bellafill®

Instructions for Use

CAUTION

Federal Law restricts this device for sale by or on the order of a physician or licensed practitioner.

DESCRIPTION

Bellafill®[1] is an implant composed of non-resorbable polymethylmethacrylate (PMMA) microspheres, 30 to 50 microns in diameter, suspended in a water-based carrier gel composed of 3.5% bovine collagen, 92.6% buffered, isotonic water for injection, 0.3% lidocaine hydrochloride, 2.7% phosphate buffer, and 0.9% sodium chloride.

INTENDED USE / INDICATIONS

Bellafill® is indicated for the correction of nasolabial folds and moderate to severe, atrophic, distensible facial acne scars on the cheek in patients over the age of 21 years.

CONTRAINDICATIONS

- Bellafill® is contraindicated for patients displaying a positive response to the required Bellafill® Skin Test. Refer to the Bellafill® Skin Test Instructions for Use for complete instructions for administration and evaluation of the Skin Test.
- Bellafill® is contraindicated for patients with severe allergies manifested by a history of anaphylaxis or history or presence of multiple severe allergies.
- Bellafill® contains lidocaine and is contraindicated for patients with known lidocaine hypersensitivity.
- Bellafill® contains bovine collagen and is contraindicated for patients with a history of allergies to any bovine collagen products, including but not limited to injectable collagen, collagen implants, hemostatic sponges, and collagen-based sutures, because these patients are likely to have hypersensitivity to the bovine collagen in Bellafill®.
- Bellafill® is contraindicated for patients undergoing or planning to undergo desensitization injections to meat products, as these injections can contain bovine collagen.
- Bellafill® is contraindicated for patients with bleeding disorders.
- Bellafill® is contraindicated for use in lip augmentation and injection into the vermilion or the wet mucosa of the lip.
- Bellafill® should not be used in patients with known susceptibility to keloid formation or hypertrophic scarring.

WARNINGS

- The safety of Bellafill® when used within 6 months of collagen, botulinum toxin, or other wrinkle therapies has not been studied.
- A Bellafill® Skin Test must be administered and evaluated prior to injection of Bellafill®. Patients demonstrating a positive skin test or 2 equivocal skin tests should not be considered candidates for treatment. Patients demonstrating an anti-bovine collagen serum IgG level outside of the normal range at baseline should not be considered candidates for treatment. A negative Skin Test does not preclude the possibility of the patient subsequently developing a delayed hypersensitivity response to the implant material following treatment exposure. Refer to the Bellafill® Skin Test Instructions for Use.
- Use of Bellafill® at specific sites in which an active inflammatory process (skin eruptions such as cysts, pimples, rashes, or hives) or infection is present should be deferred until the inflammatory process has been controlled.
- Introduction of 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, inject the product slowly and apply the least amount of pressure necessary. Rare but serious adverse events associated with the intravascular injection of soft-tissue fillers in the face have been reported and include temporary or permanent vision impairment; blindness; 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 a stroke, blanching of the skin, or unusual pain during or shortly after the procedure. Patients should receive prompt medical attention and possibly evaluation by an appropriate health care practitioner specialist should an intravascular injection occur.
- Bellafill is not indicated for use in the periocular area (e.g. tear trough), as the effects of injection in this location have not been studied. The following adverse events including, but not limited to, lumps, swelling, granulomas and vision loss due to vascular occlusion, have been reported in the post-market surveillance data with off-label injection in the periocular area.

PRECAUTIONS

- Bellafill® contains non-absorbable PMMA microspheres. Implantation is permanent and will not be reversed without physical removal.
- The safety of Bellafill® for use during pregnancy and in breastfeeding females has not been established.
- Bellafill® is packaged in a sealed tray containing individual treatment syringes with sterile needles for single patient use, packaged in a box. The tip of the syringe is sealed with a Winged cap. Do not use if the seal on the tray lid or syringe is broken or removed. Do not re-sterilize.
- The safety of injecting greater amounts than 3.5 cc per treatment site or 8.9 cc overall has not been established.
- The safety and effectiveness of Bellafill® for the treatment of non-distensible atrophic acne scars has not been established. The use of Bellafill® for ice pick or sinus tract scars has not been studied.
- The safety and effectiveness of Bellafill® for nasolabial-fold wrinkles and cheek acne scars have not been established in patients under the age of

21 years. There is limited information on the safety of Bellafill® in patients less than 36 years of age. In the pivotal Acne Scar Study of Bellafill®, the incidence of injection-site reactions in subjects less than 36 years old (30 subjects) was similar to the incidence in subjects above the age of 36 (113 subjects). The majority of these injection-site reactions were mild in severity.

The safety in patients with known susceptibility to hyperpigmentation, keloid formation, and hypertrophic scarring has not been studied. Formation of hyperpigmentation, keloids, or hypertrophic scars may occur after dermal-filler injections including Bellafill®. In the pivotal Acne Scar Study of Bellafill®, the incidence and severity of adverse events in 34 subjects with Fitzpatrick Skin Types V and VI was similar to that reported in 109 patients with Fitzpatrick Skin types I–IV and no unique adverse events associated with these patient subgroups were observed.

- As with all transcutaneous procedures, Bellafill® injection carries a risk of infection. The usual precautions associated with injectable materials should be followed.
- [1] Bellafill® formerly known as Artefill®
- The safety of Bellafill® in patients on immunosuppressive therapy or with connective tissue disorders has not been established however these patients may have an increased susceptibility or hypersensitivity response and/or accelerated clearance of their implants when injected with bovine collagen preparations. Therefore, caution should be used when treating these patients, including consideration for further skin testing.
- Bruising or bleeding may occur at Bellafill® injection sites. Use of Bellafill® in patients who have undergone therapy with thrombolytics, anticoagulants, or inhibitors of platelet aggregation within 3 weeks preceding treatment has not been studied.
- Patients should minimize exposure of the treated area to excessive sun, UV-lamp exposure, and extreme cold weather at least until any initial swelling and redness has resolved.
- If laser treatment, chemical peeling or any other procedure based on active dermal response is considered after treatment with Bellafill®, there is a possible risk of eliciting an inflammatory reaction at the implant site. This also applies if Bellafill® is administered before the skin has healed completely after such a procedure.
- The use of Bellafill® in anatomical spaces other than the dermis for correction of nasolabial folds and for acne scars on the cheek has not been studied. Refer to the Clinical Studies section for more information on implantation sites that have been studied.
- The use of Bellafill® in patients with thin or flaccid skin has not been studied and the cosmetic results for these patients are unknown.
- Long-term safety and effectiveness of Bellafill® beyond five years has not been established.
- In order to minimize the risks of potential complications, this product should only be used by health care practitioners who have appropriate training, experience, and who are knowledgeable about the anatomy at and around the site of injection.
- Health care practitioners 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.
- After use, treatment syringes and needles may be potential biohazards. Handle accordingly and dispose of in accordance with accepted medical practice and applicable local, state, and federal requirements.
- Bellafill® has an opaque, off-white appearance. In the event that the content of a syringe shows signs of separation and/or appears clear (like water), do not use the syringe, and notify Suneva Medical immediately. In the United States or Canada call 844-Bellafill (844-235-5234). Outside of the United States or Canada call +1-858-550-9999.
- Bellafill® should not be mixed with other products before implantation of the device.

