

# ARTEFILL®

## INSTRUCTIONS FOR USE

*FDA DRAFT as of 10-25-06*

**Caution: Federal Law restricts this device to physician use only.**

### DESCRIPTION

ArteFill 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.

### INDICATIONS

ArteFill® is indicated for the correction of nasolabial folds.

### CONTRAINDICATIONS

- ArteFill is contraindicated for patients displaying a positive response to the required ArteFill Skin Test. Refer to ArteFill Skin Test Instructions for Use for complete instructions for administration and evaluation of the skin test.
- ArteFill is contraindicated for patients with severe allergies manifested by a history of anaphylaxis, or history or presence of multiple severe allergies.
- ArteFill contains lidocaine and is contraindicated for patients with known lidocaine hypersensitivity.
- ArteFill 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 bovine collagen in ArteFill.
- ArteFill is contraindicated for patients undergoing or planning to undergo desensitization injections to meat products, as these injections can contain bovine collagen.
- ArteFill is contraindicated for use in lip augmentation and injection into the vermilion or the wet mucosa of the lip

- ArteFill should not be used in patients with known susceptibility to keloid formation or hypertrophic scarring.

## **WARNINGS**

- The safety of ArteFill when used within 6 months of collagen, botulinum toxin, or other wrinkle therapies has not been studied.
- An ArteFill Skin Test must be administered and evaluated prior to injection of ArteFill. 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 also should not be considered candidates for treatment. Refer to the ArteFill Skin Test Instructions for Use.
- ArteFill must not be implanted into blood vessels. Implantation of ArteFill into dermal vessels may cause vascular occlusion, infarction, or embolic phenomena.
- Use of ArteFill 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.
- Patients who are using substances that interfere with platelet function or have any condition that reduces coagulation may experience increased bruising or bleeding at injection sites.

## PRECAUTIONS

- ArteFill contains non-absorbable PMMA microspheres. Implantation is permanent and will not be reversed without excision.
- The safety of ArteFill for use during pregnancy, in breastfeeding females, or in patients under 18 years has not been established.
- ArteFill is packaged in sealed syringes and cartons. The tip of the syringe is sealed with a tamper evidence cover. Do not use if the seal on the carton or syringe is broken or removed. Do not resterilize.
- The safety of injecting greater amounts than 3.5 cc per treatment site or 8.9 cc overall has not been established.
- As with all transcutaneous procedures, ArteFill injection carries a risk of infection. The usual precautions associated with injectable materials should be followed.
- The use of ArteFill in patients receiving UV light therapy has not been studied.
- The use of ArteFill in patients on immunosuppressive therapy has not been studied.
- The use of ArteFill in patients with atrophic skin diseases or thin or flaccid skin has not been studied and the cosmetic results for these patients are unknown.
- Long-term safety and effectiveness of ArteFill beyond one year have not been established.
- 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.
- ArteFill 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 Artes Medical immediately. In the United States call toll free 888-ARTEFILL or 888-278-3345. Outside the United States call 858-875-5555.

## ADVERSE EVENTS

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

**TABLE I.**  
**ADVERSE EVENTS REPORTED AT AN INCIDENCE OF 1% OR GREATER**  
**IN US CLINICAL TRIALS OF ARTEFILL**

| Event   | Number of Events<br>(Events/subjects treated, %) |                                  |                                   |
|---|--|----------------------------------|-----------------------------------|
|   | ArteFill <sup>1</sup><br>n = 285                 | ArteFill <sup>2</sup><br>n = 106 | Control <sup>3,4</sup><br>n = 123 |
| 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)                           |

<sup>1</sup>128 ArteFill subjects in the controlled study and 157 subjects in an open label study, who were followed for 1 year after implantation.

<sup>2</sup>106 Control subjects who received ArteFill in the cross-over arm of the controlled study and were followed for 6 months after implantation.

