

# PERLANE®

**Caution:** Federal Law restricts this device to sale by or on the order of a physician or licensed practitioner.

### Description

PERLANE® is a sterile gel of hyaluronic acid generated by *Streptococcus* species of bacteria, chemically cross-linked with BDDE, stabilized and suspended in phosphate buffered saline at pH=7 and concentration of 20 mg/mL. The largest fraction of gel particles size is between 940 and 1090 microns.

### Indication

PERLANE® is indicated for implantation into the deep dermis to superficial subcutis for the correction of moderate to severe facial folds and wrinkles, such as nasolabial folds.

### Contraindications

- PERLANE® is contraindicated for patients with severe allergies manifested by a history of anaphylaxis or history or presence of multiple severe allergies.

- PERLANE® contains trace amounts of gram positive bacterial proteins, and is contraindicated for patients with a history of allergies to such material.

- PERLANE® is contraindicated for patients with bleeding disorders

- PERLANE® is contraindicated for implantation in anatomical spaces other than the dermis or superficial layer of the subcutis.

### Warnings

- Defer use of PERLANE® at specific sites in which an active inflammatory process (skin eruptions such as cysts, pimples, rashes, or hives) or infection is present until the process has been controlled.

- Injection site reactions (*e.g.*, swelling, redness, tenderness, or pain) to PERLANE® have been observed as consisting mainly of short-term minor or moderate inflammatory symptoms starting early after treatment and with less than 7 days duration. Refer to the adverse reactions section for details.

- PERLANE® must not be implanted into blood vessels. Localized superficial necrosis may occur after injection in or near dermal vessels, such as the glabellar area. It is thought to result from the injury, obstruction, or compromise of blood vessels.

- Delayed onset inflammatory papules have been reported following the use of dermal fillers. Inflammatory papules that may occur rarely should be considered and treated as a soft tissue infection.

### Precautions

- PERLANE® is packaged for single patient use. Do not resterilize. Do not use if package is opened or damaged.

- Based on US clinical studies patients should be limited to 6.0 mL per patient per treatment. The safety of injecting greater amounts has not been established.

- The safety or effectiveness of PERLANE® for the treatment of anatomic regions other than nasolabial folds has not been established in controlled clinical studies.

- Long term safety and effectiveness of PERLANE® beyond one year have not been investigated in clinical trials.

- As with all transcutaneous procedures, PERLANE® implantation carries a risk of infection. Standard precautions associated with injectable materials should be followed.

- The safety and efficacy of PERLANE® for lip augmentation has not been established.

- The safety of PERLANE® for use during pregnancy, in breastfeeding females or in patients under 18 years has not been established.

- Formation of keloids may occur after dermal filler injections including PERLANE®. Keloid formation was not observed in studies involving 509 patients (including 150 African-Americans and 25 other patients of Fitzpatrick Skin Types IV, V and VI). For additional information please refer to Studies MA-1400-02, MA-1400-01, 31GE0002, and 31GE0101 in the Clinical Trials Section.

- PERLANE® injection may cause hyperpigmentation at the injection site. In a clinical study of 150 subjects with pigmented skin (of African-American heritage and Fitzpatrick Skin Types IV, V, and VI), the incidence of post-inflammatory hyperpigmentation was 6% (9/150). 50% of these events lasted up to six weeks after initial implantation.

- PERLANE® should be used with caution in patients on immunosuppressive therapy.

- Bruising or bleeding may occur at PERLANE® injection sites. PERLANE® should be used with caution in patients who have undergone therapy with thrombolytics, anticoagulants, or inhibitors of platelet aggregation in the preceding 3 weeks.

- After use, syringes and needles should be handled as potential biohazards. Disposal should be in accordance with accepted medical practice and applicable local, state, and federal requirements.

- The safety of PERLANE® with concomitant dermal therapies such as epilation, UV irradiation, or laser, mechanical or chemical peeling procedures has not been evaluated in controlled clinical trials.

- 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 PERLANE®, there is a possible risk of eliciting an inflammatory reaction at the implant site. This also applies if PERLANE® is administered before the skin has healed completely after such a procedure.

- Injection of PERLANE® into patients with a history of previous herpetic eruption may be associated with reactivation of the herpes.

- PERLANE® is a clear, colorless gel without particulates. In the event that the content of a syringe shows signs of separation and/or appears cloudy, do not use the syringe and notify Medicis Aesthetics, Inc. at 1-800-555-5115. Glass is also subject to breakage under a variety of unavoidable conditions. Care should be taken with the handling of the glass syringe and with disposing of broken glass to avoid laceration or other injury.

- PERLANE® should not be mixed with other products before implantation of the device.

### Adverse Experiences

In two U.S. studies (*i.e.*, Study MA-1400-01 and Study MA-1400-02) involving 433 patients at 25 centers, the adverse outcomes reported in patient diaries during 14 days after treatment are presented in Tables 1–4. The physician diagnosed adverse events identified in these studies at 72 hours after injection are presented in Table 5. In Study MA-1400-01, 150 patients were injected with PERLANE® on

one side of the face and RESTYLANE® on the other side of the face. In study MA-1400-02, 283 patients were randomized to receive either PERLANE® or RESTYLANE® injection on both sides of the face. Table 6 presents all investigator-identified adverse experiences recorded at study visits 2 weeks or more after injection

|                    | PERLANE®                                | RESTYLANE®                              | PERLANE® Patients |                        |                                      |                        | RESTYLANE® Patients |             |                         |           |
|--------------------|---|---|-------------------|------------------------|--------------------------------------|------------------------|---------------------|-------------|-------------------------|-----------|
|                    | Total patients reporting symptoms n (%) | Total patients reporting symptoms n (%) | None              | Tolerable <sup>1</sup> | Affected Daily Activity <sup>2</sup> | Disabling <sup>2</sup> | None                | Tolerable   | Affected Daily Activity | Disabling |
|                    |   |   | n (%)             | n (%)                  | n (%)                                | n (%)                  | n (%)               | n (%)       | n (%)                   | n (%)     |
| Bruising           | 122 (86.5%)                             | 111 (78.2%)                             | 17 (12.2%)        | 97 (69.8%)             | 24 (17.3%)                           | 1 (0.7%)               | 28 (20.1%)          | 82 (59%)    | 28 (20.1%)              | 1 (0.7%)  |
| Redness            | 118 (83.7%)                             | 114 (80.3%)                             | 21 (15.1%)        | 105 (75.5%)            | 12 (8.6%)                            | 1 (0.7%)               | 25 (18%)            | 96 (69.1%)  | 17 (12.2%)              | 1 (0.7%)  |
| Swelling           | 128 (90.8%)                             | 127 (89.4%)                             | 11 (7.9%)         | 107 (77%)              | 19 (13.7%)                           | 2 (1.4%)               | 12 (8.6%)           | 102 (73.4%) | 23 (16.5%)              | 2 (1.4%)  |
| Pain               | 114 (80.9%)                             | 108 (76.1%)                             | 25 (18%)          | 96 (69.1%)             | 18 (12.9%)                           | 0 (0%)                 | 31 (22.3%)          | 93 (66.9%)  | 14 (10.1%)              | 1 (0.7%)  |
| Tenderness         | 130 (92.2%)                             | 123 (86.6%)                             | 9 (6.5%)          | 112 (80.6%)            | 18 (12.9%)                           | 0 (0%)                 | 16 (11.5%)          | 109 (78.4%) | 12 (8.6%)               | 2 (1.4%)  |
| Itching            | 45 (31.9%)                              | 67 (47.2%)                              | 94 (67.6%)        | 40 (28.8%)             | 3 (2.2%)                             | 2 (1.4%)               | 72 (51.8%)          | 66 (47.5%)  | 1 (0.7%)                | 0 (0%)    |
| Other <sup>3</sup> | 1 (0.7%)                                | 3 (2.1%)                                | NA                | NA                     | NA                                   | NA                     | NA                  | NA          | NA                      | NA        |

<sup>1</sup> Missing values are not reported.