ADVERSE EVENTS

Nasolabial Fold and Acne Scar Indications:

A total of 1,542 patients have been treated with Bellafill® (or a previous generation) in four U.S. clinical studies. Three of the four studies were conducted on 1,399 patients treated with Bellafill® in support of the indication for the correction of Nasolabial Folds. One of the four studies was conducted on 143 patients treated with Bellafill® in support of the indication for the correction of moderate to severe, atrophic, distensible facial acne scars on the cheek in patients over the age of 21 years.

a) U.S. Controlled Nasolabial Fold (NLF) Clinical Trials

All adverse events (AEs), including those attributed and not attributed to treatment, reported in Bellafill® or Control subjects at an incidence of 1% or greater in U.S. studies are presented in **Table 1** below in descending order according to frequency in the Bellafill® group.

TABLE 1: ADVERSE EVENTS REPORTED AT AN INCIDENCE OF 1% OR GREATER IN U.S. NASOLABIAL FOLD CLINICAL TRIALS OF BELLAFILL®

Event	Number of Events (Events/Subjects Treated, %)		
	Bellafill®[1] n=285	Bellafill®[2] n=106	Control n=123[3,4]
Lumpiness at injection area more than one month after injection	13 (4.6%)	–	4 (3.3%)
Persistent swelling or redness	10 (3.5%)	3 (2.8%)	13 (10.6%)
Increased sensitivity	5 (1.8%)	2 (1.9%)	–
Rash, itching more than 48 hours after injection	4 (1.4%)	–	2 (1.6%)
Sensitization reactions	–	–	6 (4.9%)
Abscess	–	–	3 (2.4%)
Visibility of puncture area	–	–	2 (1.6%)

[1] 128 Bellafill® subjects in the controlled study and 157 subjects in an open-label study, who were followed for 1 year after implantation.
[2] 106 Control subjects who received Bellafill® in the crossover arm of the controlled study and were followed for 6 months after implantation.
[3] 123 subjects who received the Control treatment in the controlled study and were followed for 6 months after implantation.
[4] The Control treatment in the study was a commercially available collagen implant (Zyplast®).

No systemic adverse events were reported at an incidence of 1% or greater. One severe adverse event (granuloma or enlargement of the implant) and 14 moderate adverse events (persistent swelling or redness, lumpiness at injection site more than 1 month after injection, blurred vision, flu-like symptoms, abscess, granuloma or enlargement of the implant, alopecia areata) were reported for Bellafill® subjects. Nine severe adverse events (lumpiness at injection site more than 1 month after injection, abscess, infection, granuloma or enlargement of the implant, sensitization reactions, increased sensitivity, persistent swelling or redness), and 12 moderate adverse events (persistent swelling or redness, rash, itching more than 48 hours after injection, sensitization reactions, lumpiness at injection site more than 1 month after injection, visibility of the puncture area, abscess) were reported for Control subjects.

Local adverse events reported in Bellafill® subjects at an incidence of less than 1% in U.S. studies, whether or not they were determined to be related to the implant, were sensitization reactions, abscess, visibility of the puncture area, blurred vision, flu-like symptoms, recurrence of existing herpes labialis, granuloma or enlargement of the implant, acneiform lesions, occasional tenderness, redness and visible capillaries, alopecia areata, and dry skin. Systemic adverse events reported at an incidence of less than 1% were mild chest congestion and fainting. One subject was diagnosed with breast cancer, determined by the investigator not to be related to the implant.

For Control subjects, local adverse events reported at an incidence of less than 1%, whether or not they were determined to be related to the implant, were increased sensitivity, flu-like symptoms, granuloma or enlargement of the implant, infection, and acneiform reaction. One subject died of trauma unrelated to the implant.

ADVERSE EVENTS LASTING LONGER THAN TWO WEEKS
The following is a summary of the reported duration of adverse events lasting longer than 2 weeks in Bellafill® subjects (n=391 subjects) in U.S. studies: lumpiness at injection site more than 1 month after injection (n=12 events), duration varied from 4 weeks to unresolved at 26 weeks; persistent swelling or redness (n=8 events), duration varied from 5 weeks to unresolved at 26 weeks; increased sensitivity (n=7 events), duration varied from 4 weeks to unresolved at 26 weeks; rash and itching (n=2 events), duration varied from 3 weeks to 6 weeks; sensitization reactions (n=2 events), duration varied from 19 weeks to unresolved at 26 weeks; visibility of the puncture site (n=1 event), duration was 13 weeks; granuloma or enlargement of the implant (n=4 events), duration varied from 10 weeks to unresolved at 26 weeks; other local complications (n=5 events), duration was unresolved at 26 weeks. One subject suffered from breast cancer unrelated to the implant.

Reported duration of adverse events lasting longer than 2 weeks in Control subjects (n=123 subjects): lumpiness at injection site more than 1 month after injection (n=2 events), duration varied from 13 weeks to unresolved at 26 weeks; persistent swelling or redness (n=12 events), duration varied from 7 weeks to unresolved at 26 weeks; increased sensitivity (n=1 event), duration was unresolved at 26 weeks; rash and itching (n=2 events), duration was unresolved at 26 weeks; sensitization reactions (n=4 events), duration varied from 7 weeks to unresolved at 26 weeks; abscess (n=2 events), durations were unresolved at 26 weeks; visibility of the puncture site (n=1 event), duration was unresolved at 26 weeks; granuloma or enlargement of the implant (n=1 event), duration was unresolved at 26 weeks; flu-like symptoms (n=1 event), duration was unresolved at 26 weeks. One subject died from an accident unrelated to the implant.

ADVERSE EVENTS REPORTED THREE MONTHS OR LONGER AFTER TREATMENT
Among the 391 subjects treated with Bellafill®, adverse events with reported onset dates 3 months or more after treatment were lumpiness at the injection site (6), rash and itching (3), sensitization reaction (2), increased sensitivity (2), persistent swelling and redness (1), granuloma or granulomatous inflammation (1), alopecia areata (1), visibility of the puncture site (1), and redness and visible capillaries near the area of injection (1).