<sup>3</sup> a commercially available collagen implant for the treatment of soft tissue defects of the face

<sup>4</sup>123 subjects who received the Control treatment in the controlled study and were followed for 6 months after implantation.

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 ArteFill 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 ArteFill subjects at an incidence of less than 1% in US 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.

The following is a summary of the reported duration of adverse events lasting longer than 2 weeks in ArteFill subjects (n=391 subjects) in US 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.

Among the 391 subjects treated with ArteFill, 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).

### **Potential Adverse Events**

Clinical experience with similar products used outside United States suggest that the following adverse events that did not occur in US clinical trials might occur: hypersensitivity to bovine collagen, severe anaphylaxis reaction, drainage of fluid from the injection site, and nodule formation requiring excision or drug treatment.

## US CLINICAL TRIALS

### a) Controlled Trial

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

The primary effectiveness endpoint was a comparison of the cosmetic correction provided by ArteFill 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 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 2.

**Table 2.**  
**Subject and Baseline Characteristics**

| <b>Demographic</b>            | <b>ArteFill<br/>(n = 128)</b> | <b>Control<br/>(n = 123)</b> |
|-------------------------------|-------------------------------|------------------------------|
| <b>Gender</b>                 |                               |                              |
| Male                          | 11 (8.6%)                     | 11 (8.9%)                    |
| Female                        | 117 (91.4%)                   | 112 (91.1%)                  |
| <b>Age, years</b>             |                               |                              |
| Mean                          | 53.2                          | 51.2                         |
| Range                         | 28-82                         | 29-78                        |
| <b>Ethnicity</b>              |                               |                              |
| Caucasian                     | 100 (78.1%)                   | 101 (82.1%)                  |
| Hispanic                      | 21 (16.4%)                    | 20 (16.3%)                   |
| Asian                         | 1 (0.8%)                      | 1 (0.8%)                     |
| Other <sup>1</sup>            | 6 (4.7%)                      | 1 (0.8%)                     |
| <b>Facial Area Treated</b>    |                               |                              |
| Nasolabial Folds              | 108 (84.4%)                   | 104 (84.6%)                  |
| <b>Wrinkle Severity</b>       | <b>Mean Value</b>             | <b>Mean Value</b>            |
| Nasolabial Folds <sup>2</sup> | 1.74                          | 1.45                         |

1. "Other" ethnicities, as reported by ArteFill 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 ArteFill 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 ArteFill - 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 (ArteFill) 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 (ArteFill) and 0.15 points (Control) were determined for nasolabial folds. At 12 months after treatment, a nasolabial wrinkle severity difference of 0.98 points (compared to baseline) was recorded for ArteFill 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 Tables 3 and 4, respectively.

**Table 3.**  
**Mean number of treatment sessions per product**

| Area             | ArteFill     | Control       |
|------------------|--------------|---------------|
| Nasolabial Folds | 2.28 (n=108) | 2.18 (n= 104) |

**Table 4.**  
**Mean volume of product used per side (Left/Right)**

| Treatment Area   | ArteFill (cc) | Control (cc)  |
|------------------|---------------|---------------|
| Nasolabial Folds | 0.82 (n=108)  | 1.46 (n= 104) |

### b) Open Label Study

This open-label, single-arm, multi-center study assessed the safety of ArteFill 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. 126/157 (80.2%) subjects completed the 1-year study. The safety data collected in this study were included in Table 1.

### c) Collagen Immunoreactivity

The immunoreactivity of the collagen component was evaluated in the randomized study. All patients were required to have a skin test prior to being considered for injection with ArteFill. In this trial, 128 patients received ArteFill Skin Test as their first injection. The 123 patients in the control group received skin tests with the control collagen. Of the 123 patients in the control group, 106 patients received the ArteFill skin test after 6 months when they decided to receive ArteFill in the cross-over portion of the study.

