**GLOSSARY OF TERMS:**

**Actinic keratosis** - A rough, scaly patch on your skin that develops from years of exposure to the sun
**Active acne** - Acne where there are currently pustules, cysts or lesions on the skin at the time of evaluation
**Adverse Event** - A negative reaction to a medication or treatment
**Anesthetic** - A substance that induces insensitivity to pain, a numbing agent.
**Anticoagulant** – Blood thinner
**Cardiac abnormality** – Abnormal heart/blood vessel structure or function
**Contact dermatitis** – A rash that occurs at the site of exposure to a substance capable of producing an irritant skin response.
**Diabetes** – A disease in which your blood glucose, or blood sugar, levels are too high
**Eczema** – A condition that makes your skin red and itch
**Fitzpatrick Skin Types** – A numerical classification system for human skin color
**Hemorrhagic** – Accompanied by or produced by an escape of blood from a ruptured blood vessel, especially when bleeding excessively
**Hemostatic** – The stopping of blood flow
**Immunosuppressive** – Partially or completely suppressing the immune response of an individual
**Isotretinoin** – Vitamin A derivative that is used to treat acne. Common brand names: Accutane, Myorisan
**Keloid scars** – A scar that grows outside the boundaries of the original scar.
**Orbital rim** – The portion of the skull that outlines the border of the eye socket
**Papules** – A small bump (up to 1 cm in diameter) on the skin with no visible fluid within
**Psoriasis** - a common skin condition that causes cells to build up rapidly on the surface of the skin to form thick, silvery scales and itchy, dry, red patches that are sometimes painful
**Rosacea** – A disease that affects your skin and sometimes your eyes. It causes redness and pimples.
**Scleroderma** – A number of rare diseases that involve the hardening and tightening of the skin and connective tissues
**Sequelae** – Any complications that follow a medical illness or event
**Side effect** – An expected reaction to a medication or treatment that is used in an approved manner
**Skin striae** – A linear mark, slight ridge, or groove
**Transdermal** – Under the skin
**Vesicle** – A small blister on the skin

## 1. PRODUCT DESCRIPTION

**a. What is it, and how does it work?**

SkinPen® Precision System is a minimally invasive, micro-needling device intended for use on facial acne scars. The SkinPen Precision System is comprised of a reusable motor unit designed to be attached to sterile, disposable cartridges that house 14 micro- needles (~250 um diameter) on a reciprocating head which when activated and placed properly against the skin can create hundreds to thousands of "micro" punctures into the skin. The procedure creates many microscopic punctures in the skin's outer layers. As these punctures heal, the remodeling process works to improve the appearance of facial acne scars. SkinPen Precision's® patent-pending cartridge design inhibits the entrance of fluids into the device which along with the BioSheath and routine cleaning help to prevent potential cross-contamination of the motor unit between uses. It is for prescription use only.

**b. Who is a candidate?**

The SkinPen Precision System is intended to be used as a treatment to improve the appearance of facial acne scars in adults aged 22 years or older. The SkinPen® Precision System's clinical study was conducted on adult men and women ranging from light to very dark skin (Fitzpatrick skin types).

## 2. CONTRAINDICATIONS

**a. Are there any reasons why I should not receive a SkinPen® Precision treatment?**

The use of the SkinPen® Precision System should not be used on patients who:

- Have active skin cancer in the treatment area(s)
- Have open wounds, sores, or irritated skin in the treatment area(s)
- Have an allergy to stainless steel or anesthetics
- Have a hemorrhagic (bleeding) disorder or hemostatic (bleeding) dysfunction
- Are pregnant or nursing
- Are currently taking drugs with the ingredient isotretinoin (such as Accutane)

**NOTE:** This product is not intended for transdermal (under the skin) delivery of topical products such as cosmetics, drugs, or biologics.