Among the 123 Control subjects, adverse events with reported onset dates 3 months or more after treatment were abscess (1), infection (1), lumpiness (1), acneiform reaction (1), flu-like symptoms (1), persistent swelling or redness (1), and trauma fatality not related to the implant (1).

b) U.S. Controlled Acne Scar Clinical Trial

The U.S. Acne Scar pivotal study (Study SUN-11-001) involved 147 treated subjects at 10 centers. At baseline, subjects were randomized to receive Bellafill® in the cheeks or (Control group) saline. At 6 months, all Control subjects were eligible to receive treatment with Bellafill®.

Of the 147 subjects treated in the study, 143 subjects received a treatment with Bellafill® at either baseline/Day 0 (Period I) or at Month 6 (Period II, Track B). Therefore the safety information reflects the combination of patient outcomes for the initial (n=97) and crossover (n=46) Bellafill® subjects (i.e., 97 + 46 = 143 total) compared to the 50 subjects who were initially enrolled in the Control treatment arm.

Subject Diary:
Subjects were asked to keep diary cards and grade symptoms of erythema, swelling, bruising, pain, itching, lumps/bumps and discoloration. Subjects'

scores for the severity of these events after initial treatment are presented in **Table 2** and durations are provided in **Table 3**, respectively. Subjects who observed any signs or symptoms (89.2%), experienced them shortly after Bellafill® treatment and the majority were mild to moderate in intensity. Subjects typically reported these diary card symptoms as resolved in 1-7 days. Similar subject diary outcomes were noted following touch-up treatment injections.

TABLE 2: MAXIMUM INTENSITY OF SIGNS/SYMPTOMS AFTER INITIAL BELLAFILL® TREATMENT FROM SUBJECT DIARY (n=130)*

Sign/Symptom (R&L side combined)	None n (%)	Mild n (%)	Moderate n (%)	Severe n (%)
Any sign/symptom	14 (10.8%)	54 (41.5%)	51 (39.2%)	11 (8.5%)
Swelling	40 (30.8%)	48 (36.9%)	38 (29.2%)	4 (3.1%)
Erythema	44 (33.8%)	60 (46.2%)	23 (17.7%)	3 (2.3%)
Pain	47 (36.2%)	52 (40.0%)	28 (21.5%)	3 (2.3%)
Bruising	53 (40.8%)	49 (37.7%)	23 (17.7%)	5 (3.8%)
Lumps/bumps	55 (42.3%)	45 (34.6%)	27 (20.8%)	3 (2.3%)
Itching	97 (74.6%)	26 (20.0%)	7 (5.4%)	0 (0.0%)
Discoloration	102 (78.5%)	21 (16.2%)	6 (4.6%)	1 (0.8%)

*Number of treated subjects returning diaries, combined for Period I and Period II data. Percentages are based on the number of subjects returning diaries.

TABLE 3: DURATION OF SIGNS/SYMPTOMS AFTER INITIAL BELLAFILL® TREATMENT FROM SUBJECT DIARY (N=130)*

Sign/Symptom (R&L side combined)	Any	1 day	2–7 days	8–14 days
Any sign/symptom	116 (89.2%)	7 (5.4%)	61 (46.9%)	48 (36.9%)
Erythema	86 (66.2%)	34 (26.2%)	39 (30.0%)	13 (10.0%)
Swelling	90 (69.2%)	15 (11.5%)	65 (50.0%)	10 (7.7%)
Bruising	77 (59.2%)	7 (5.4%)	44 (33.8%)	26 (20.0%)
Pain	83 (63.8%)	17 (13.1%)	57 (43.8%)	9 (6.9%)
Itching	33 (25.4%)	10 (7.7%)	19 (14.6%)	4 (3.1%)
Lumps/bumps	75 (57.7%)	14 (10.8%)	44 (33.8%)	17 (13.1%)
Discoloration	28 (21.5%)	5 (3.8%)	13 (10.0%)	10 (7.7%)

*Number of treated subjects returning diaries, combined for Period I and Period II data.
Percentages are based on the number of subjects returning diaries.

Physician-Diagnosed Adverse Events
46/143 of the Bellafill® and 16/50 of the Control subjects experienced at least one all cause (related and unrelated) Treatment-Emergent Adverse Event (TEAEs). TEAEs that occurred in ≥4% of the subjects (related and unrelated) (i.e., 51/143 of the Bellafill® and 12/50 of the Control subjects) are presented below in **Table 4.**

TABLE 4: TREATMENT-EMERGENT AEs IN ≥ 4% OF THE SUBJECTS SORTED BY SYSTEM ORGAN CLASS (SOC) AND PREFERRED TERM

System Organ Class Code	Preferred Term (PT)	Bellafill® n=143*		Control n=50	
		Subjects	Events	Subjects	Events
General Disorders and Administration Site Conditions		22 (15.4%)	27	1 (2.0%)	1
	Burning sensation	**1 (0.7%)**	**1**	**0 (0.0%)**	**0**
	Device breakage	1 (0.7%)	1	0 (0.0%)	0
	Fatigue	2 (1.4%)	2	0 (0.0%)	0
	Injection site bruising	3 (2.1%)	3	0 (0.0%)	0
	Implant site mass	1 (0.7%)	1	0 (0.0%)	0
	Injection site discoloration	1 (0.7%)	1	0 (0.0%)	0
	Injection site pain	3 (2.1%)	3	0 (0.0%)	0
	Injection site reactions	6 (4.2%)	6	0 (0.0%)	0
	Pruritus	1 (0.7%)	1	0 (0.0%)	0
	Swelling	3 (2.1%)	3	0 (0.0%)	0
	Tenderness	5 (3.5%)	5	1 (2.0%)	1
Infections and Infestations		**14(9.8%)**	**16**	**4 (8.0%)**	**6**
	Bacterial infection	1 (0.7%)	1	0 (0.0%)	0
	Bronchitis	0 (0.0%)	0	1 (2.0%)	1
	Ear infection	1 (0.7%)	1	0 (0.0%)	0
	Hordeolum	1 (0.7%)	1	0 (0.0%)	0
	Influenza	1 (0.7%)	1	0 (0.0%)	0
	Influenza-like illness	2 (1.4%)	2	2 (4.0%)	3
	Meningitis	1 (0.7%)	1	0 (0.0%)	0
	Nasopharyngitis	4 (2.8%)	4	0 (0.0%)	0
	Oral infection	0 (0.0%)	0	1 (2.0%)	1
	Pharyngitis	1 (0.7%)	1	0 (0.0%)	0
	Pharyngitis streptococcal	1 (0.7%)	1	1 (2.0)	1
	Sinusitis	2 (1.4%)	2	0 (0.0%)	0
	Skin papilloma	1 (0.7%)	1	0 (0.0%)	0
Musculoskeletal and Connective Tissue Disorders		**5 (3.5%)**	**5**	**5 (10.0%)**	**5**
	Arthralgia	2 (1.4%)	2	0 (0.0%)	0
	Back pain	2 (1.4%)	2	2 (4.0%)	2