*Results of the skin tests* – In the randomized study there were no positive skin tests in the 128 patients first randomized to receive ArteFill treatment or the 106 control patients who elected to receive ArteFill injections in the cross-over cohort. Of the 141 patients who received the collagen control skin test, 6 had a positive skin test and were excluded from the study.

*Serum IgG* – In the randomized study 4 ArteFill and 2 control patients were not treated because they displayed abnormal baseline serum IgG levels against collagen during screening. One subject in the ArteFill 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 patient's IgG levels returned to the normal range by 3 months after treatment.

## **INDIVIDUALIZATION OF TREATMENT**

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

## **HOW SUPPLIED**

ArteFill is an aseptic product that is required to pass a USP sterility test before release. It is supplied in a sealed tray containing 5 syringes, 3 containing 0.8 cc and 2 containing 0.4 cc, packaged in a box. Each syringe contains: 20% polymethylmethacrylate beads 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.

Each syringe is sealed for single patient use. The tip of the syringe is sealed with a tamper evidence cover. Do not use if the tamper evidence cover is broken or removed. Do not re-sterilize.

The tray lid is also sealed with a tamper evidence cover. Do not use if the package is damaged or the cover is broken or removed.

## **IMMUNOGENICITY TEST PROCEDURE**

Four (4) weeks prior to treatment, patients will be given a 0.1 cc test injection of collagen intradermally in the volar forearm, to determine a patient's sensitivity to the treatment material. For a complete discussion of the ArteFill 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. An ArteFill Skin Test Results Card will 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.

### **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**

ArteFill is indicated for correction of nasolabial folds.

1. Prior to treatment with ArteFill, the results of the skin test must be carefully evaluated; the patient must not have a response to the required ArteFill Skin Test. For a complete discussion of the ArteFill Skin Test, refer to the Instructions for Use supplied with skin test syringes.
2. Prior to treatment with ArteFill, 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 might 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 ArteFill.
4. The patient's soft tissue contour deficiencies should be characterized with regard to etiology, distension, stress at the site, and depth of lesion. Pretreatment photographs are recommended.
5. The ArteFill syringe must be brought to room temperature before injection.
6. After ensuring that the patient has thoroughly washed the treatment area with soap and water, the area should be swabbed with alcohol or other antiseptic.
7. ArteFill is implanted through a 26 G needle. Best results with ArteFill are achieved in defects requiring deep dermal implant placement and not into the subcutaneous fat. The rate and degree of subsidence of correction in the implanted area varies with patient, treatment site, and plane of implant placement. Correction should be conservative during initial treatment.
8. The best cosmetic result can be achieved by moving the needle back and forth 2 to 3 times beneath each skin fold being treated while maintaining constant pressure throughout the implantation procedure (tunneling technique). The injection pressure is correct if the implant flows slowly and evenly, without great exertion. This technique results in subdermal strands, which form a support structure beneath the wrinkle to prevent further wrinkling.
9. If needles become occluded or dull during a treatment session, replacement may be necessary.
10. Gentle pressure on the skin with the fingertips may facilitate even distribution of ArteFill immediately after implant placement.
11. Successive implantations at intervals of 2 or more weeks may be necessary to achieve the desired level of correction.
12. The area and the borders of ArteFill injection should be recorded on an illustration of a face for later comparison.
13. The physician should instruct the patient to report to him or her any evidence of adverse texture change in the surrounding implantation site. Other problems possibly associated with the use of ArteFill should be promptly brought to the attention of the physician.
14. The syringe and any unused material should be discarded after a single treatment visit.
15. 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**

ArteFill should be stored at standard domestic refrigerator temperatures. **DO NOT FREEZE.**

ArteFill 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 Artes Medical immediately. In the United States call toll-free 888-ARTEFILL (888-278-3345). Outside the United States call 858-875-5555.

## **PATIENT COUNSELING**

ArteFill Patient Brochures are available by contacting Artes Medical. Patients should be told that more than one treatment session might be required to achieve the desired correction.