<sup>2</sup> Prospective definitions for: tolerable, affected daily activity and disabling were not provided in the diary or protocol.

<sup>3</sup> Two patients reported pimples (one PERLANE®/one RESTYLANE®); one RESTYLANE® patient reported a sore throat; one RESTYLANE® patient reported a runny nose; degree of disability was not reported for any of the four events.

|                    | PERLANE®                                | RESTYLANE®                              | PERLANE® Patients |                        |                                      |                        | RESTYLANE® Patients |             |                         |           |
|--------------------|---|---|-------------------|------------------------|--------------------------------------|------------------------|---------------------|-------------|-------------------------|-----------|
|                    | Total patients reporting symptoms n (%) | Total patients reporting symptoms n (%) | None              | Tolerable <sup>1</sup> | Affected Daily Activity <sup>2</sup> | Disabling <sup>1</sup> | None                | Tolerable   | Affected Daily Activity | Disabling |
|                    |   |   | n (%)             | n (%)                  | n (%)                                | n (%)                  | n (%)               | n (%)       | n (%)                   | n (%)     |
| Bruising           | 74 (49.3%)                              | 70 (46.7%)                              | 75 (50.3%)        | 67 (45%)               | 7 (4.7%)                             | 0 (0%)                 | 79 (44.3%)          | 66 (53%)    | 4 (2.7%)                | 0 (0%)    |
| Redness            | 92 (61.3%)                              | 87 (58%)                                | 57 (38.3%)        | 85 (57%)               | 7 (4.7%)                             | 0 (0%)                 | 62 (41.6%)          | 81 (54.4%)  | 6 (4%)                  | 0 (0%)    |
| Swelling           | 121 (80.7%)                             | 125 (83.3%)                             | 28 (18.8%)        | 108 (72.5%)            | 11 (7.4%)                            | 2 (1.3%)               | 24 (16.1%)          | 109 (73.2%) | 14 (9.4%)               | 2 (1.3%)  |
| Pain               | 103 (68.7%)                             | 96 (64%)                                | 46 (30.9%)        | 90 (60.4%)             | 12 (8.1%)                            | 1 (0.7%)               | 53 (35.6%)          | 84 (56.4%)  | 11 (7.4%)               | 1 (0.7%)  |
| Tenderness         | 130 (86.7%)                             | 122 (81.3%)                             | 19 (12.8%)        | 116 (77.9%)            | 13 (8.7%)                            | 1 (0.7%)               | 27 (18.1%)          | 110 (73.8%) | 11 (7.4%)               | 1 (0.7%)  |
| Itching            | 58 (38.7%)                              | 53 (35.3%)                              | 91 (61.1%)        | 54 (36.2%)             | 4 (2.7%)                             | 0 (0%)                 | 96 (64.4%)          | 49 (32.9%)  | 4 (2.7%)                | 0 (0%)    |
| Other <sup>4</sup> | 3 (2%)                                  | 3 (2%)                                  | NA                | 3 (100%)               | 0 (%)                                | 0 (%)                  | NA                  | 3 (100%)    | 0 (%)                   | 0 (%)     |

<sup>1</sup> Missing values are not reported.

<sup>2</sup> Events are reported as local events; because of the design (split-face) of the study, causality of the systemic adverse events cannot be assigned.

<sup>3</sup> Prospective definitions for: tolerable, affected daily activity and disabling were not provided in the diary or protocol.

<sup>4</sup> Two patients reported mild transient headache and one patient reported mild ‘twitching’; neither could be associated with a particular product.

### Potential Adverse Events:

In postmarket surveillance of RESTYLANE® in the U.S. and both RESTYLANE® and PERLANE® in other countries, presumptive bacterial infections, inflammatory adverse events, allergic adverse events, and necrosis have been reported. Reported treatments have included systemic steroids, systemic antibiotics, and intravenous administrations of medications. Additionally, delayed inflammatory reaction to RESTYLANE® has been observed with swelling, redness, tenderness, induration and rarely acneform papules at the injection site with onset as long as several weeks after the initial treatment. Average duration of these effects is two weeks.

Adverse reactions should be reported to Medicis Aesthetics, Inc. at 1-866-222-1480.

### U.S. Clinical Studies

| MA-1400-02: Prospective, Randomized, Blinded, Controlled Clinical Study |  |
|---|--|
| Design  | 1:1 randomized, prospective study at 17 US centers, which compared the safety and effectiveness of PERLANE® and RESTYLANE® following treatment to baseline condition. Patients were randomized to either PERLANE® or RESTYLANE® treatment. A touch-up was allowed 2 weeks after initial treatment. Patients were partially masked; evaluating physicians were independent and masked; treating physicians were unmasked. Effectiveness was studied with 6 months follow-up. Safety was studied with 6 months follow-up.  |
| Endpoints   | Effectiveness <p>Primary:</p> <p>The difference in effect of PERLANE® at week 12 versus baseline condition on the visual severity of the nasolabial folds, as assessed by the Blinded Evaluator.</p> <p>The primary study and point was wrinkle severity 12 weeks after optimal correction was achieved. Wrinkle severity was evaluated on a five-step validated Wrinkle Severity Rating Scale (WSRS) (<i>i.e.</i>, none, mild, moderate, severe, extreme) by a live evaluator blinded to treatment. Patient success was defined as maintaining at least a one point improvement on the WSRS at 12 weeks after optimal correction was achieved. The percent of patient successes was calculated for each treatment group. Each group was compared to its own baseline, with no comparison with PERLANE® to RESTYLANE®.</p> <p>Secondary:</p> <p>Wrinkle Severity Rating Scale (WSRS) assessed at other follow-up points (2, 6, and 24 weeks after optimal correction) by the Blinded Evaluator, the investigator and the patient and compared to baseline score by the same evaluator. Duration of effect defined as 6 months or timepoint, if earlier, at which less than 50% of patients had at least a 1-grade response remaining in both nasolabial folds (NLFs).</p> <p>Safety assessments included: collection of patient symptoms in a 14-day diary; investigator evaluation of adverse experiences at 72 hours, and at 2, 6, 12, and 24 weeks; development of humoral or cell-mediated immunity; and the relationship of adverse experiences to injection technique.</p> |

in studies MA-1400-01, MA-1400-02, 31GE0101 and 31GE0002. In Study 31GE0101, 150 Canadian patients were injected with both PERLANE® and Hylaform®. In Study 31GE0002, 68 Scandinavian patients underwent both PERLANE® and Zyplast® injections.