Hand fracture	0 (0.0%)	0	1 (2.0%)	1
Pain in extremity	1 (0.7%)	1	0 (0.0%)	0
Tendonitis	0 (0.0%)	0	1 (2.0%)	1
Wrist fracture	0 (0.0%)	0	1 (2.0%)	1
Skin and Subcutaneous Tissue Disorders	10 (6.9%)	15	2 (4.0%)	2
Acne	1 (0.7%)	1	0 (0.0%)	0
Actinic keratosis	1 (0.7%)	1	0 (0.0%)	0
Dermatitis atopic	1 (0.7%)	1	0 (0.0%)	0
Dermatitis contact	2 (1.4%)	2	0 (0.0%)	0
Erythema	1 (0.7%)	1	0 (0.0%)	0
Herpes Zoster	1 (0.7%)	1	0 (0.0%)	0
Papule	1 (0.7%)	1	1 (2.0%)	1
Rash	2 (1.4%)	4	0 (0.0%)	0
Seborrheic dermatitis	1 (0.7%)	1	0 (0.0%)	0
Squamous cell carcinoma of skin	1 (0.7%)	1	0 (0.0%)	0
Urticaria	1 (0.7%)	1	0 (0.0%)	0

* n=143 is based on 97 subjects treated with Bellafill® from Study Period I and 46 Period II Control subjects that crossed over and were treated with Bellafill®.

Five serious adverse events (SAEs) were noted during the study; cholecystitis, lower-back nerve impingement, recurrence of breast cancer, West Nile meningitis, and exacerbation of depression. None were deemed related to study treatment. There were no deaths during the study.

Adverse events of special interest were followed separately for the study. These included hyper- and hypopigmentation, hypertrophic scarring or keloid formation, and the appearance of granulomas. None of these adverse events were reported.

Fourteen (14) Bellafill® and no Control subjects experienced treatment-related adverse events (TRAEs). Twelve (12) adverse events were mild, one (1) case of injection site reaction was moderate in severity, and one (1) injection site bruising was severe in intensity. Eleven (11) events resolved and three (3) cases of injection site reaction (lumpiness directly after injection) persisted throughout the study. Two (2) of these events were deemed by the investigator to be mild and one (1) event was deemed to be of moderate severity. All treatment-related adverse events (TRAEs) reported in Bellafill® subjects by severity and duration are presented in **Table 5** and **6**, respectively.

TABLE 5: SUMMARY OF TRAE (BY SEVERITY)

System Organ Class/ Preferred Term		Subject (n=143)	Events
Any TRAE		**14 (9.8%)**	**14**
	Mild	12 (8.4%)	12
	Moderate	1 (0.7%)	1
	Severe	1 (0.7%)	1
General Disorders and Administration Site Conditions			
Implant site mass		**1 (0.7%)**	**1**
	Mild	1 (0.7%)	1
	Moderate	0	0
	Severe	0	0
Injection site pain		**3 (2.1%)**	**3**
	Mild	3 (2.1%)	3
	Moderate	0	0
	Severe	0	0

Injection site reactions (i.e., lumpiness and papule formation)		**4 (2.8%)**	**4**
	Mild	3 (2.1%)	3
	Moderate	1 (0.7%)	1
	Severe	0	0
Swelling		**1 (0.7%)**	**1**
	Mild	1 (0.7%)	1
	Moderate	0	0
	Severe	0	0
Injection site bruising		**3 (2.1%)**	**3**
	Mild	2 (1.4%)	2
	Moderate	0	0
	Severe	1 (0.7%)	1
Tenderness		**1 (0.7%)**	**1**
	Mild	1 (0.7%)	1
	Moderate	0	0
	Severe	0	0
Skin and Subcutaneous Tissue Disorders			
Acne		**1 (0.7%)**	**1**
	Mild	1 (0.7%)	1
	Moderate	0	0
	Severe	0	0

TABLE 6: SUMMARY OF TRAE (BY DURATION)

SOC/PT		Subject (n=143)	Events
Any TRAE	**n**	**14**	**14**
	Mean #days (SD)	30.8 (53.8)	
	Median (min max)	16 (1,180)	
General Disorders and Administration Site Conditions			
Implant site mass	**n**	**1**	**1**
	Mean #days (SD)	180 (0)	
	Median (min max)	180 (180,180)	
Injection site pain	**n**	**3**	**3**
	Mean #days (SD)	3.7 (1.5)	
	Median (min max)	4 (2,5)	
Injection site reactions (i.e. lumpiness and papule formation)	**n**	**4***	**4**
	Mean #days (SD)	76 (0)	
	Median (min max)	76 (76,76)	
Swelling	n	1	1
	Mean #days (SD)	1 (0)	
	Median (min max)	1 (1,1)	
Injection site bruising	**n**	**3**	**3**
	Mean #days (SD)	17.3 (0.6)	
	Median (min max)	17 (17,18)	
Tenderness	**n**	**1**	**1**
	Mean #days (SD)	3 (0)	
	Median (min max)	3 (3,3)	
Skin and Subcutaneous Tissue Disorders			
Acne	**n**	**1**	**1**
	Mean #days (SD)	16 (0)	
	Median (min max)	16 (16,16)	

* Data does not include 3 subjects each with 1 unresolved event.

c) U.S. 5-Year Post Approval Study (PAS001-Study P521-01)

In agreement with FDA, Suneva Medical conducted a 5-year prospective study of Bellafill® as an injectable implant for the correction of nasolabial folds (NLF).

The primary objectives were to determine the incidence of granuloma formation and the incidence of adverse events at each follow-up period. The secondary objective was to determine the subject's assessment of satisfaction using a five-point scale at each follow-up visit over the 5-year time period.

This was a multi-center (23 sites), open-label study in which one thousand and eight (1,008) subjects were followed for a 5-year period after their completion of NLF correction with Bellafill®. Treatments were administered according to the approved labeling for the Bellafill® NLF indication. Subjects underwent up to three injection sessions over 6 weeks as needed to obtain the best possible correction.

Follow-up for AEs and satisfaction data was completed by mail or telephone questionnaire survey at 6, 12, and 18 months, and 2, 3 and 4 years post-treatment. Subjects were seen and examined in person at the 5-year post-treatment visit. If the questionnaire responses submitted at any timepoint indicated a potential adverse event in the treatment area and/or the face, the subjects were asked to return to the study site for evaluation.

Adverse events reported by subjects were confirmed and adjudicated by the investigators. Any event that an Investigator thought might potentially be a granulomatous lesion was biopsied and sent to an independent pathology lab for evaluation and diagnosis.

Primary Endpoints (safety): (1) Incidence of clinically identified and histologically confirmed granulomas tabulated by event and by subject; (2) incidence of serious unanticipated AEs stratified by severity and relation to treatment and tabulated by event and by subject; (3) incidence of anticipated AEs categorized as granulomas, serious unanticipated AEs, and AEs tabulated by event and within each study period.