To place an order contact Artes Medical, Inc. In the United States call toll-free 888-ARTEFILL (888-278-3345). Outside the United States call ++1-858-875-5555. Order may also be sent by fax to 858-875-5556 or email to [customersupportservice@artemedical.com](mailto:customersupportservice@artemedical.com).

Artes Medical, Inc.  
5870 Pacific Center Blvd.  
San Diego, CA 92121  
United States of America

Toll Free Phone 888-ARTEFILL (888-278-3345)  
Outside the US Phone 858-875-5555  
Fax 858-875-5556  
[customersupportservice@artemedical.com](mailto:customersupportservice@artemedical.com)  
[www.artemedical.com](http://www.artemedical.com)  
[www.artefill.com](http://www.artefill.com)

7007REVxx

Artes Medical, Inc.  
**ArteFill Patient Labeling**  
**Version 5 to FDA with Photos**  
**10/24/06**

ArteFill Logo

ArteFill.

Q What is ArteFill?

A ArteFill is an injectable filler for the correction of wrinkles known as smile lines. It contains 20% tiny round, non-resorbable and smooth particles (PMMA microspheres) and 80% purified bovine collagen gel with 0.3% lidocaine, an anesthetic.

Q How is ArteFill different from temporary dermal fillers?

A All temporary fillers are eventually absorbed by the body. That's why they require frequent repeat injections. ArteFill is different. The unique microspheres in ArteFill are not absorbed by the body. These microspheres provide the support your skin needs for wrinkle correction.

Q How does ArteFill work?

A ArteFill is a dual-acting injectable wrinkle filler. First, ArteFill visibly corrects the wrinkle. Then the microspheres provide the support your skin needs for wrinkle correction.

Q Is ArteFill safe?

A Yes. Clinical studies have shown ArteFill to be safe and effective correction of smile lines.

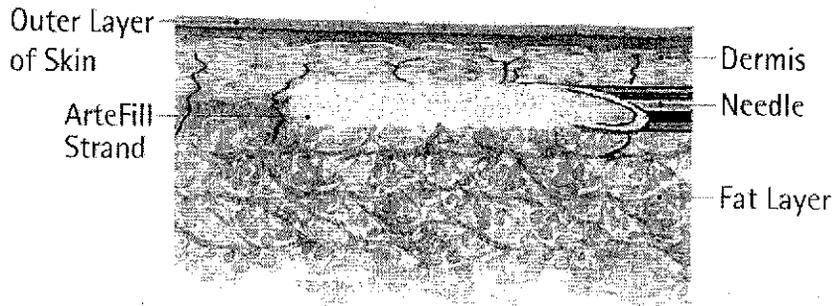
Q Why is a skin test necessary prior to treatment with ArteFill?

A A skin test is a safety precaution to make sure that you are not allergic to the bovine collagen or anesthetic in ArteFill.

Q How is ArteFill injected?

A ArteFill is injected underneath the wrinkle, just above the skin's fat layer. ArteFill provides the soft, supportive foundation that your skin needs for wrinkle correction.

Figure 1. How ArteFill is Injected



Q Can anyone have ArteFill treatments? (Contraindications)

A No. Some people are not good candidates for ArteFill. ArteFill is contraindicated in those who:

- have a positive reaction to the ArteFill skin test.
- have a history of severe allergies and hypersensitivity (anaphylaxis).
- are allergic to the anesthetic (lidocaine) in ArteFill.
- have a history of allergies to any bovine collagen products.
- are prone to thick scarring (hypertrophic) formation and/or excessive scarring (keloid).
- are undergoing or planning to undergo desensitization injections to meat products.

Q Are there any other treatment concerns with ArteFill?

A Yes.

- If you have any skin outbreaks (e.g., cysts, pimples, rashes, hives, infection) near the injection site, you should postpone treatment until they clear.
- If you are taking aspirin (NSAIDs) or anti-inflammatory drugs or have any medical condition that affects your blood, you may experience increased bruising or bleeding at the injection sites.

