF-SRS grade at Week 24 as evaluated by the investigator, and the proportion of subjects with the NLF-SRS grade reduced by ≥1 point versus Baseline at Week 24.

c. Subject Demographics

A total of 60 subjects were treated. All were White (Caucasian) with a median age of 55.5 years.

d. Effectiveness Results

The average NLF severity based on the NLF-SRS had improved by a mean of 1.80 grades from Baseline to Week 24. The proportion of subjects with an improvement (reduction) of ≥1 NLF severity grade was 97%. (Table 13)

Table 13. Change in NLF severity from Baseline to Week 24

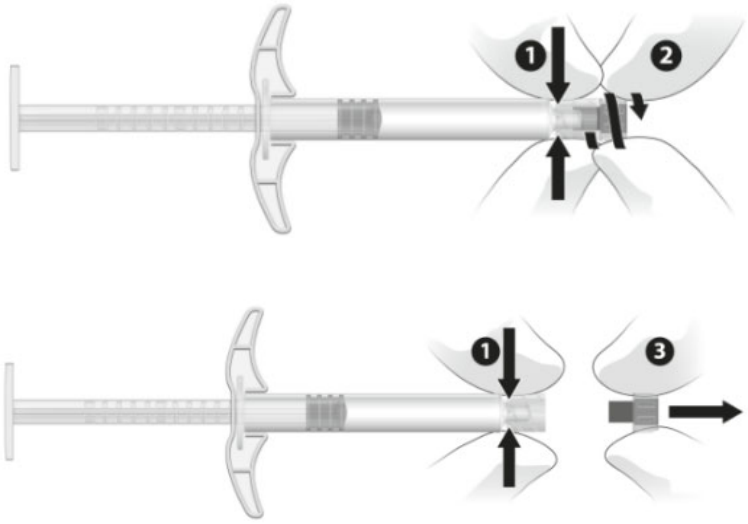
Analysis set	N	Visit	Mean (SD) of change in NLF severity	Number (%)[a] of subjects with ≥1 grade reduction
ITT	59	Week 4	-1.98 (0.40)	59 (98.3)
	59	Week 24	-1.80 (0.60)	58 (96.7)
	59	Week 36	-1.67 (0.61)	58 (96.7)
PP	58	Week 4	-1.98 (0.41)	58 (100.0)
	58	Week 24	-1.79 (0.60)	57 (98.3)
	58	Week 36	-1.66 (0.61)	57 (98.3)

[a] Percentages are based on the number of subjects in the analysis set.
ITT = intent-to-treat, N = number of subjects with evaluable data, NLF = nasolabial fold, PP = per protocol, SD = standard deviation.

8. INSTRUCTIONS FOR USE

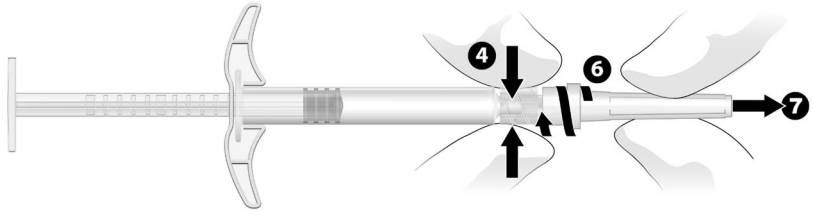
A. To Attach Needle to Syringe

Hold the Luer-Lock adapter as shown in (1). To remove the tip cap, twist (2) and pull carefully (3).



Hold the syringe as shown in (4). Open the enclosed needle case and insert the needle firmly (5).

Holding the Luer-Lock (4), tightly secure the needle by twisting it clockwise (6) and pull off the needle cap before use (7).