|                    | PERLANE®                                | RESTYLANE®                              | PERLANE® Patients           |             |            |          | RESTYLANE® Patients         |            |            |          |
|--------------------|---|---|-----------------------------|-------------|------------|----------|-----------------------------|------------|------------|----------|
|                    | Total patients reporting symptoms n (%) | Total patients reporting symptoms n (%) | Number of days <sup>2</sup> |             |            |          | Number of days <sup>2</sup> |            |            |          |
|                    |   |   | 1 n (%)                     | 2–7 n (%)   | 8–13 n (%) | 14 n (%) | 1 n (%)                     | 2–7 n (%)  | 8–13 n (%) | 14 n (%) |
| Bruising           | 122 (86.5%)                             | 111 (78.2%)                             | 6 (4.9%)                    | 81 (66.4%)  | 28 (23%)   | 7 (5.7%) | 9 (8.1%)                    | 69 (62.8%) | 30 (27%)   | 3 (2.7%) |
| Redness            | 118 (83.7%)                             | 114 (80.3%)                             | 19 (16.1%)                  | 87 (73.7%)  | 8 (6.8%)   | 4 (3.4%) | 31 (26.2%)                  | 71 (62.3%) | 9 (7.9%)   | 3 (2.6%) |
| Swelling           | 128 (90.8%)                             | 127 (89.4%)                             | 6 (4.7%)                    | 100 (78.1%) | 17 (13.3%) | 5 (3.9%) | 12 (9.4%)                   | 93 (73.2%) | 19 (15.0%) | 2 (2.4%) |
| Pain               | 114 (80.9%)                             | 108 (76.1%)                             | 46 (40.4%)                  | 66 (57.9%)  | 2 (1.8%)   | 0 (0%)   | 37 (34.3%)                  | 69 (63.9%) | 2 (1.9%)   | 0 (0%)   |
| Tenderness         | 130 (92.2%)                             | 123 (86.6%)                             | 24 (18.5%)                  | 89 (68.5%)  | 16 (12.3%) | 1 (0.8%) | 21 (17.1%)                  | 92 (74.8%) | 9 (7.3%)   | 1 (0.8%) |
| Itching            | 45 (31.9%)                              | 67 (47.2%)                              | 19 (42.2%)                  | 23 (51.1%)  | 3 (6.7%)   | 0 (0%)   | 22 (32.8%)                  | 38 (56.7%) | 6 (9.0%)   | 1 (1.5%) |
| Other <sup>3</sup> | 1 (0.7%)                                | 3 (2.1%)                                | 1 (100%)                    | 0 (0%)      | 0 (0%)     | 0 (0%)   | 3 (100%)                    | 0 (0%)     | 0 (0%)     | 0 (0%)   |

<sup>1</sup> Missing values are not reported.

<sup>2</sup> Data are cumulated from up to four injection sites per patient with earliest and latest timepoint for any reaction provided.

<sup>3</sup> Two patients reported pimples (one PERLANE®/one RESTYLANE®); one RESTYLANE® patient reported a sore throat; one RESTYLANE® patient reported a runny nose; degree of disability was not reported for any of the four events.

|                    | PERLANE®                                | RESTYLANE®                              | PERLANE® Patients           |            |            |          | RESTYLANE® Patients         |            |            |          |
|--------------------|---|---|-----------------------------|------------|------------|----------|-----------------------------|------------|------------|----------|
|                    | Total patients reporting symptoms n (%) | Total patients reporting symptoms n (%) | Number of days <sup>2</sup> |            |            |          | Number of days <sup>2</sup> |            |            |          |
|                    |   |   | 1 n (%)                     | 2–7 n (%)  | 8–13 n (%) | 14 n (%) | 1 n (%)                     | 2–7 n (%)  | 8–13 n (%) | 14 n (%) |
| Bruising           | 74 (49.3%)                              | 70 (46.7%)                              | 23 (31.1%)                  | 44 (59.5%) | 6 (8.1%)   | 1 (1.4%) | 13 (18.6%)                  | 51 (72.9%) | 6 (8.6%)   | 0 (0%)   |
| Redness            | 92 (61.3%)                              | 87 (58%)                                | 38 (41.3%)                  | 52 (56.5%) | 2 (2%)     | 0 (0%)   | 33 (37.9%)                  | 52 (59.8%) | 2 (2.3%)   | 0 (0%)   |
| Swelling           | 121 (80.7%)                             | 125 (83.3%)                             | 22 (18.2%)                  | 85 (70.2%) | 11 (9.1%)  | 3 (2.5%) | 3 (2.4%)                    | 89 (71.2%) | 12 (9.6%)  | 1 (0.8%) |
| Pain               | 103 (68.7%)                             | 96 (64%)                                | 32 (31.1%)                  | 67 (65%)   | 2 (1.9%)   | 2 (1.9%) | 27 (28.1%)                  | 67 (69.8%) | 2 (2.1%)   | 0 (0%)   |
| Tenderness         | 130 (86.7%)                             | 122 (81.3%)                             | 26 (20%)                    | 94 (72.3%) | 6 (4.6%)   | 4 (3.1%) | 28 (23%)                    | 87 (71.3%) | 7 (5.7%)   | 0 (0%)   |
| Itching            | 58 (38.7%)                              | 53 (35.3%)                              | 29 (50%)                    | 26 (44.8%) | 2 (3.4%)   | 1 (1.7%) | 22 (41.5%)                  | 27 (50.9%) | 4 (7.5%)   | 0 (0%)   |
| Other <sup>4</sup> | 3 (2%)                                  | 3 (2%)                                  | 3 (100%)                    | 0 (0%)     | 0 (0%)     | 0 (0%)   | 3 (100%)                    | 0 (0%)     | 0 (0%)     | 0 (0%)   |

<sup>1</sup> Missing values are not reported.

<sup>2</sup> Events are reported as local events; because of the design (split-face) of the study, causality of the systemic adverse events cannot be assigned.

<sup>3</sup> Data are cumulated from up to two injection sites per patient with earliest and latest timepoint for any reaction provided.

<sup>4</sup> Two patients reported mild transient headache and one patient reported mild ‘twitching’; neither could be associated with a particular product.