## 3. PRECAUTIONS

**a. What precautions should my doctor advise me about?**

The SkinPen® Precision System has not been evaluated in the following patient populations. Therefore, if you have a history of the following conditions or have taken the following medications, please let your doctor know, as treatment with the SkinPen Precision System may not be appropriate for you: Actinic (solar) keratosis; active acne; collagen vascular diseases or cardiac abnormalities; diabetes; eczema, psoriasis and other chronic conditions in the treatment area or on other areas of the body; immunosuppressive therapy; history of contact dermatitis; raised moles in the treatment area; rosacea; active bacterial or fungal infection, active viral herpes simplex infections (such as cold sores); warts; keloid scars; patients on anticoagulants (also known as 'blood thinners'); scars and stretchmarks less than one year old; scleroderma; and wound-healing deficiencies. Inform your provider if you have any of the above conditions. Your doctor will determine whether treatment with the SkinPen Precision System is right for you.

Let your doctor know if you are allergic or sensitive to any of the following ingredients which are in the Skinfuse Lift HG hydrogel: purified water, glycerin, carbomer, potassium hydroxide, disodium EDTA, phenoxythanol, caprylyl glycol, sorbic acid. If you are, SkinPen® Precision treatment may not be safe for you.

## 4. CLINICAL STUDY

**a. How was the product studied?**

**A clinical study was conducted to support the safety and effectiveness of the SkinPen Precision System for the treatment of acne scars on the face.**

The single center study was conducted on a total of 41 subjects, 20 of which were exclusive to the SkinPen Precision device (7 male and 13 female), aged 21 years and older from various ethnic groups with multiple skin tones (pale to dark skin). The other 21 subjects were treated with a prototype device. Treatments were given on day 1, day 30, and day 60, with follow-up visits at 1 month and 6 months after the final (day 60) treatment. Treatments were conducted by a trained aesthetician (skin care specialist). The face was cleaned and numbed prior to treatment. A thin layer of Skinfuse Lift HG was applied prior to treatment to protect against abrasion and friction during the procedure. The aestheticians were instructed to start at the lowest depth setting and gradually increase the depth until redness was observed. Following treatment, Skinfuse Lift HG was applied to prevent the skin from drying out post procedure.

[1]Jwala Karnik, Leslie Baumann, Suzanne Bruce, Valerie Callender, Steven Cohen, Pearl Grimes, John Joseph, Ava Shamban, James Spencer, Ruth Tedaldi, William Philip Werschler, Stacy R. Smith, "A double-blind, randomized, multicenter, controlled trial of suspended polymethylmethacrylate microspheres for the correction of atrophic facial acne scars" Journal of the American Academy of Dermatology 71(1):77-83 (2014).

**Table 3: Summary of Demographic Information**

| | SkinPen Precision System | | All Subjects | |
|---|---|---|---|---|
| **N** | 20 | | 41 | |
| **Age (years)** | | | | |
| Mean (standard deviation) | 43.8 (12.7) | | 44 (11.9) | |
| Minimum, Median, Maximum | 23, 48, 60 | | 21, 46, 60 | |
| | N | (%) | N | (%) |
| **Sex** | | | | |
| Male | 7 | 35 | 13 | 31.7 |
| Female | 13 | 65 | 28 | 68.3 |
| **Ethnicity** | | | | |
| Hispanic or Latino | 6 | 30 | 13 | 31.7 |
| Not Hispanic or Latino | 14 | 70 | 28 | 68.3 |
| **Race** | | | | |
| American Indian or Alaska | 1 | 5 | 2 | 4.9 |
| Asian | 3 | 15 | 9 | 22.0 |
| Black or African American | 6 | 30 | 10 | 24.4 |
| White | 10 | 50 | 20 | 48.8 |
| **Fitzpatrick Skin Type** | | | | |
| II | 2 | 10 | 3 | 7.3 |
| III | 4 | 20 | 10 | 24.4 |
| IV | 7 | 35 | 17 | 41.5 |
| V | 4 | 20 | 7 | 17.1 |
| VI | 3 | 15 | 4 | 9.8 |

At each clinical visit, digital images were taken of each subject's facial acne scars. These images were graded by two separate Board Certified Dermatologists after completion of the study using the following assessment tools and timepoints [Table 4]. The dermatologists were blinded, which means they did not know which treatment or time point was represented in each photo. Details of each of these assessment tools are provided below in Tables 5-7. The results of the study are provided in Tables 8-12.