B. Healthcare Professional Instructions

1. saypha MagIQ is a cross-linked gel formulation that can be injected using a fine gauge needle (e.g., 27G ½") for correction of facial wrinkles and folds (such as nasolabial folds). The use of other needles and cannulas has not been studied.
2. Before and after treatment, health care professionals are encouraged to conduct vision assessments, including visual acuity, extraocular motility, and visual field testing.
3. Health care practitioners are encouraged to be prepared with the following in the event of an intravascular injection:
    - Ensuring supplies are immediately available, as recommended by the American Society for Dermatologic Surgery guidelines [1]
    - Identifying a local ophthalmologist or ophthalmology subspecialist to be available in the event of an ophthalmic adverse event related to a dermal filler injection
    - Conducting a basic neurologic examination in the event of an ophthalmic adverse event due to the association of such events with central nervous system deficits
    - If a neurological complication is suspected the patient shall be sent to a local emergency room emergently.
4. Prior to treatment, the patient's medical history should be obtained, and the patient should be fully apprised of the indications, contraindications, warnings, precautions, treatment reactions, adverse reactions, and method of administration. Patients should also be advised that supplemental touch-up treatments may be required to achieve and maintain desired correction.
5. The patient's soft tissue deficiencies should be characterized with regard to etiology, distensibility, stress at the site, and depth of lesion. Pre-treatment photographs are recommended.
6. Although lidocaine in saypha MagIQ aids in relieving pain, supplementary anesthesia may be used for additional pain management during and after injection.
7. After ensuring that the patient has thoroughly washed the treatment area with soap and water, the area should be swabbed with alcohol or other antiseptic.
8. Do not attempt to bend or otherwise manipulate the needle before or during treatment.
9. Before injection, press the plunger rod carefully until a small droplet is visible at the tip of the needle.
10. If the needle is bent or blocked, do not increase the pressure on the plunger rod. Instead, stop the injection and replace the needle.
11. After insertion of the needle, and just before injection, the plunger rod should be withdrawn slightly to aspirate and verify the needle is not intravascular. If blood is withdrawn, this could

[1] Jones DH, Fitzgerald R, Cox SE, et al. Preventing and treating adverse events of injectable fillers: evidence-based recommendations from the American Society for Dermatologic Surgery Multidisciplinary Task Force. *Dermatol Surg*. 2021;47(2):214-226.

indicate intravascular placement; therefore, stop immediately, reposition the needle and repeat the retraction step again. The absence of blood does not necessarily exclude intravascular placement; therefore, it is important to inject the product slowly and apply the least amount of pressure necessary.

12. After the first small amount of material has been injected into the patient, wait a few seconds to allow the lidocaine to take effect before proceeding with the rest of the injection.
13. The injection technique, injection depth, and volume administered may vary based on the patient's treatment needs. Injecting the product too superficially or uneven may result in visible lumps and/or bluish discoloration (Tyndall effect).
14. The insertion of the needle may lead to superficial needle stick/puncture wounds.
15. Lateral movements of the needle should be avoided since these can result in a fan-like dissection of the sub-epidermal plane and vascular damage, thus increasing the risk of local undesired side effects such as hematoma, swelling, skin discoloration, pain or tenderness at the injection site.
16. Evenly inject saypha MagIQ by applying slow and even pressure on the plunger rod. It is important that the injection be stopped before the needle is pulled out of the skin to prevent material from leaking out or being placed too superficially in the skin.
17. In the clinical study, the typical injection volume to achieve optimal correction of moderate to severe nasolabial folds per treatment site was approximately 1.0 mL at initial treatment and 0.4 mL at touch-up treatment. This may vary depending on the goals the patient wished to achieve. Injection volumes after repeat treatment tended to be lower, with the typical injection volume to achieve optimal correction being approximately 0.7 mL per treatment site.
18. Inject low volumes in two or more sessions instead of high volumes in one session. Do not overcorrect. A new injection may be placed at a previously injected location from two weeks after the original treatment. There is no non-clinical data available regarding the safety of administering more than 2.4 mL of saypha MagIQ during each treatment session.
19. If immediate blanching occurs, the injection should be stopped, and the area massaged until it returns to a normal color. Blanching may represent a vessel occlusion. If normal skin coloring does not return, do not continue with the injection. Treat in accordance with American Society for Dermatologic Surgery guidelines[1].
20. After the injections are complete, the treated site may be gently massaged so that the product contours to the surrounding tissues and is evenly distributed. If overcorrection occurs, massage the area with your fingers or against an underlying superficial bone to obtain optimal results.
21. With patients who have localized swelling, the degree of correction is sometimes difficult to judge at the time of treatment. In these cases, it is better to invite the patient back to the office for a touch-up treatment.