In addition, you should inform your doctor if:

- you have had any treatments for smile lines in the last 6 months
- you are receiving UV light therapy
- you are currently on immuno-suppressive therapy (medication commonly prescribed for those who have undergone an organ transplant, or are suffering from rheumatoid arthritis, psoriasis, inflammatory bowel disease, or cancer).

It's important that you share your medical information with your doctor. Together, you can make an informed decision as to whether ArteFill is right for you.

Q Are there any further precautions with ArteFill?

A Yes, you should know:

- ArteFill contains microspheres that help provide the support for wrinkle correction. Treatment results are lasting. The microspheres can only be surgically removed.
- The safety of ArteFill in pregnant or breastfeeding women, and individuals under 18, has not been established.
- There is always a risk of infection with any injection. Discuss the symptoms of infection with your doctor so you will be able to recognize them.
- Check to see if your doctor is properly trained to provide ArteFill.

Q Are there any possible side effects with ArteFill?

A As with any injectable wrinkle filler, you can expect mild swelling and reddening at the treatment site. These side effects are usually gone within 24 hours. Occasionally, there is mild bruising that typically disappears in three to seven days. Less common side effects include rash and itching more than 48 hours after treatment, persistent swelling or redness, and increased sensitivity at some or all injection sites. Two other rare potential side effects of all dermal fillers may be lumps and granulomas, both of which can be treated by your physician.

Be sure to call your doctor immediately if you notice any unusual skin reactions around the treatment area.

Q How does ArteFill treatment compare to temporary fillers?

A The treatment itself is similar. It involves injections with a fine needle and takes only a few minutes. You can resume your normal activities immediately.

Q When will I see results with ArteFill and how long will the results last?

A You will see results immediately. In the U.S. clinical study, full wrinkle correction was maintained throughout the study.

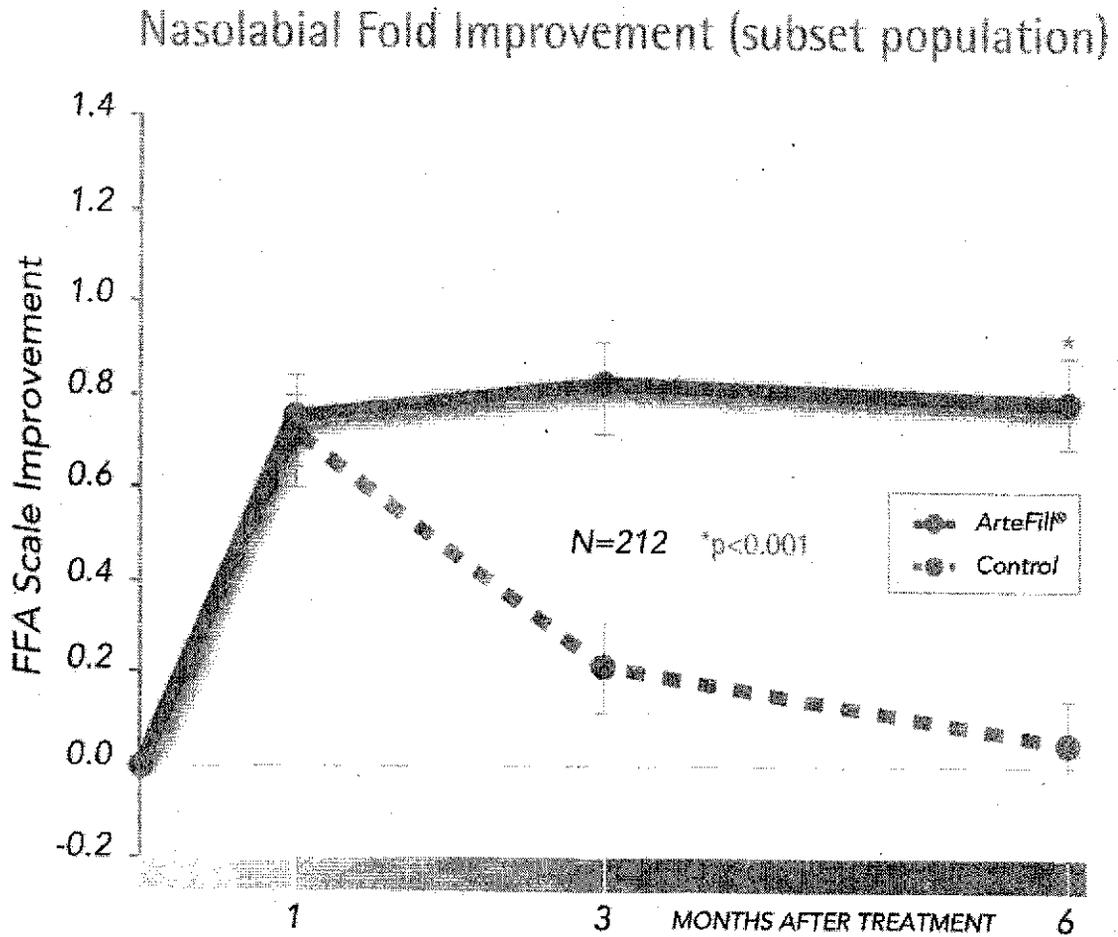
Q What clinical studies were conducted on ArteFill?