#### MA-1400-02: Prospective, Randomized, Blinded, Controlled Clinical Study

| Outcomes   | <p><b>Demographics:</b></p> <p>The study enrolled 283 (<i>i.e.</i>, 141 PERLANE® and 142 RESTYLANE®) patients with moderate to severe NLF wrinkles. The patients were predominantly healthy ethnically diverse females. Bilateral NLFs and oral commissures were corrected in most patients with 1.9 mL to 4.6 mL of PERLANE®. The greatest amount used in any patient was 9.0 mL.</p> <p>Gender – Female: 266 (94%); Male: 17 (6%)</p> <p>Ethnicity – White: 226 (80%); Hispanic or Latino: 31 (11%); African American: 23 (8%); Asian: 3 (1%)</p> <p><b>Efficacy:</b></p> <p>The results of the blinded evaluator assessment of NLF wrinkle severity for PERLANE® and control (RESTYLANE®) are presented in Table 7. In the primary effectiveness assessment at 12 weeks, 87% of the PERLANE® and 77% of the control patients had maintained at least a 1 point improvement over baseline.</p>   |   |                            |   |                            |   |         |     |           |     |           |          |     |           |     |           |          |     |          |     |           |
|------------|--|---|----------------------------|---|----------------------------|---|---------|-----|-----------|-----|-----------|----------|-----|-----------|-----|-----------|----------|-----|----------|-----|-----------|
|            | <table border="1"> <caption>Table 7. Blinded Evaluator Wrinkle Severity Response Scores</caption> <thead> <tr> <th>Time point</th> <th>No. of PERLANE® Patients</th> <th>No. of PERLANE® Pts. maintaining <input type="checkbox"/>1 Unit Improvement of NLF on WSRS</th> <th>No. of RESTYLANE® Patients</th> <th>No. of RESTYLANE® Pts. maintaining <input type="checkbox"/>1 Unit Improvement of NLF on WSRS</th> </tr> </thead> <tbody> <tr> <td>6 weeks</td> <td>136</td> <td>121 (89%)</td> <td>136</td> <td>113 (83%)</td> </tr> <tr> <td>12 weeks</td> <td>141</td> <td>122 (87%)</td> <td>140</td> <td>108 (77%)</td> </tr> <tr> <td>24 weeks</td> <td>138</td> <td>87 (63%)</td> <td>140</td> <td>103 (74%)</td> </tr> </tbody> </table> <p>All p values &lt;0.0001 based on t-test compared to baseline condition</p> <p><b>Antibody Testing:</b></p> <p>15/141 (10.6%) subjects displayed a pre-treatment antibody response against PERLANE® (which was believed to be related to co-purifying <i>Streptococcus</i> capsule antigens). One subject also developed a measurable increase in antibody titer after PERLANE® injection. 4/16 (27%) patients with antibodies against PERLANE® had adverse experiences at the injection site, which was similar to the local adverse event rate observed in the entire PERLANE® population (<i>i.e.</i>, 49/141 (35%)). With the exception of one moderate bruising event, all the adverse experiences in the patients with a humoral response against PERLANE® were mild in severity. No severe events were noted and the subject who developed an antibody response after PERLANE® injection did not experience any adverse event at the injection site. Immediate type skin testing demonstrated that no patient developed IgE to PERLANE®. Post-exposure histopathology of skin biopsies of an implant site on each patient demonstrated that no patient developed cell-mediated immunity to PERLANE®.</p> | Time point  | No. of PERLANE® Patients   | No. of PERLANE® Pts. maintaining <input type="checkbox"/> 1 Unit Improvement of NLF on WSRS   | No. of RESTYLANE® Patients | No. of RESTYLANE® Pts. maintaining <input type="checkbox"/> 1 Unit Improvement of NLF on WSRS | 6 weeks | 136 | 121 (89%) | 136 | 113 (83%) | 12 weeks | 141 | 122 (87%) | 140 | 108 (77%) | 24 weeks | 138 | 87 (63%) | 140 | 103 (74%) |
| Time point | No. of PERLANE® Patients   | No. of PERLANE® Pts. maintaining <input type="checkbox"/> 1 Unit Improvement of NLF on WSRS | No. of RESTYLANE® Patients | No. of RESTYLANE® Pts. maintaining <input type="checkbox"/> 1 Unit Improvement of NLF on WSRS |                            |   |         |     |           |     |           |          |     |           |     |           |          |     |          |     |           |
| 6 weeks    | 136  | 121 (89%)   | 136                        | 113 (83%)   |                            |   |         |     |           |     |           |          |     |           |     |           |          |     |          |     |           |
| 12 weeks   | 141  | 122 (87%)   | 140                        | 108 (77%)   |                            |   |         |     |           |     |           |          |     |           |     |           |          |     |          |     |           |
| 24 weeks   | 138  | 87 (63%)  | 140                        | 103 (74%)   |                            |   |         |     |           |     |           |          |     |           |     |           |          |     |          |     |           |
|            | <p><b>MA-1400-01: Prospective, Randomized, Blinded, Controlled Clinical Study</b></p>  |   |                            |   |                            |   |         |     |           |     |           |          |     |           |     |           |          |     |          |     |           |
| Design     | 1:1 randomized, prospective study at 10 US centers, which compared the safety and effectiveness of PERLANE® and RESTYLANE® following treatment to baseline condition in 150 patients with pigmented skin and predominantly African-American ethnicity. Patients were randomized to either PERLANE® or RESTYLANE® treatment in a “within-patient” model of augmentation correction of bilateral nasolabial folds (NLFs) and oral commissures with one treatment assigned to one side and the other treatment to the other side. A touch-up was allowed 2 weeks after initial treatment. Patients and treating physicians were partially masked. Evaluations were performed by live investigator assessment for the primary analysis. Effectiveness was studied with 6 months follow-up. Safety was studied with 6 months follow-up.   |   |                            |   |                            |   |         |     |           |     |           |          |     |           |     |           |          |     |          |     |           |