**Table 4: Study Endpoints**

| | |
|---|---|
| **Primary effectiveness endpoints** | Acne Scar Assessment Scale graded by two blinded dermatologists using photographs taken at baseline, day 30, day 60, 1-month post-treatment, and 6-months post-treatment |
| | Clinician's Global Aesthetic Improvement Assessment graded by two blinded dermatologists using photographs taken at 1-month post-treatment, and 6-months post-treatment |
| **Secondary effectiveness endpoints** | Self-assessed Scar Improvement Scale completed by subjects at baseline, 1-month post-treatment, and 6-months post-treatment |
| | Subject Global Aesthetic Improvement Scale completed by subjects at baseline, 1-month post-treatment, and 6-months post-treatment |
| | Patient Satisfaction Questionnaire completed by subjects at 1-month post-treatment and 6-months post-treatment |
| **Safety Endpoint** | Subject safety diaries provided to the subject at each treatment visit (day 1, 30, and 60) and completed for 30 days to record treatment responses |
| | Adverse event monitoring at each visit; baseline, day 30, day 60, 1-month post-treatment, and 6-months post-treatment |

The photo grading included the following effectiveness assessments:

- Acne Scar Assessment Scale[1]

**Table 5: Acne Scar Assessment Scale**

| Grade | Term | Description |
|---|---|---|
| 0 | Clear | No depressions are seen in the treatment area. Macular discoloration may be seen. |
| 1 | Very mild | A single depression is easily noticeable with direct lighting (deep). Most or all of the depressions seen are only readily apparent with tangential lighting (shallow). |
| 2 | Mild | A few to several, but less than half of all the depressions are easily noticeable with direct lighting (deep). Most of the depressions seen are only readily apparent with tangential lighting (shallow). |
| 3 | Moderate | More than half of the depressions are apparent with direct lighting (deep). |
| 4 | Severe | All or almost all the lesions can be seen with direct lighting (deep). |

In addition to the clinician graded effectiveness measures, the following patient-reported measures were recorded throughout the study:

- Self-assessed Scar Improvement Scale

**Table 6: Self-assessed Scar Improvement Scale**

| Rating | Description |
|---|---|
| -1 | Exacerbation of Acne Scars |
| 0 | No change in appearance of acne scars |
| 1 | 1% - 25% improvement in appearance of acne scars |
| 2 | 25% - 50% improvement in appearance of acne scars |
| 3 | 50% - 75% improvement in appearance of acne scars |
| 4 | 75% - 99% improvement in appearance of acne scars |

- Subject Global Aesthetic Improvement Scale

**Table 7: Subject Global Aesthetic Improvement Scale**

| Rating | Description |
|---|---|
| 1 | **Very Much Improved:** Optimal cosmetic result. |
| 2 | **Much Improved:** Marked improvement in appearance from the initial condition, but not completely optimal. |
| 3 | **Improved:** Obvious improvement in appearance from initial condition. |
| 4 | **No Change:** The appearance is essentially the same as the original condition. |
| 5 | **Worse:** The appearance is worse than the original condition. |

(Continued on reverse side.)

- Patient Satisfaction Questionnaire

Three questions were asked to the subjects in the study regarding their level of satisfaction with the treatment. It was included as a secondary endpoint in the study. See individual questions and results in the section below.

Safety information was collected throughout the study using subject safety diaries. Safety diaries were provided to the subject at each treatment visit (day 1, 30, and 60). The subject was instructed to record any observations related to treatment including common treatment responses. Common treatment responses are side effects that result from treatment which resolve on the order of days. Common treatment responses that persist may be categorized as adverse events when assessed by the investigator at the next visit.