A Artes Medical conducted two clinical studies in the United States to demonstrate the safety and effectiveness of ArteFill. One study was primarily to determine ArteFill's safety and the second study was to determine both the safety and effectiveness of ArteFill.

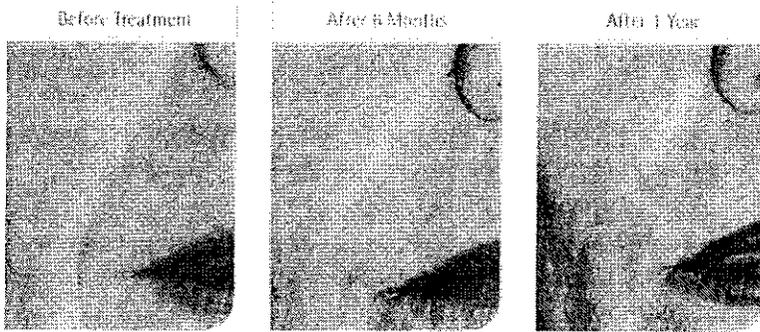
- **Clinical Study #1.** In this safety study, both the doctors and the patients knew that ArteFill was being injected. This multi-center study reviewed the safety of ArteFill injections for the correction of facial wrinkles. 157 patients were enrolled and monitored at 3, 6, and 12 months after treatment. 126 out of the 157 patients (80%) completed the 1-year study. The safety data from this study was combined with the safety data from the controlled study to define the safety record for ArteFill.

- **Clinical Study #2.** A controlled study conducted at 8 research clinics compared the safety and efficacy of ArteFill and a commercially available collagen implant for the treatment of facial wrinkles in a total of 251 patients. The patients were randomly divided into two groups with 128 patients receiving ArteFill and 123 receiving collagen injections. After 6 months, the effect of ArteFill was compared to the collagen patients who served as the control group. Photographs were taken of all of the treated wrinkles at each office visit and evaluated by a separate group of doctors who were not involved in treating the patients. These doctors evaluated the coded photographs using a standardized rating scale to grade the effectiveness of both the ArteFill and control collagen results. Safety was evaluated by comparing the number and severity of side effects during and for 12 months after treatment.