**MA-1400-01: Prospective, Randomized, Blinded, Controlled Clinical Study**

| Endpoints  | <p>Effectiveness</p> <p>Primary:<br/>The difference in effect of PERLANE® at week 12 versus baseline condition on the visual severity of the NLFs.</p> <p>The primary study endpoint was wrinkle severity 12 weeks after optimal correction was achieved. Wrinkle severity was evaluated with a five-step validated Wrinkle Severity Rating Scale (WSRS) (i.e., none, mild, moderate, severe, extreme) by an on-site Blinded Evaluator. Patient success was defined as maintaining at least a one point improvement on the WSRS at 12 weeks after optimal correction was achieved. The percent of patients successes was calculated for each group. Each treatment group was compared to its own baseline, with no comparison of PERLANE® to RESTYLANE®</p> <p>Secondary:<br/>Wrinkle Severity Rating Scale (WSRS) was assessed at other follow-up points (2, 6, and 24 weeks after optimal correction) by the investigator and the patient and compared to baseline score by the same evaluator. A photographic assessment of patient outcomes was also performed. Duration of effect defined as 6 months or timepoint, if earlier, at which less than 50% of patients had at least a 1-grade response at both nasolabial folds.</p> <p>Safety assessments included: collection of patient symptoms in a 14-day diary; investigator evaluation of adverse experiences at 72 hours, and at 2, 6, 12, and 24 weeks; the development of humoral or cell-mediated immunity; and the relationship of adverse experiences to injection technique.</p>  |   |                                  |   |                                    |   |                                    |         |     |           |        |           |        |          |     |           |        |           |        |          |     |           |        |           |        |
|------------|---|---|----------------------------------|---|------------------------------------|---|------------------------------------|---------|-----|-----------|--------|-----------|--------|----------|-----|-----------|--------|-----------|--------|----------|-----|-----------|--------|-----------|--------|
| Outcomes   | <p><b>Demographics:</b></p> <p>The study enrolled 150 patients with moderate to severe NLF wrinkles. The patients were predominantly healthy African-American females.</p> <p>Gender – Female: 140/150 (93%); Male 10/150 (7%)</p> <p>Ethnicity – White: 2 (1.3%); Hispanic or Latino: 9 (6%); African-American: 137 (91%); American Indian: 2 (1.3%)</p> <p>Fitzpatrick Skin Type – I to III: 0 (0%); IV: 44 (29%); V: 68 (45%); VI: 38 (25%)</p> <p><b>Efficacy:</b></p> <p>The results of the live blinded evaluator assessment of wrinkle severity for PERLANE® and control (RESTYLANE®) are presented in Table 8 and are based on the Intent-to-Treat analysis. In the primary effectiveness assessment at 12 weeks, 92% of the PERLANE-treated and 93% of the RESTYLANE-treated NLF maintained at least a 1 point over baseline.</p> <table border="1"> <caption>Table 8. Live Evaluator Wrinkle Severity Response Scores</caption> <thead> <tr> <th>Time point</th> <th>No. of patients</th> <th>No. of PERLANE® Pts. maintaining □ 1 Unit Improvement on WSRS</th> <th>95% PERLANE® Confidence Interval</th> <th>No. of RESTYLANE® Pts. maintaining □ 1 Unit Improvement on WSRS</th> <th>95% RESTYLANE® Confidence Interval</th> </tr> </thead> <tbody> <tr> <td>6 weeks</td> <td>148</td> <td>140 (95%)</td> <td>90–99%</td> <td>142 (96%)</td> <td>92–99%</td> </tr> <tr> <td>12 weeks</td> <td>149</td> <td>137 (92%)</td> <td>87–97%</td> <td>139 (93%)</td> <td>89–98%</td> </tr> <tr> <td>24 weeks</td> <td>147</td> <td>104 (71%)</td> <td>63–77%</td> <td>108 (73%)</td> <td>66–81%</td> </tr> </tbody> </table> <p>All p-values &lt;0.0001 based on t-test compared to baseline condition</p> <p><b>Antibody Testing:</b></p> <p>6/150 (4%) subjects displayed a pre-treatment antibody response against PERLANE® (which was believed to be related to co-purifying <i>Streptococcus</i> capsule antigens). No subjects developed a measurable increase in antibody titer after PERLANE® injection. 0/6 (0%) patients with antibodies against PERLANE® had adverse experiences at the injection site as compared to the local adverse event rate observed in the entire PERLANE® population (i.e., 14/150 (9%)). All the adverse experiences in the patients with a humoral response against PERLANE® were mild in severity. Immediate type skin testing demonstrated that no patient developed IgE to PERLANE®. Post-exposure histopathology of skin biopsies of an implant site on each patient demonstrated that no patient developed cell-mediated immunity to PERLANE®</p> | Time point  | No. of patients                  | No. of PERLANE® Pts. maintaining □ 1 Unit Improvement on WSRS   | 95% PERLANE® Confidence Interval   | No. of RESTYLANE® Pts. maintaining □ 1 Unit Improvement on WSRS | 95% RESTYLANE® Confidence Interval | 6 weeks | 148 | 140 (95%) | 90–99% | 142 (96%) | 92–99% | 12 weeks | 149 | 137 (92%) | 87–97% | 139 (93%) | 89–98% | 24 weeks | 147 | 104 (71%) | 63–77% | 108 (73%) | 66–81% |
| Time point | No. of patients   | No. of PERLANE® Pts. maintaining □ 1 Unit Improvement on WSRS | 95% PERLANE® Confidence Interval | No. of RESTYLANE® Pts. maintaining □ 1 Unit Improvement on WSRS | 95% RESTYLANE® Confidence Interval |   |                                    |         |     |           |        |           |        |          |     |           |        |           |        |          |     |           |        |           |        |
| 6 weeks    | 148   | 140 (95%)   | 90–99%                           | 142 (96%)   | 92–99%                             |   |                                    |         |     |           |        |           |        |          |     |           |        |           |        |          |     |           |        |           |        |
| 12 weeks   | 149   | 137 (92%)   | 87–97%                           | 139 (93%)   | 89–98%                             |   |                                    |         |     |           |        |           |        |          |     |           |        |           |        |          |     |           |        |           |        |
| 24 weeks   | 147   | 104 (71%)   | 63–77%                           | 108 (73%)   | 66–81%                             |   |                                    |         |     |           |        |           |        |          |     |           |        |           |        |          |     |           |        |           |        |