22. Patients may experience treatment site reactions, which typically resolve within 14 days. An ice pack may be applied using gentle pressure for a short period following treatment to minimize swelling and reduce pain.
23. The healthcare professional should instruct the patient to promptly report back any problems associated with the use of saypha MagIQ.
24. After use, treatment syringes and needles are biohazards. Handle and dispose of these items in accordance with accepted medical practice and applicable local, state, and federal requirements.

C. Patient Instructions

Please also instruct your patients of the following:

- Patients should seek immediate medical help if they experience changes in vision, signs of stroke, white appearance of the skin or unusual pain during or shortly after treatment. Patients should seek medical advice as soon as any undesired side effects occur.
- Within the first 24 hours, patients should avoid strenuous exercise and extensive sun or heat exposure. Exposure to any of the above may cause temporary redness, swelling, and/or itching at the injection site.
- Within the first 2 days, the patient should avoid massaging the treatment area as this increases the risk of implant mobility and impaired wound healing.
- If the treated area is swollen, an ice pack may be applied to the site for a short period.

9. HOW SUPPLIED

saypha MagIQ is supplied in individual treatment syringes with two 27G ½" needles for single patient use and ready for injection (implantation). The volume in each syringe is as stated on the syringe label and the carton. The contents of the syringe are sterile and non-pyrogenic. Do not re-sterilize. Do not use if package is opened or damaged.

As long as the syringe is stored in its original packaging (carton/blister), the viscoelastic implant inside the intact syringe is guaranteed to be sterile until the use-by date printed on the folding box and the label on the syringe. The syringe constitutes the sterile barrier. A compromised sterile barrier may lead to a non-sterile implant that could cause bacterial infections associated with skin inflammation and irritation, erythema, pain, fever, and abscess. Therefore, do not use the syringe beyond the use-by date or if it is cracked or broken.

10. SHELF LIFE AND STORAGE

saypha MagIQ must be used prior to the use-by date printed on the packaging and syringe label.

Store the device in the original blister and folding box at 5–25°C/41–77°F, in a dry place and protected from sunlight, heat and frost.

To place an order, contact 1-800-636-7546.

Distributed by:
Obagi Cosmeceuticals LLC,
Long Beach, CA, 90806

Manufactured by:
CROMA-PHARMA GmbH
Industriezeile 6
2100 Leobendorf
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Patents: See www.obagi.com/saypha

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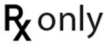
Revision: 09/2025

Symbols Glossary

Symbol	Symbol Title	Explanatory Text
	Manufacturer	Indicates the medical device manufacturer
	Use-by date	Indicates the date after which the medical device is not to be used
	Batch code	Indicates the manufacturer's batch code so that the batch or lot can be identified
	Catalogue number	Indicates the manufacturer's catalogue number so that the medical device can be identified
	Distributor	Indicates the entity distributing the medical device into the locale
	Sterilized using steam or dry heat	Indicates a medical device that has been sterilized using steam or dry heat
	Do not re-sterilize	Indicates a medical device that is not to be re-sterilized
	Do not use if package is damaged and consult instructions for use	Indicates that a medical device that should not be used if the package has been damaged or opened and that the user should consult the instructions for use for additional information
	Single sterile barrier system	Indicates a single sterile barrier system
	Fragile, handle with care	Indicates a medical device that can be broken or damaged if not handled carefully
	Keep away from sunlight	Indicates a medical device that needs protection from light sources
	Keep dry	Indicates a medical device that needs to be protected from moisture

Symbol	Symbol Title	Explanatory Text
	Temperature limit	Indicates the temperature limits to which the medical device can be safely exposed
	Do not re-use	Indicates a medical device that is intended for one single use only
	Consult instructions for use or consult electronic instructions for use	Indicates the need for the user to consult the instructions for use
	Medical device	Indicates the item is a medical device
	Unique device identifier	Indicates a carrier that contains unique device identifier information
	Prescription Device	Caution: Federal (USA) law restricts this device to sale by or on the order of a licensed physician or properly licensed practitioner.