Subjects were informed of the following potential common treatment responses in the informed consent process: skin will be red and flushed similar to a moderate sunburn, skin tightness and mild sensitivity to the touch, redness, burning, tingling, stinging, itching, and/or scaling/dryness, edema (swelling), tenderness/ discomfort, a possibility of developing an infection (an increase in redness, warmth, itching, or pus formation). The diaries included space for daily recording of observations for the 30 days in between treatment visits. Adverse events were assessed by the investigator at each subsequent visit.

**RISKS:**

**a. What side effects were seen in the clinical study?**

**Common Treatment Responses:**

At the 6-month post-treatment visit, no adverse events were seen.

The following common treatment responses were reported in the subject safety diaries which were sent home with the subject:

- Dryness in 5/41 (12%) subjects lasting from 1-6 days
  - o These responses were reported by 3 subjects with FST III, 1 subject with FST VI, and 1 subject with FST V
- Rough Skin in 3/41 (7%) of subjects lasting from 1-2 days
  - o These responses were reported by 1 subject with FST III, and 2 subjects with FST V
- Tightness in 2/41 (4%) of subjects lasting from 1-2 days
  - o These responses were reported by 2 subjects with FST VI
- Redness, Itching, Peeling Discomfort and Tenderness in 13/41 (31%) of subjects lasting 1-3 days
  - o These responses were reported by 6 subjects with FST III, 2 subjects with FST VI, 3 subjects with FST V, and 2 subjects with FST V
- Burning in 4/41 (9%) of subjects lasting 1-3 days
  - o These responses were reported by 1 subject with FST III, 1 subject with FST VI, and 2 subjects with FST V

**b. What adverse events were seen in the clinical study?**

1 subject reported an insect/bug bite on the inner right thigh that was determined to be moderate and unlikely related to SkinPen prototype device. 1 subject (1/41, 2.4%) experienced an Adverse Event (skin striae [linear marks, ridges, or grooves] on the forehead and both sides of the face) that was determined to be mild and possibly related to use of the SkinPen Precision System. This Adverse Event was thought to be due to subject exposure to excess sunlight soon after treatment which was against study instructions, yet resolved without any additional complications.

**c. What are other possible adverse events?**

Although not seen in the clinical study, patients may experience reactivation of herpes simplex virus (coldsore), pigment changes that include lighter or darker skin in the area treatment that resolves over time, or no change in their acne scars.

**Benefits:**

**What will a SkinPen Precision Treatment accomplish, and what did the clinical study show?**

The study doctors reported using the Acne Scar Assessment Scale:

Results of the photo grading indicated a significant improvement in acne scar assessment at 6 months post-treatment when compared with baseline with 55% (11/20) of subjects showing improvement at 6-months post-treatment when compared with baseline. At 6-months post-treatment, the remaining 9 subjects(45%) reported no change in score when compared to baseline. The visual improvements seen in the photo grading results were considered to be clinically meaningful.

**Table 8: Results of Photo Grading of Acne Scar Assessment Scale for SkinPen Precision System**

| Time Point | N | Mean | Standard Deviation | Minimum | Median | Maximum |
|---|---|---|---|---|---|---|
| Baseline | 20 | 2.80 | 0.52 | 2.00 | 3.00 | 4.00 |
| Day 30 | 20 | 2.78 | 0.57 | 2.00 | 2.75 | 4.00 |
| Day 60 | 20 | 2.70 | 0.55 | 2.00 | 2.50 | 3.50 |
| 1-Month Post-Treatment | 20 | 2.68 | 0.49 | 2.00 | 2.50 | 3.50 |
| 6-Months Post-Treatment | 20 | 2.35 | 0.69 | 1.50 | 2.50 | 3.50 |

**Table 9: Change from Baseline for Photo Grading of Acne Scar Assessment Scale for SkinPen Precision System**

| Time Point | N | Subject Improved (%) | Subject Worsened (%) | Mean Change | Standard Deviation for Change | Mean Change (%) |
|---|---|---|---|---|---|---|
| Day 30 | 20 | 30.0 | 20.0 | -0.03 | 0.50 | -0.9 |
| Day 60 | 20 | 35.0 | 20.0 | -0.10 | 0.50 | -3.6 |
| 1-Month Post-Treatment | 20 | 40.0 | 20.0 | -0.13 | 0.58 | -4.5 |
| 6-Months Post-Treatment | 20 | 55.0 | 0.0 | -0.45 | 0.46 | -16.1 |