Results confirmed both the short and long term (5-year) safety of Bellafill®, as no device-related serious adverse events (SAEs) or unanticipated AEs were noted and the general adverse event profile was similar to prior NLF studies.

A total of 887 AEs were reported among 416 of the 1,008 treated subjects. A total of 101 SAEs were reported among 75 treated subjects; none of these SAEs were considered device-related, and all were unanticipated. Of these 101 serious adverse events the majority were moderate to severe (86). The most commonly reported SAEs were "other systemic complications (46)" and "other local complications (43)" non device–related SAEs.

A total of 177 device-related AEs among 118 treated subjects were observed. Of the 177 treatment-related adverse events, the majority (131, 74%) were mild in severity. Forty-two (24%) of these related events were moderate in severity and four (2.0%) were considered severe. The most commonly reported device related adverse events were "lumpiness at the injection site" (29%) followed by "redness" (11%). See **Table 7**.

The duration of device related adverse events is provided in **Table 8**. Most of the device related adverse events were resolved during the study period. Thirty-two related adverse events (18%) were deemed to be ongoing. The number of device related adverse events observed within the first month, 1-6 months, and beyond 6 months were comparable. The most common ongoing device related event was "lumpiness at the injection site" (12. 7%).

TABLE 7: SUMMARY OF DEVICE-RELATED ADVERSE EVENT SEVERITY (n=1,008)

AE Category	Device-Related AE Severity			
	Mild	Moderate	Severe	Total
Lumpiness at injection site	46	6	0	52
Redness	19	1	0	20
Other local complications	13	5	0	18
Granuloma or enlargement of the implant	7	9	2	18[1]
Swelling	8	8	1	17
Pain/ Tenderness	10	4	0	14
Skin blanching or discoloration at injection site	6	3	0	9
Increased sensitivity	8	0	0	8
Itching and/or burning	7	0	0	7
Other systemic complications	0	4	0	4
Hardness at the injection area	1	1	1	3
Rash	2	0	0	2
Scab and/or Scar	0	1	0	1
Recurrence of pre-existing Herpes labialis	1	0	0	1
Tingling, numbness, temp pain in various areas of the body	1	0	0	1
Stinging	1	0	0	1
Small veins in the implant area	1	0	0	1
Total	131	42	4	177

[1]These 18 events occurred in 17 subjects. One subject had bilateral, biopsy-proven granuloma.

TABLE 8: SUMMARY OF DEVICE-RELATED ADVERSE EVENT BY DURATION

AE Category	Device-Related AE Severity					
	≤ 30 Days	30–180 days	> 180 Days	Ongoing	Missing[1]	Total
Other systemic complications	2	0	1	1	0	4
Other local complications	5	5	3	4	1	18
Lumpiness at injection site	8	11	19	12	2	52
Redness	7	6	6	1	0	20
Swelling	12	2	2	1	0	17
Granuloma or enlargement of the implant	0	3	5	10	0	18[2]
Pain/ Tenderness	6	2	6	0	0	14
Itching and/or burning	2	2	2	1	0	7
Increased sensitivity	1	2	5	0	0	8
Skin blanching or discoloration at injection site	5	2	1	1	0	9
Rash	1	0	1	0	0	2
Hardness at the injection area	0	1	1	1	0	3
Scab and/or Scar	0	1	0	0	0	1
Recurrence of pre-existing Herpes labials	1	0	0	0	0	1
Tingling, numbness, temp pain in various areas of the body	1	0	0	0	0	1
Stinging	1	0	0	0	0	1
Small veins in the implant area	0	0	1	0	0	1
Total	52	37	53	32	3	177

[1]AEs with missing durations.
[2] These 18 events occurred in 17 subjects. One subject had bilateral, biopsy-proven granuloma.

Granulomas were encountered in 17 of 1,008 subjects (1.69%). All cases were considered at least possibly related to the treatment; however, none were identified as SAEs. The majority of these cases 15 of 17, (88%) were assessed as mild or moderate in severity by the investigator and typically responded to medical therapy. Eight of seventeen (47%) cases resolved during the course of the study, 8/17 (47%) showed improvement by study exit and were still being treated at the time of study exit, and a single lesion remaining stable at study exit, although improved from the time of diagnosis (see **Table 9**).

TABLE 9: THE TIME TO ONSET AND DURATION OF GRANULOMA FORMATION IN BELLAFILL® PATIENTS (N=1,008)

Months from Last Treatment to Onset Date	Duration (Months)	Status at Study Exit
5	Ongoing	No change (stable)
10	3	Resolved
11	9	Resolved
12	3	Resolved
21	8	Resolved
22	4	Resolved
28	Ongoing	Improved
29	Ongoing	Improved
35	Ongoing	Improved
35	21	Resolved

35	16	Resolved
37	Ongoing	Improved
39	Ongoing	Improved
41	18	Resolved
42	Ongoing	Improved
57	Ongoing	Improved
61	Ongoing	Improved

POST-MARKETING SURVEILLANCE

Since product approval for the correction of nasolabial folds, the adverse events received via Bellafill® post-marketing surveillance in on-label or off-label settings have been infrequent. Those events that were reported in five or more instances include (in order of decreasing frequency reported) lumps/bumps, swelling, nodules, bruising, granuloma, redness, and reported allergic reactions. Time to onset for these events typically ranged from immediate to three-and-a-half years post-injection. The majority of the events (when severity was reported) were mild in severity and no events were characterized as serious. Outcomes for these events ranged from resolution to ongoing at the time of last contact. The treatments for these events included massage, ice packs, warm compresses, antibiotics, antihistamines, various energy treatments, oral and intralesional steroids, and device excision.

Adverse events possibly related to intravascular injection have been reported. Symptoms ranged from possible skin discoloration to bumps to skin necrosis. Time of onset (when known) ranged from the day of injection to 3 days post treatment. The majority of the intravascular injection events were mild in severity and no events were reported as serious. Treatments included nitroglycerin paste, aspirin, and warm compresses. These events resolved or were resolving within one month after onset.

A single case of blindness was reported as a Medical Device Report (MDR) after Bellafill® injection. The patient was injected in the right canthal area (periorbital), and experienced immediate onset of loss of vision in the right eye. Treatments included IV saline, direct pressure release in the anterior chamber of the eye, and treatment in a hyperbaric oxygen chamber. The patient's vision did not return. In this patient case, periorbital injection of Bellafill® was outside the recommended Indications for Use (see Warnings section).

Adverse reactions should be reported to Suneva Medical, Inc., at 1-858-550-9999.

U.S. CLINICAL TRIALS

a) CONTROLLED NASOLABIAL FOLD TRIAL

A prospective, multi-center, double-masked, randomized trial compared Bellafill® and a commercially available collagen implant for the treatment of soft-tissue defects of the face. A total of 251 (i.e., 128 Bellafill® and 123 Control) subjects were enrolled and the nasolabial folds of 212 (i.e., 108 Bellafill® and 104 Control) subjects were treated.