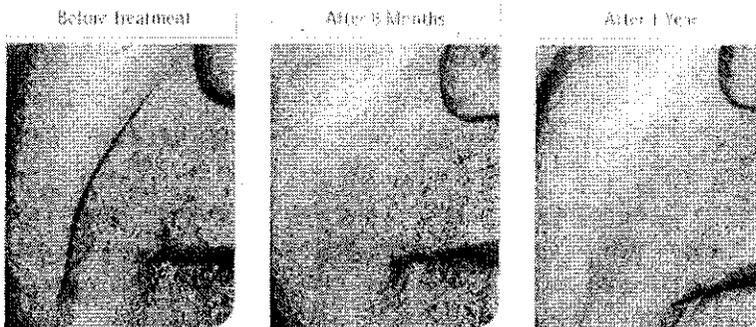
Figure 2.



The effectiveness of ArteFill and the control collagen to correct smiles lines (nasolabial folds) is shown in Figure 2. One month after treatment, both ArteFill and the control collagen had a similar effect on improving the wrinkle. At the 3 month evaluation, ArteFill maintained its effect while the control collagen had a lesser effect. At the 6 month evaluation, ArteFill had maintained its effect while the control group had lost its effect. This was the primary point at which effectiveness was determined.



Individual results may vary



Individual results may vary

Q Is one treatment enough to get the look I want?

A Most people get the results they want with one or two treatments, depending on the depth of their wrinkles and folds. When you have your follow-up appointment in four to six weeks, you and your doctor can decide if you would like to further enhance your results. With **ArteFill Progressive Enhancement™** (gradual wrinkle correction), your doctor can tailor your treatment program to meet your individual needs. This personalized approach helps to ensure that you get the look you desire.

Q Where can I get ArteFill treatment?

A ArteFill is only available through ArteFill-trained physicians. To find an ArteFill-trained doctor near you, please visit [www.artefill.com](http://www.artefill.com) or call 888.ARTEFILL (888.278.3345).

## Glossary

Anaphylaxis or anaphylactic shock – A sudden, severe and maybe fatal allergic reaction to a particular substance marked by a drop in blood pressure, itching, swelling and difficulty in breathing.

Anesthetic -- A substance that blocks pain

ArteFill Progressive Enhancement™ -- A gradual and personalized ArteFill wrinkle correction, where treatments are tailored to meet individual needs

Bovine collagen -- Collagen from a calf (see collagen)

Collagen -- A protein that provides the structural support for skin

Contraindicated -- Something that makes a particular treatment inadvisable

Corticosteroids -- Medication often used to treat swelling and redness (inflammation)

Desensitization -- Medical therapy to make someone less sensitive to a specific substance (allergen) by adding amounts slowly over time to build up resistance

Granuloma -- A delayed reaction after injection of any dermal filler that may appear as a swollen lump

Hypertrophic -- Thick scarring

Keloid -- Excessive scarring

Lidocaine -- The anesthetic in ArteFill (see anesthetic)

NSAIDs -- Non-steroidal anti-inflammatory drugs

Immuno-suppressive therapy -- Medications commonly prescribed for those who have undergone an organ transplant, or are suffering from rheumatoid arthritis, psoriasis, inflammatory bowel disease, or cancer

Injectable -- Able to be injected with a needle

PMMA (Polymethylmethacrylate) -- A non-degradable plastic material used for dozens of medical purposes over the last century

PMMA Microspheres – The tiny round and smooth particles that help provide the wrinkle correction of ArteFill

ArteFill logo

For more information and to locate an ArteFill-trained physician in your area, visit  
[www.artefill.com](http://www.artefill.com).

Artes Medical logo

5870 Pacific Center Blvd.  
San Diego, CA 92121  
United States of America  
888.ARTEFILL (278.3345)  
858.550.9999  
[info@artemedical.com](mailto:info@artemedical.com)  
[www.artemedical.com](http://www.artemedical.com)

Reference

ArteFill Instructions for Use. San Diego, CA; Artes Medical, Inc.; 2006.

©2006 Artes Medical, Inc.

Before and after photos are ArteFill patients.

7066REVxx