**Non-U.S. Clinical studies**

**31GE0101: Prospective, Randomized, Blinded, Controlled Clinical Study**

| Design                    | <p>1:1 randomized, prospective study at 6 Canadian centers, which compared the safety and effectiveness of PERLANE® and Hylaform®. Patients were randomized to either PERLANE® or Hylaform® in a “within-patient” model of augmentation correction of bilateral nasolabial folds (NLFs) with one treatment assigned to one side and the other treatment to the other side. A touch-up was allowed 2 weeks after initial treatment. Patients were partially masked; evaluating physicians were independent and masked; treating physicians were partially masked.</p> <p>Effectiveness was studied with 6 months follow-up. Safety was studied with 6 months follow-up.</p>  |   |  |   |  |          |     |           |          |            |     |           |          |          |     |           |          |                           |   |                                   |                                      |          |   |            |            |          |          |     |            |            |          |          |   |            |            |           |          |
|---------------------------|---|---|--|---|--|----------|-----|-----------|----------|------------|-----|-----------|----------|----------|-----|-----------|----------|---------------------------|---|-----------------------------------|--------------------------------------|----------|---|------------|------------|----------|----------|-----|------------|------------|----------|----------|---|------------|------------|-----------|----------|
| Endpoints                 | <p>Effectiveness</p> <p>Primary:<br/>The difference in effect of PERLANE® as compared to Hylaform® on the visual severity of the NLFs, as assessed by a Blinded Evaluator at 6 months after baseline.</p> <p>The primary evaluation parameter was a five-step validated Wrinkle Severity Rating Scale (WSRS) score (absent, mild, moderate, severe, extreme) by the Blinded Evaluator at 6 months. Success was defined as maintaining at least a one point improvement of the NLF on the WSRS at 6 months after optimal correction was achieved. The percent of successful NLFs after PERLANE® and control treatments were compared, as well as a within-patient matched analysis (McNemar’s Test).</p> <p>Secondary:<br/>Wrinkle Severity Rating Scale (WSRS) was assessed at other follow-up points (2 weeks and 3, 4, 5, and 6 months after optimal correction) by the Blinded Evaluator and the patient. Global Aesthetic Improvement (GAI): very much improved / much improved / improved / no change / worse, assessed at same timepoints by patient.</p> <p>Safety assessments included: investigator evaluation of adverse experiences at all time points.</p>  |   |  |   |  |          |     |           |          |            |     |           |          |          |     |           |          |                           |   |                                   |                                      |          |   |            |            |          |          |     |            |            |          |          |   |            |            |           |          |
| Outcomes                  | <p><b>Demographics:</b></p> <p>The study enrolled 150 patients with moderate to severe nasolabial fold wrinkles. The patients were predominantly healthy white females. The study was completed by 140 of 150 patients at six months and additional safety data were available in 122 of 150 patients at 9 months.</p> <p>Gender – Female: 140 (93%); Male: 10 (7%)</p> <p>Ethnicity – White: 142/150 (95%); Non-caucasian: 8/150 (5%)</p> <p><b>Efficacy:</b></p> <p>The results of the blinded evaluator assessments are presented in Table 9 and are based on an Intent-to-Treat (ITT) analysis. At 6 months, 113/150 (75%) of the PERLANE-treated NLFs maintained at least a single point improvement on the WSRS compared to 57/150 (38%) of the control-treated NLFs.</p> <table border="1"> <caption>Table 9. Blinded Evaluator Wrinkle Severity Response Rates</caption> <thead> <tr> <th>Time point</th> <th>Number of NLFs</th> <th>No. of PERLANE® NLFs maintaining □ 1 Unit Improvement on WSRS</th> <th>No. of Hylaform® NLFs maintaining □ 1 Unit Improvement on WSRS</th> </tr> </thead> <tbody> <tr> <td>3 months</td> <td>150</td> <td>131 (87%)</td> <td>94 (63%)</td> </tr> <tr> <td>4.5 months</td> <td>150</td> <td>110 (73%)</td> <td>69 (46%)</td> </tr> <tr> <td>6 months</td> <td>150</td> <td>113 (75%)</td> <td>57 (38%)</td> </tr> </tbody> </table> <p>Table 10 shows the results for the within-patient investigator assessment of NLF on the WSRS.</p> <table border="1"> <caption>Table 10. Evaluating Investigator’s Assessment of NLF Severity; Score Change From Pre-Treatment Until 3, 4.5, and 6 Months After Last Treatment</caption> <thead> <tr> <th>Mos. after last treatment</th> <th>PERLANE® is superior to Hylaform® n (%)</th> <th>PERLANE® equal to Hylaform® n (%)</th> <th>Hylaform® superior to PERLANE® n (%)</th> <th>p-value*</th> </tr> </thead> <tbody> <tr> <td>3</td> <td>95 (63.3%)</td> <td>46 (30.7%)</td> <td>9 (6.0%)</td> <td>p&lt; 0.001</td> </tr> <tr> <td>4.5</td> <td>87 (58.0%)</td> <td>54 (36.0%)</td> <td>9 (6.0%)</td> <td>p&lt; 0.001</td> </tr> <tr> <td>6</td> <td>96 (64.0%)</td> <td>42 (28.0%)</td> <td>12 (8.0%)</td> <td>p&lt; 0.001</td> </tr> </tbody> </table> <p>* McNemar’s test with %-n/N, where N=Number of subjects in the ITT population</p> | Time point  | Number of NLFs   | No. of PERLANE® NLFs maintaining □ 1 Unit Improvement on WSRS | No. of Hylaform® NLFs maintaining □ 1 Unit Improvement on WSRS | 3 months | 150 | 131 (87%) | 94 (63%) | 4.5 months | 150 | 110 (73%) | 69 (46%) | 6 months | 150 | 113 (75%) | 57 (38%) | Mos. after last treatment | PERLANE® is superior to Hylaform® n (%) | PERLANE® equal to Hylaform® n (%) | Hylaform® superior to PERLANE® n (%) | p-value* | 3 | 95 (63.3%) | 46 (30.7%) | 9 (6.0%) | p< 0.001 | 4.5 | 87 (58.0%) | 54 (36.0%) | 9 (6.0%) | p< 0.001 | 6 | 96 (64.0%) | 42 (28.0%) | 12 (8.0%) | p< 0.001 |
| Time point                | Number of NLFs  | No. of PERLANE® NLFs maintaining □ 1 Unit Improvement on WSRS | No. of Hylaform® NLFs maintaining □ 1 Unit Improvement on WSRS |   |  |          |     |           |          |            |     |           |          |          |     |           |          |                           |   |                                   |                                      |          |   |            |            |          |          |     |            |            |          |          |   |            |            |           |          |
| 3 months                  | 150   | 131 (87%)   | 94 (63%)   |   |  |          |     |           |          |            |     |           |          |          |     |           |          |                           |   |                                   |                                      |          |   |            |            |          |          |     |            |            |          |          |   |            |            |           |          |
| 4.5 months                | 150   | 110 (73%)   | 69 (46%)   |   |  |          |     |           |          |            |     |           |          |          |     |           |          |                           |   |                                   |                                      |          |   |            |            |          |          |     |            |            |          |          |   |            |            |           |          |
| 6 months                  | 150   | 113 (75%)   | 57 (38%)   |   |  |          |     |           |          |            |     |           |          |          |     |           |          |                           |   |                                   |                                      |          |   |            |            |          |          |     |            |            |          |          |   |            |            |           |          |
| Mos. after last treatment | PERLANE® is superior to Hylaform® n (%)   | PERLANE® equal to Hylaform® n (%)                             | Hylaform® superior to PERLANE® n (%)                           | p-value*  |  |          |     |           |          |            |     |           |          |          |     |           |          |                           |   |                                   |                                      |          |   |            |            |          |          |     |            |            |          |          |   |            |            |           |          |
| 3                         | 95 (63.3%)  | 46 (30.7%)  | 9 (6.0%)   | p< 0.001  |  |          |     |           |          |            |     |           |          |          |     |           |          |                           |   |                                   |                                      |          |   |            |            |          |          |     |            |            |          |          |   |            |            |           |          |
| 4.5                       | 87 (58.0%)  | 54 (36.0%)  | 9 (6.0%)   | p< 0.001  |  |          |     |           |          |            |     |           |          |          |     |           |          |                           |   |                                   |                                      |          |   |            |            |          |          |     |            |            |          |          |   |            |            |           |          |
| 6                         | 96 (64.0%)  | 42 (28.0%)  | 12 (8.0%)  | p< 0.001  |  |          |     |           |          |            |     |           |          |          |     |           |          |                           |   |                                   |                                      |          |   |            |            |          |          |     |            |            |          |          |   |            |            |           |          |