Subjects reported using the Self-assessed Scar Improvement Scale:

Treatment with SkinPen Precision produced an improvement in SASIS scores at 1-month post-treatment and 6-months post-treatment. At 1-month post-treatment, 17 (85%) subjects reported some percentage of improvement in the appearance of their acne scars, with 3 (15%) subjects reporting no change. At 6-months post-treatment, 18 (90%) subjects reported some percentage of improvement in the appearance of their acne scars, with 2 (10%) subjects reporting no change. The average value for the population was = 1.65 and 1.70, at 1-month post-treatment and 6-months post-treatment respectively (1%-25% improvement in appearance of acne scars) when compared with a score of 0 (no change in appearance of acne scars). No subjects reported a negative score (i.e., worsening of acne scars) at either post-treatment timepoint.

Subjects reported using the Subject Global Aesthetic Improvement Scale:

Treatment with SkinPen Precision produced an improvement in SGAIS scores at 1 month post-treatment and 6 months post-treatment. At 1-month post-treatment, 7 (35%) subjects reported much improved, 9 (45%) subjects reported improved, and 4 (20%) subjects reported no change. At 6-months post-treatment, 2 (10%) subjects reported very much improved, 8 (40%) subjects reported much improved, 8 (40%) subjects reported improved, and 2 (10%) subjects reported no change. The mean value for the population was = 2.85 and 2.50, at 1-month post-treatment and 6-months post-treatment improved when compared with a score of 4 (no change). No subjects reported a score of 5 (worse) at either post treatment timepoint.

Subjects reported using the Patient Satisfaction Questionnaire:

The results of the patient satisfaction questionnaire for all subjects indicated that a greater number of subjects (11/20, 55%) selected favorable responses regarding treatments at 1 month and 6 months post-treatment for the following inquiries:

- Question 1: Do you notice any improvement in how your acne scars look in the treated area?

**Table 10: Results of Patient Satisfaction Questionnaire - Question 1**

| Time Point | Yes [N (%)] | No [N, (%)] |
|---|---|---|
| 1-Month Post-Treatment | 16 (80.0) | 4 (20.0) |
| 6-Months Post-Treatment | 18 (90.0) | 2 (10.0) |

- Question 2: How would you characterize your satisfaction with the treatment?

**Table 11: Results of Patient Satisfaction Questionnaire – Question 2**

| Time Point | Extremely Satisfied [N (%)] | Satisfied [N (%)] | Slightly Satisfied [N (%)] | Neither Satisfied nor Dissatisfied [N (%)] |
|---|---|---|---|---|
| 1-Month Post-Treatment | 3 (15.0) | 9 (45.0) | 5 (25.0) | 3 (15.0) |
| 6-Months Post-Treatment | 3 (15.0) | 9 (45.0) | 5 (25.0) | 1 (5.0) |

| Time Point | Slightly Dissatisfied [N (%)] | Dissatisfied [N (%)] | Very Dissatisfied [N (%)] |
|---|---|---|---|
| 1-Month Post-Treatment | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| 6-Months Post-Treatment | 1 (5.0) | 1 (5.0) | 0 (0.0) |

- Question 3: Would you recommend this treatment to your friends and family members?

**Table 12: Results of Patient Satisfaction Questionnaire – Question 3**

| Time Point | Yes [N (%)] | No [N, (%)] |
|---|---|---|
| 1-Month Post-Treatment | 18 (90.0) | 2 (10.0) |
| 6-Months Post-Treatment | 18 (90.0) | 2 (10.0) |

## 5. BEFORE TREATMENT INFORMATION

**a. What happens in the office before the SkinPen® Precision treatment?**

Note that each doctor may have a unique process for assessing and treating patients. The following is an example of what you would likely experience with a typical SkinPen® Precision treatment. Before the SkinPen® Precision treatment, your doctor will ask you questions about your medical history, as well as your treatment goals. Your doctor will discuss whether you are an appropriate candidate for a SkinPen® Precision System treatment and review what to expect during and after a treatment, including common treatment responses and adverse events.