The primary effectiveness endpoint was a comparison of the cosmetic correction provided by Bellafill® and Control treatments at the end of a 6-month period after injection, evaluated by means of a validated facial-fold assessment scale (FFA Scale) using standardized photographs as reference. The numerical values for the FFA Scale were: zero – no folds; one – folds just perceptible (i.e., ~0.1 mm); two – shallow folds with some defined edges (i.e., ~0.2 mm); three – moderately deep folds with some well-defined edges (i.e., ~0.5 mm); four – deep folds with most edges well defined and some redundant folds (i.e., ~1.0 mm;) and five – very deep folds with most edges well defined and some redundant folds (i.e., ~2.0 mm). Comparisons to the reference photos were made at pre-treatment and at each follow-up visit. Safety was evaluated by comparing the incidence and severity of clinical events during and for 12 months after treatment completion.

Subject and Baseline Characteristics are presented in **Table 10**.

TABLE 10: SUBJECT AND BASELINE CHARACTERISTICS

Demographic		Bellafill® (n=128)	Control (n=123)
GENDER			
	Male	11 (8.6%)	11 (8.9%)
	Female	117 (91.4%)	112 (91.1%)
AGE, YEARS			
	Mean	53.2	51.2
	Range	28–82	29–78

ETHNICITY			
	Caucasian	100 (78.1%)	101 (82.1%)
	Hispanic	21 (16.4%)	20 (16.3%)
	Asian	1 (0.8%)	1 (0.8%)
	Other[1]	6 (4.7%)	1 (0.8%)
FACIAL AREA TREATED			
	Nasolabial Folds	108 (84.4%)	104 (84.6%)
WRINKLE SEVERITY		Mean Value	Mean Value
	Nasolabial Folds[2]	1.74	1.45

[1] "Other" ethnicities, as reported by Bellafill® subjects, were Mexican/Greek/English, Italian, Hispanic/Irish, American Indian, Native American, Middle Eastern. "Other" ethnicity, as reported by a Control subject, was Persian.
[2] Subjects in the Bellafill®-treated group had a higher baseline fold severity than those in the Control group. The difference was statistically significant (p=0.039).

RESULTS
The mean improvement in nasolabial fold wrinkle severity, as characterized by the masked observers, for subjects from before treatment to 6 months after completion of treatment was: Bellafill® – 0.77 points, and Control – 0.00 points. The difference was statistically significant (p = < 0.001).

ADDITIONAL ANALYSIS
At 1 month after treatment, 0.75 points (Bellafill®) and 0.74 points (Control) differences from baseline for nasolabial fold wrinkle severity were recorded. At 3 months after treatment, differences of 0.81 points (Bellafill®) and 0.15 points (Control) were determined for nasolabial fold. At 12 months after treatment, a nasolabial wrinkle severity difference of 0.98 points (compared to baseline) was recorded for Bellafill® subjects. No assessment of nasolabial fold wrinkle severity was performed at 12 months after treatment for Control subjects.

The number of treatment sessions and volumes administered in nasolabial folds over the course of the study are displayed in **Table 11** and **12**, respectively.

TABLE 11: MEAN NUMBER OF TREATMENT SESSIONS PER PRODUCT

Treatment Area	Bellafill®	Control
Nasolabial Folds	2.28 (n=108)	2.18 (n=104)

TABLE 12: MEAN VOLUME OF PRODUCT USED PER SIDE (LEFT/RIGHT)

Treatment Area	Bellafill® (cc)	Control (cc)
Nasolabial Folds	0.82 (n=108)	1.46 (n=104)

b) OPEN-LABEL NASOLABIAL-FOLD STUDY

This open-label, single-arm, multi-center study assessed the safety of Bellafill® injections for the correction of soft-tissue defects of the face. 157 subjects were enrolled and monitored at 3, 6, and 12 months post-treatment. Approximately 80% (126/157) of subjects completed the 1-year study. The safety data collected in this study were included in **Table 1**.

c) CONTROLLED ACNE SCAR STUDY

A prospective, multi-center, randomized, double-blind, controlled trial assessing the effectiveness and safety of Bellafill® for the correction of facial atrophic acne scars was conducted. A total of 147 (97 Bellafill® and 50 Saline Control) subjects were enrolled and treated in the controlled phase of the study.

The primary effectiveness endpoint was a responder analysis in which the criteria for success at 6 months was defined as 50% or more of treated scars improving by 2 or more points, based on the blinded-investigator assessment utilizing the validated four-point Acne Scar Rating Scale (ASRS). The objective was to show that Bellafill® was superior to Control in treating acne scars. The ASRS (**Table 13**) is a four-point, static scale, ranging from minimal to severe, that relies on the depth of individual scars for severity assessment.

TABLE 13: ACNE SCAR RATING SCALE (ASRS)

Score	Description
1	**Minimal** – Depth up to 0.5mm. Visibility = Perceptible with tangential lighting
2	**Mild** – Depth >0.5mm to <1.5mm. Visibility = Moderately detectable with tangential lighting
3	**Moderate** – Depth = ≥1.5mm to <2.5mm. Visibility = Easily seen with tangential lighting
4	**Severe** – Depth = ≥2.5mm in depth. Visibility = Substantial shadowing with tangential lighting

Subject and Baseline Characteristics are presented in **Table 14**.

TABLE 14: SUBJECT AND BASELINE CHARACTERISTICS

Demographic	Bellafill® (n=97)	Control (n=50)
GENDER		
Male	37 (38.1%)	20 (40.0%)
Female	60 (61.9%)	30 (60.0%)
AGE, YEARS		
Mean	44.6	45.3
Range	21–67	22–63
RACE		
Caucasian	70 (72.2%)	38 (76.0%)
Black	20 (20.6%)	8 (16.0%)
American Indian/ Native Alaskan	2 (2.1%)	0 (0.0%)
Native Hawaiian/ Pacific Islander	1 (1.0%)	0 (0.0%)
Asian	4 (4.1%)	4 (8.0%)
Other	0 (0.0%)	0 (0.0%)
ETHNICITY		
Non-Hispanic	77 (79.4%)	37 (74.0%)
Hispanic	20 (20.6%)	13 (26.0%)

The number and severity of scars per subject are shown in **Table 15**. There were no differences between treatment groups regarding the number of qualifying scars or their severity. The median number of scars to be treated for each subject was 8.0 in each group (mean value shown below) with a median Acne Scar Rating Scale (ASRS) severity of 3.2 in each group.