**31GE0002: Prospective, Randomized, Blinded, Controlled Clinical Study**

| Design     | <p>1:1 randomized, prospective study at 2 Scandinavian centers, which compared the safety and effectiveness of PERLANE® and Zyplast®. Patients were randomized to either PERLANE® or Zyplast® in a “within-patient” model of augmentation correction of bilateral nasolabial folds (NLFs) with one treatment assigned to one side and the other treatment to the other side. Patients were partially masked; evaluating physicians were independent and masked; treating physicians were partially masked. A touch-up was allowed 2 weeks after the initial treatment. Retreatment was allowed at 6 or 9 months.</p> <p>Effectiveness was studied with 9 months follow-up. Safety was studied with 12 months follow-up.</p>  |  |   |  |   |          |           |            |            |           |        |           |            |            |          |        |           |            |            |           |        |           |            |            |           |        |
|------------|--|--|---|--|---|----------|-----------|------------|------------|-----------|--------|-----------|------------|------------|----------|--------|-----------|------------|------------|-----------|--------|-----------|------------|------------|-----------|--------|
| Endpoints  | <p>Effectiveness</p> <p>Primary:<br/>Superiority of correction of the NLF by PERLANE® as compared to Zyplast® based on the visual severity of the NLF, as assessed by a Blinded Evaluator at 6 months after optimal correction was achieved.</p> <p>The primary evaluation parameter was a five-step validated Wrinkle Severity Rating Scale (WSRS) score (absent, mild, moderate, severe, extreme) by the Blinded Evaluator at 6 months. NLF success was defined as maintaining at least a one point improvement on the WSRS at 6 months after optimal correction was achieved. The within patient comparison of PERLANE® and control treatments was evaluated in a matched analysis (McNemar’s Test).</p> <p>Secondary:<br/>Superiority of correction of the NLF by PERLANE® or Zyplast® based on the visual severity of the NLFs, as assessed by a Blinded Evaluator at 9 months after baseline.</p> <p>Safety assessments included: investigator evaluation of adverse experiences at all time points.</p>   |  |   |  |   |          |           |            |            |           |        |           |            |            |          |        |           |            |            |           |        |           |            |            |           |        |
| Outcomes   | <p><b>Demographics:</b></p> <p>The study enrolled 68 patients with correctable NLF wrinkles. The patients were predominantly healthy white females.</p> <p>Gender – Female: 65 (96%); Male: 3 (4%)</p> <p>Ethnicity – White: 68/68 (100%)</p> <p><b>Efficacy:</b></p> <p>The results of the blinded evaluator assessments are presented in Table 11. At the primary effectiveness time point of 6 months, the PERLANE-treated NLF experienced more improvement from baseline (judged by the WSRS) in 50% of the subjects; the control-treated side experienced more improvement in 10.3% of the subjects.</p> <table border="1"> <caption>Table 11. Evaluating Investigator’s Assessment: Difference in the Severity Rating Scale From Pre-Treatment Until 2, 4, 6, and 9 Months After Baseline</caption> <thead> <tr> <th>Time point</th> <th>PERLANE® NLF is superior to control NLF n (%)</th> <th>PERLANE® NLF is equal to control NLF n (%)</th> <th>Control NLF is superior to PERLANE® NLF n (%)</th> <th>p-Value¹</th> </tr> </thead> <tbody> <tr> <td>2 months²</td> <td>32 (47.1%)</td> <td>28 (41.2%)</td> <td>8 (11.8%)</td> <td>0.0001</td> </tr> <tr> <td>4 months²</td> <td>38 (55.9%)</td> <td>25 (36.8%)</td> <td>5 (7.4%)</td> <td>0.0001</td> </tr> <tr> <td>6 months²</td> <td>34 (50.0%)</td> <td>27 (39.7%)</td> <td>7 (10.3%)</td> <td>0.0003</td> </tr> <tr> <td>9 months³</td> <td>21 (48.8%)</td> <td>16 (37.2%)</td> <td>6 (14.9%)</td> <td>0.0039</td> </tr> </tbody> </table> <p>¹ McNemar’s test<br/>² Percent=n/Number of subjects in the ITT population at Month 6<br/>³ Percent=n/Number of subjects in the ITT population Month 9; includes only patients not retreated (n=43)</p> | Time point                                 | PERLANE® NLF is superior to control NLF n (%) | PERLANE® NLF is equal to control NLF n (%) | Control NLF is superior to PERLANE® NLF n (%) | p-Value¹ | 2 months² | 32 (47.1%) | 28 (41.2%) | 8 (11.8%) | 0.0001 | 4 months² | 38 (55.9%) | 25 (36.8%) | 5 (7.4%) | 0.0001 | 6 months² | 34 (50.0%) | 27 (39.7%) | 7 (10.3%) | 0.0003 | 9 months³ | 21 (48.8%) | 16 (37.2%) | 6 (14.9%) | 0.0039 |
| Time point | PERLANE® NLF is superior to control NLF n (%)  | PERLANE® NLF is equal to control NLF n (%) | Control NLF is superior to PERLANE® NLF n (%) | p-Value¹                                   |   |          |           |            |            |           |        |           |            |            |          |        |           |            |            |           |        |           |            |            |           |        |
| 2 months²  | 32 (47.1%)   | 28 (41.2%)                                 | 8 (11.8%)                                     | 0.0001                                     |   |          |           |            |            |           |        |           |            |            |          |        |           |            |            |           |        |           |            |            |           |        |
| 4 months²  | 38 (55.9%)   | 25 (36.8%)                                 | 5 (7.4%)                                      | 0.0001                                     |   |          |           |            |            |           |        |           |            |            |          |        |           |            |            |           |        |           |            |            |           |        |
| 6 months²  | 34 (50.0%)   | 27 (39.7%)                                 | 7 (10.3%)                                     | 0.0003                                     |   |          |           |            |            |           |        |           |            |            |          |        |           |            |            |           |        |           |            |            |           |        |
| 9 months³  | 21 (48.8%)   | 16 (37.2%)                                 | 6 (14.9%)                                     | 0.0039                                     |   |          |           |            |            |           |        |           |            |            |          |        |           |            |            |           |        |           |            |            |           |        |

**How Supplied**

PERLANE® is supplied in a 1 mL disposable glass syringe with a Luer-lok fitting. The gel particle contents of the syringe are sterile. A □ irradiated sterilized needle, 27 G x ½”, is co-packed with each syringe. PERLANE® can be stored at a temperature of up to 25°C (77°F). Do not freeze and protect from sunlight. Refrigeration is not required.

A patient record label is a part of the syringe label. Remove it by pulling the flap marked with three small arrows. This label is to be attached to patient records to ensure traceability of the product.

INSTRUCTIONS FOR USE CAN BE FOUND AT: <http://www.RestylaneUSA.com>

**STORAGE**

- PERLANE® should be stored at a temperature of up to 25°C (77°F). Do not freeze and protect from sunlight. Refrigeration is not required.
- PERLANE® is a gel without visible particulates. In the event that the contents of the syringe show signs of separation, do not use the syringe and notify Medicis Aesthetics, Inc. at 1-866-222-1480.

US PATENT 5,827,937

**Manufactured for**  
Medicis Aesthetics, Inc.  
8125 N. Hayden Road  
Scottsdale, AZ 85258  
U.S.A.  
Phone: 1-866-222-1480

**Manufactured by**  
Q-Med AB  
Seminariegatan 21  
SE-752 28 Uppsala  
Sweden

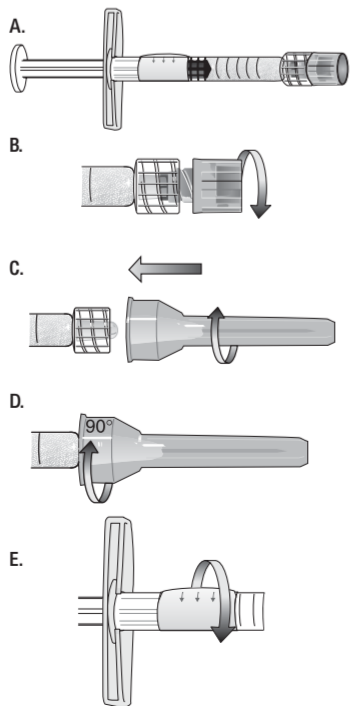
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**HOW SUPPLIED**

PERLANE® is supplied in a disposable glass syringe with a Luer-lok fitting (A). A gamma irradiated sterilized needle, 27 G x 1/2”, is co-packed with each syringe of PERLANE®. A patient record label is a part of the syringe label. This label is to be attached to patient records to ensure traceability of the product. The contents of the syringe are sterile. The volume in each syringe is as stated on the syringe label and on the carton.