You may be cautioned to avoid sun exposure and stop topical retinoid therapy 24 hours prior to procedure. You should allow at least 24 hours after autoimmune therapies before a treatment. You should wait six months following oral isotretinoin (such as Accutane) use before receiving treatment.

Your doctor will also examine your treatment area, and may take photos. Different options for pain management will be discussed, and if pretreatment numbing is desired, a topical anesthetic agent may be used. The treatment area will be cleaned and then prepared with isopropyl alcohol or other antiseptic before the treatment.

## 6. TREATMENT DESCRIPTION

**a. What happens during the treatment?**

A layer of Skinfuse Lift HG is applied to the treatment area to protect the skin against abrasion and friction of the SkinPen® Precision device during treatment. **NOTE:** Let your doctor know if you are allergic or sensitive to any of the following ingredients which are in the Skinfuse Lift HG hydrogel: purified water, glycerin, carbomer, potassium hydroxide, disodium EDTA, phenoxythanol, caprylyl glycol, sorbic acid. If you are, the SkinPen® Precision treatment may not be safe for you. The doctor then selects a depth on the microneedle cartridge to begin treatment on the patient and begins the treatment. As the SkinPen® Precision glides over the skin micro-channels are created on the skins surface. Gauze may be used to pat down the affected area after treatment, and it is suggested to apply a generous layer of Skinfuse Lift HG to prevent the skin from drying out post treatment.

**b. Does microneedling with the SkinPen® Precision hurt?**

The SkinPen® Precision treatment may cause some minor discomfort during after the treatment. Your doctor may recommend that a topical numbing agent be used during treatment to further minimize discomfort.

## 7. AFTER TREATMENT INFORMATION

**a. What should I expect following the treatment?**

**In the SkinPen® Precision clinical study, the most common treatment responses experienced were:**

Dryness, rough skin, tightness, redness, itching, peeling, discomfort, tenderness, and burning. These conditions resolved over time without any further complications.

Although not seen in the clinical study, you may experience reactivation of herpes simplex virus (cold sore), pigment changes that include lighter or darker skin in the area treatment that resolves over time, or no change in their acne scars.

Your doctor will also tell you what to expect following a SkinPen® Precision system treatment. Within the first 72 hours post-treatment you should avoid sweaty exercise and sun exposure. Exposure to these conditions could led to: itching, burning, stinging, and tingling), scaling/dryness, redness, swelling, and tenderness/discomfort.

**b. Will I need more than one treatment to achieve my desired results?**

You should discuss treatment goals with your doctor. In the clinical study patients were treated in a series of 3 treatments spaced 4 weeks apart. It is recommended to avoid other facial aesthetic treatments the month following your SkinPen Precision treatment.

**c. Do the results last forever?**

While individual results may vary, in the clinical study, the results were evaluated 6 months after the third (final) treatment. After this, additional treatments may be needed to maintain your desired result.

## 8. WHEN TO CALL YOUR DOCTOR?

**a. When should I call my doctor?**

**Call your doctor immediately if you experience:**

1. Signs of infection such as an increase in redness, warmth, itching, or pus formation. This would typically happen within a day or two after the treatment.
2. Allergic reactions to the test material (s). Rare allergic reactions can consist of severe contact dermatitis (rash) or itching, swelling, or difficulty breathing. This risk is increased for individuals with a history of allergies, and individuals with asthma and/or a history of hives, and itching.

**Be sure to call your doctor if you:**

1. Any additional treatment responses not discussed above.

## 9. ADDITIONAL INFORMATION

**a. What should I do if I have additional questions?**

For further questions and information, please call Bellus Medical at 1.888.372.3982.


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