TABLE 15: ACNE SCAR CHARACTERISTICS AT BASELINE

Number and Severity of Scars		Bellafill® (n=97)	Control (n=50)
Number of qualified scars subject			
	Mean ± SD	8.9 ± 4.6	8.5 ± 3.7
Mean scar severity	N	97	50
	Mean ± SD	3.3 ± 0.3	3.3 ± 0.3
Average volume/subject (mL) –Total	N	97	50
	Mean ± SD	1.50 ± 1.03	2.61 ± 1.80

Note: Mean ± standard deviation.

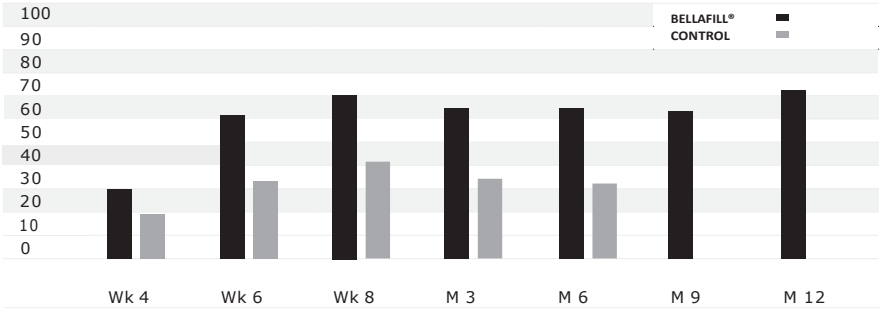
RESULTS

The primary effectiveness endpoint was analyzed as a responder analysis, in which the criterion for success was defined as 50% or more of treated scars on a patient improved by two or more points on the ASRS at the 6-month visit (as evaluated by a live, blinded evaluator). The observed success rate at 6 months in the Bellafill® group was 56/87 (64%- and significantly higher (p=0.0005) than in the Control group 15/46 (33%).

Bellafill® was found to be effective in all Fitzpatrick skin types, and for male and female subjects.

A secondary effectiveness endpoint was a responder analysis (i.e., success was defined as 50% or more of treated scars on a patient improved by two or more points) determined via ASRS at each time point by a live, blinded evaluator. The observed success rates in unblinded assessments at 9 and 12 months for the Bellafill® group were 48/78 (61.5%) and 58/82 (70.7%). See **Figure 1**.

Figure 1: Proportion (%) of Responders Assessed by the Blinded Evaluator Based on the Observed Estimate



	W4	W6	W8	M3	M6	M9	M12
Bellafill® Treatment	26.9%	60.0%	66.7%	62.4%	64.4%	61.5%	70.7%
Control Treatment	18.8%	33.3%	40.9%	35.7%	32.6%	NA	NA
Bellafill® Responders / Number of Subjects	25/93	60/75	54/81	53/85	56/87	48/78	58/82
Control Responders / Number of Subjects	9/48	14/42	18/44	15/42	15/46	NA	NA

ADDITIONAL EFFECTIVENESS ANALYSES

In addition to assessing patient responder rates, the response rate of individual scars was also compared. In this analysis where scars with a greater-than or equal-to two-point improvement on the ASRS over baseline were considered responders, 442/789 (56.0%) of scars in the Bellafill® group and 118/397 (29.7%) of scars in the Control group were judged as successes. Bellafill® injections were superior to Control treatment at all study visits after the Week 4 touch-up injection. Independent, masked review of photographs (IPR) from the Month 6 visit by three board-certified physicians revealed a higher ASRS response rate for Bellafill® than Control subjects, but these rates were lower than those determined by live, blinded evaluators.

Subjects blinded to the treatment rated the overall degree of improvement in their treated scars using a five-point, non-validated Subject Global Aesthetic Improvement Scale (SGAIS) where 5 was "much improved," 3 was "no change," and 1 was "much worse." Seventy-seven percent (77.0%) of subjects (67/87) treated with Bellafill® and forty one percent (41.3%) treated with Control (19/46) reported improvement in their global appearance at 6 months after their injection. Subjects who were treated with Bellafill® continued to report improvement in their global appearance in an unblinded assessment at Month 9 (84.6%) 66/78 and at Month 12 (83.1%) 69/83.

BENEFIT / RISK CONCLUSIONS

The benefits as determined by the improvements seen on the Acne Scar Rating Scale and patient satisfaction scale as well as the risks as assessed from short-term adverse outcomes seen after injection and rare late adverse events, are sufficiently well understood for patients to make informed decisions about device use.

d.) U.S. 5-Year Post Approval Study (PAS001-Study P521-01)

This was an open-label uncontrolled study in which 23 sites enrolled 1,008 subjects with a completion rate of 87% at the end of the 5-year study. The primary objectives were to determine the incidence of granuloma formation and the incidence of adverse events at each follow-up period. The secondary objective was to determine the subject's assessment of satisfaction using a five-point scale at each follow-up visit over the 5-year time period."

The Effectiveness Endpoint was based on: Subject satisfaction using a five-point scale, where 1 = very satisfied, 2 = satisfied, 3 = somewhat satisfied, 4 = dissatisfied, and 5 = very dissatisfied.

Study Visits and Length of Follow-up: After treatment, subsequent follow-up was conducted by mail or telephone questionnaire survey at 6, 12, and 18 months, and 2, 3, and 4 years post-treatment. Subjects were seen and examined in person at 5-years post-treatment visit.

The study population is shown in **Table 16**, below. The population enrolled is typical of individuals seeking correction of NLFs in current clinical practice.

TABLE 16: DEMOGRAPHIC SUMMARY

Characteristic	n (%) n=1,008
GENDER	
Male	112 (11.1%)
Female	896 (88.9%)
ETHNICITY	
Hispanic or Latino	138 (13.7%)
Not Hispanic or Latino	870 (86.3%)
RACE[1]	
White	886 (87.9%)
Black	54 (5.4%)
Asian	12 (1.2%)
American Indian/Native Alaskan	11 (1.1%)
Native Hawaiian/Pacific Islander	2 (0.2%)
Other[2]	54 (5.4%)
AGE (yrs.)	
Mean	53.76
Range	22–86

[1] Subjects were permitted to report more than one race; therefore, the total number of subjects exceeds the number of subjects in the study (n=1,008).
[2] "Other" race responses include the following:
Argentinian, Black / Korean, Hispanic or Latino, Hispanic-Portuguese, Indian, Iranian, Latino, Mexican, Mexican American, Portuguese, Puerto Rican, Spanish (Spain)

RESULTS: EFFECTIVENESS – SUBJECT SATISFACTION

Based on subject assessment of satisfaction (using an unbalanced and unvalidated scale), patients reported satisfaction with Bellafill® treatment throughout the entire study. One year after the final treatment the mean subject satisfaction rating was 1.80 (where 1 = very satisfied and 2 = satisfied). At 5 years after the last treatment, 83% of subjects were either very satisfied or satisfied with their treatment outcome and the mean Satisfaction score was 1.70.

e) COLLAGEN IMMUNOREACTIVITY

All subjects were required to have a skin test prior to being considered for injection with Bellafill®.