**DIRECTIONS FOR ASSEMBLY**

- Assembly of needle to syringe**  
For safe use of PERLANE® it is important that the needle is properly assembled. Improper assembly may result in separation of the needle and syringe during implantation. See pictures A through E.
- Unscrew the tip cap (B) of the syringe carefully.
  - Grasp the narrow part of the needle shield loosely; mount the needle on the Luer-lok (C) by turning it clockwise until you feel counterpressure.
  - Grasp the wider part of the needle shield firmly (D).
  - Press and turn the needle shield 90° (a quarter turn).
  - The quarter turn is necessary to lock the needle onto the syringe.
  - Remove the patient record label marked with three small arrows (E) and attach to patient chart.
  - Pull off the needle shield.



**PRE-TREATMENT GUIDELINES**

Prior to treatment, the patient should avoid taking aspirin, nonsteroidal anti-inflammatory medications, St. Johns Wort, or high doses of Vitamin E supplements. These agents may increase bruising and bleeding at the injection site.

**TREATMENT PROCEDURE**

- It is necessary to counsel the patient and discuss the appropriate indication, risks, benefits and expected responses to the PERLANE® treatment. Advise the patient of the necessary precautions before commencing the procedure. A consent form should be utilized.
- Assess the patient’s need for appropriate anesthetic treatment for managing comfort, i.e., topical anesthetic, local or nerve block.
- The patient’s face should be washed with soap and water and dried with a clean towel. Cleanse the area to be treated with alcohol or another suitable antiseptic solution.
- Sterile gloves are recommended while injecting PERLANE®.
- Before injecting, press rod carefully until a small droplet is visible at the tip of the needle.
- PERLANE® is administered using a thin gauge needle (27 G x 1/2”). The needle is inserted at an approximate angle of 30° parallel to the length of the wrinkle or fold. PERLANE® should be injected into the deep dermis to superficial layer of the subcutis. If PERLANE® is injected too superficially this may result in visible lumps and/or bluish discoloration.
- Inject PERLANE® applying even pressure on the plunger rod. It is important that the injection is stopped just before the needle is pulled out of the skin to prevent material from leaking out or ending up too superficially in the skin.
- Only correct to 100% of the desired volume effect. Do not overcorrect. With cutaneous deformities the best results are obtained if the defect can be manually stretched to the point where it is eliminated. The degree and duration of the correction depend on the character of the defect treated, the tissue stress at the implant site, the depth of the implant in the tissue and the injection technique.
- Typical usage for each treatment session is specific to the site as well as wrinkle severity rating scale (WSRS). In a prospective study of midface wrinkle correction, the median total dose was 3.0 mL. Based on U.S. clinical studies, the maximum recommended dose per treatment is 6.0 mL.

**INJECTION TECHNIQUES**

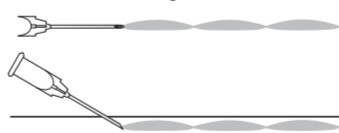
- PERLANE® can be injected by a number of different techniques that depend on the treating physician’s experience and preference, and patient characteristics.
- Serial puncture (F)** involves multiple, closely spaced injections along wrinkles or folds. Although serial puncture allows precise placement of the filler, it produces multiple puncture wounds that may be undesirable to some patients.
- Linear threading (G)** is accomplished by fully inserting the needle into the middle of the wrinkle or fold and injecting the filler along the track as a “thread.” Although threading is most commonly practiced after the needle has been fully inserted and is being withdrawn, it can also be performed while advancing the needle (“push-ahead” technique).
- Serial threading is a technique that utilizes elements of both approaches.
- Cross-hatching (H)** consists of a series of parallel linear threads injected at intervals of five to ten mm followed by a new series of threads injected at right angles to the first set to form a grid. This technique is particularly useful in facial contouring when coverage of the treatment region needs to be maximized.
- Note! The correct injection technique is crucial for the final result of the treatment.** Dissection of the sub-epidermal plane with lateral movement of the needle, rapid flows (>0.3 mL/min), rapid injection or high volumes may result in an increase in short-term episodes of bruising, swelling, redness, pain, or tenderness at the injection site.

- When the injection is completed, the treated site should be gently massaged so that it conforms to the contour of the surrounding tissues. If an overcorrection has occurred, massage the area firmly between your fingers or against an underlying superficial bone to obtain optimal results.
- If so called “blanching” is observed, i.e., the overlying skin turns a whitish color, the injection should be stopped immediately and the area massaged until it returns to a normal color.
- If the wrinkle needs further treatment, the same procedure should be repeated until a satisfactory result is obtained. Additional treatment with PERLANE® may be necessary to achieve the desired correction.
- If the treated area is swollen directly after the injection, an ice pack can be applied on the site for a short period. Ice should be used with caution if the area is still numb from anesthetic to avoid thermal injury.
- Patients may have mild to moderate injection site reactions, which typically resolve in a few days.

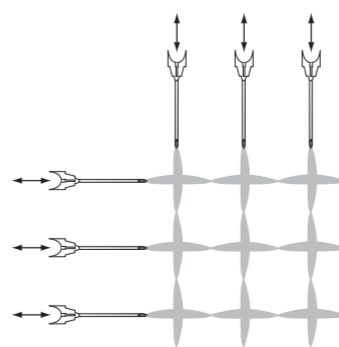
**F. Serial Puncture**



**G. Linear Threading**



**H. Cross-hatching**



**STERILE NEEDLE, 1 x 27 G x 1/2”**

- Follow national, local or institutional guidelines for use and disposal of medical sharp devices. Obtain prompt medical attention if injury occurs.
- To help avoid needle breakage, do not attempt to straighten a bent needle. Discard it and complete the procedure with a replacement needle.
- Do not reshield used needles. Recapping by hand is a hazardous practice and should be avoided.
- Discard unshielded needles in approved sharps collectors.

**SHELF LIFE AND STORAGE**

PERLANE® must be used prior to the expiration date printed on the package. Store at a temperature of up to 25° C (77° F). Do not freeze and protect from sunlight. Refrigeration is not needed. Do not resterilize PERLANE® as this may damage or alter the product.

After full correction of a treatment area is attained, any remaining PERLANE® may be used in another appropriate treatment area. A PERLANE® syringe should be completely used or discarded immediately following treatment.

PERLANE® is packaged in a glass syringe. Glass is subject to breakage under a variety of unavoidable conditions. Care should be taken with the handling of the glass syringe and with disposing of broken glass to avoid laceration or other injury. Do not use if the package is damaged. Immediately return the damaged product to Medicis Aesthetics Inc.

Rx only

**Ordering Information**  
Medicis Aesthetics, Inc. and its distributor, McKesson Speciality, are your only sources for FDA-approved PERLANE®. Purchasing from any other agent is illegal.

To order, call 877-520-0500.

PERLANE® is a registered trademark of HA North American Sales AB.