Results of the Skin Tests – In the randomized NLF study, there were no positive skin tests in the 128 patients first randomized to receive Bellafill® treatment or the 106 Control subjects who elected to receive Bellafill® injections in the crossover cohort. Of the 141 subjects who received the collagen Control skin test, 6 had a positive skin test and were excluded from the study.

Serum IgG – In the randomized NLF study, 4 Bellafill® and 2 Control subjects were not treated because they displayed abnormal baseline serum IgG levels against collagen during screening. One subject in the Bellafill® group transitioned from a normal IgG level before administration of the skin test to a value above the normal range at 1 month after treatment. This subject's IgG levels returned to the normal range by 3 months after treatment.

Acne Scar Study: 175 subjects received the Bellafill® Skin Test. Three subjects (1.7%) demonstrated a positive skin test and were excluded.

5-Year Post Approval Study: 1,211 subjects received the Bellafill® Skin Test. Eight subjects (0.7%) demonstrated a positive skin test and were excluded.

INDIVIDUALIZATION OF TREATMENT

A complete medical history should be obtained to determine whether the patient is an appropriate candidate for treatment with Bellafill®.

HOW SUPPLIED

Bellafill® is an aseptic product that is required to pass a USP sterility test before release. It is supplied in a sealed tray containing individual treatment syringes with sterile needles for single patient use, packaged in a box. Each sterile single use syringe contains: 20% polymethylmethacrylate microspheres and 80% bovine collagen solution containing 3.5% bovine collagen, 2.7% phosphate buffer, 0.9% sodium chloride, 0.3% lidocaine hydrochloride, and 92.6% water for injection.

The tray lid is sealed with a cover. Do not use if the cover is broken or removed. Do not re-sterilize.

IMMUNOGENICITY TEST PROCEDURE

Four (4) weeks prior to treatment, patients will be given a 0.1cc test injection of Bellafill® Skin Test material subcutaneously in the volar forearm, to determine a patient's sensitivity to the treatment material. For a complete discussion of the Bellafill® Skin Test, refer to the Instructions for Use supplied with test syringes.

Test Interpretation

The patient should observe the test site daily during the 4-week test period and notify the physician immediately if any effects indicative of a positive or equivocal response are observed or if systemic effects are experienced. A Bellafill® Skin Test Results Card should be provided to the patient at the time of the skin test to help the patient assess the test site.

Positive Response

A positive response consists of erythema of any degree, induration, tenderness, and swelling, with or without pruritus, which can appear immediately following implantation and persists for more than 24 hours or appears more than 24 hours following implantation for any length of time.

Equivocal Response

An equivocal response is one in which there is no localized skin reaction, but the patient does elicit a possible systemic reaction such as a rash, arthralgia (aching joints), or myalgia (aching muscles) that occurs at any time during the 4-week observation period. If an equivocal response is observed, a second injection in the opposite arm is required, with observation for an additional 4 weeks. Patients demonstrating a positive or equivocal response in this second test should not be treated.

DIRECTIONS FOR USE

Bellafill® is indicated for the correction of nasolabial folds and moderate to severe, atrophic, distensible facial acne scars on the cheek in patients over the age of 21 years.

1. Prior to treatment with Bellafill®, the results of the skin test must be carefully evaluated; the patient must not have a positive or equivocal second response to the required Bellafill® Skin Test. For a complete discussion of the Bellafill® Skin Test, refer to the Instructions for Use supplied with skin test syringes.
2. Prior to treatment with Bellafill®, the patient should be fully informed of the indications, contraindications, warnings, precautions, treatment responses, adverse reactions, and method of administration. Patients also should be advised that supplemental touch-up treatments may be required to achieve correction.
3. A complete medical history should be obtained to determine whether the patient is an appropriate candidate for treatment with Bellafill®.
4. The patient's soft-tissue contour deficiencies should be characterized with regard to etiology, distensibility, and depth of lesion. Pretreatment photographs are recommended.
5. Scars selected for treatment should be atrophic distensible scars.
6. The Bellafill® syringe must be brought to room temperature before injection.
7. After ensuring that the patient has thoroughly washed the treatment area with soap and water, the area should be cleaned with alcohol or other antiseptic.
8. Bellafill® is implanted through a 26 G needle. Best results with Bellafill® are achieved in defects requiring deep dermal implant placement and not into the subcutaneous fat. The rate and degree of correction in the implanted area varies with patient, treatment site, and plane of implant placement. Correction should be conservative during initial treatment.
9. Before injecting the patient, depress the syringe plunger until Bellafill® is visible at the tip of the needle.
10. The best cosmetic result for NLFs can be achieved by a standard linear threading technique, moving the needle back and forth beneath the skin being treated and maintaining constant injection pressure while withdrawing the needle (retrograde liner threading). Injection for acne scar can use both the retrograde linear threading and serial puncture techniques. The injection pressure is correct if the implant flows slowly and evenly, without great exertion. This technique forms a support structure beneath the skin to prevent further wrinkling and/or to maintain the scar correction.
11. If needles become occluded or dull during a treatment session, replacement may be necessary.
12. Gentle massage of the skin with the fingertips may facilitate even distribution of Bellafill® immediately after implant placement.
13. The area and the borders of the Bellafill® injection should be recorded on an illustration of a face for later comparison.

14. The physician should instruct the patient to report to him or her any evidence of adverse texture change in the surrounding treatment site. Other problems possibly associated with the use of Bellafill® should be promptly brought to the attention of the physician.
15. The syringe and any unused material should be discarded after a single treatment visit.
16. Correction should be limited to no more than 100% of the skin defect during treatment. One or two touch-up implantations at intervals of at least 2 weeks may be required to achieve the desired effect. The interval at which touch-up implantations are needed depends on the nature of the defect, the amount of implant injected, the site of placement, and the dynamics at the corrected sites.

STORAGE DIRECTIONS

Bellafill® should be stored at standard domestic refrigerator temperatures (2 – 8˚C). **DO NOT FREEZE**. Do not remove syringes from tray until ready for use.

Bellafill® has an off-white appearance. In the event that the content of a syringe shows signs of separation and/or is clear (like water), do not use the syringe and notify Suneva Medical immediately. In the United States or Canada, call toll-free 844-Bellafill (844-235-5234). Outside of the United States or Canada call ++1-858-550-9999.

PATIENT COUNSELING

Patients considering treatment with Bellafill® should be provided with the patient labeling, which is available by contacting Suneva Medical. Patients should be told that more than one treatment session might be required to achieve the desired correction.

ORDERING

To place an order, contact Suneva Medical, Inc. In the United States or Canada, call toll-free 844-Bellafill (844-235-5234). Outside of the United States or Canada: call ++1-858-550-9999. Orders may also be sent by fax to 858-550-9997 or email to orders@sunevamedical.com.

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