

Dermik Laboratories
A Division of Aventis Pharmaceuticals Inc.

SCULPTRA™
(injectable poly-L-lactic acid)

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

BEFORE USING PRODUCT, READ THE FOLLOWING INFORMATION THOROUGHLY.

DEVICE DESCRIPTION

SCULPTRA™ is an injectable implant that contains microparticles of poly-L-lactic acid, a biocompatible, biodegradable, synthetic polymer from the alpha-hydroxy-acid family. **SCULPTRA** is reconstituted prior to use by the addition of Sterile Water for Injection, USP (SWFI) to form a sterile non-pyrogenic suspension.

INTENDED USE / INDICATIONS

SCULPTRA is intended for restoration and/or correction of the signs of facial fat loss (lipoatrophy) in people with human immunodeficiency virus.

CONTRAINDICATIONS

- **SCULPTRA** should not be used in any person who has hypersensitivity to any of the components of the product.

WARNINGS

- Use of **SCULPTRA** in any person with active skin inflammation or infection in or near the treatment area should be deferred until the inflammatory or infectious process has been controlled.
- Do not overcorrect (overfill) a contour deficiency because the depression should gradually improve within several weeks as the treatment effect of **SCULPTRA** occurs (see **PATIENT TREATMENT**).
- Injection procedure reactions to **SCULPTRA** have been observed consisting mainly of hematoma, bruising, edema, discomfort, inflammation, and erythema. The most common device related adverse effect was the delayed occurrence of subcutaneous papules, which were confined to the injection site and were typically palpable, asymptomatic and non-visible. Refer to **ADVERSE EVENTS** for details.

- Special care should be taken to avoid injection into the blood vessels. An introduction into the vasculature may occlude the vessels and could cause infarction or embolism.

PRECAUTIONS

- **SCULPTRA** should only be used by health care providers with expertise in the correction of volume deficiencies in patients with human immunodeficiency virus after fully familiarizing themselves with the product, the product educational materials, and the entire package insert.
- **SCULPTRA** vials are for single patient use only. Do not reuse or resterilize the vial. Do not use if package or vial is opened or damaged.
- Long-term safety and effectiveness of **SCULPTRA** beyond two years have not been investigated. Dermik is conducting a post approval study to evaluate the safety and effectiveness of **SCULPTRA** beyond two years.
- **SCULPTRA** should be used in the deep dermis or subcutaneous layer. Avoid superficial injections. Special care must be taken when using **SCULPTRA** in areas of thin skin. Refer to **PATIENT TREATMENT** for instructions regarding injection techniques.
- Safety and effectiveness of treatment in the periorbital area have not been established.
- As with all transcutaneous procedures, **SCULPTRA** injection carries a risk of infection. Standard precautions associated with injectable materials should be followed.
- As with all injections, patients treated with anti-coagulants may run the risk of a hematoma or localized bleeding at the injection site.
- Universal precautions must be observed when there is a potential for contact with patient body fluids. The injection session must be conducted with aseptic technique.
- 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.
- The safety of **SCULPTRA** for use during pregnancy, in breastfeeding females or in patients under 18 years has not been established.
- No studies of interactions of **SCULPTRA** with drugs or other substances or implants have been made.
- The safety and effectiveness data from clinical trials of **SCULPTRA** in non-Caucasians and women with human immunodeficiency virus are limited. Dermik is conducting a post approval study in non-Caucasians and women with human immunodeficiency virus.

- The safety of using **SCULPTRA** in patients with increased susceptibility to keloid formation and hypertrophic scarring has not been studied. Dermik is conducting a post approval study to determine the likelihood of keloid formation and hypertrophic scars in patients with human immunodeficiency virus receiving **SCULPTRA** injections.
- The patient should be informed that he or she should minimize exposure of the treatment area to excessive sun and UV lamp exposure until any initial swelling and redness has resolved.

ADVERSE EVENTS

Adverse event data from four clinical studies that included 277 patients are summarized in Tables 1 & 2 below.

**TABLE 1:
NUMBER OF PATIENTS WITH TREATMENT-RELATED ADVERSE EVENTS OBSERVED IN
CLINICAL STUDIES WITH TWO-YEAR FOLLOW-UP**

	VEGA STUDY 50 Patients	C&W STUDY*** 29 Patients	AVERAGE DURATION (DAYS)
INJECTION PROCEDURE RELATED ADVERSE EVENTS			
Bruising	3 (6%)	11(38%)	6
Edema	2 (4%)	2 (7%)	3
Discomfort	0	3 (10%)	3
Hematoma	14 (28%)	0	17
Inflammation	0	3 (10%)	3
Erythema	0	3 (10%)	3
DEVICE-RELATED ADVERSE EVENTS			
			AVERAGE ONSET** (Months)
Injection site subcutaneous papule*	26 (52%)	9 (31%)	7

*Subcutaneous papules refer to lesions of 5 mm or less, typically palpable, asymptomatic and non-visible.

**Onset data available from VEGA study only. Duration not noted for subcutaneous papules because most were ongoing at study completion.

*** Safety data were collected *post hoc* for 27 of the patients at approximately two years from study start.

**TABLE 2:
NUMBER OF PATIENTS WITH TREATMENT-RELATED ADVERSE EVENTS OBSERVED IN
CLINICAL STUDIES WITH ONE-YEAR FOLLOW-UP**

	APEX 002 STUDY 99 Patients	BLUE PACIFIC STUDY 99 patients
INJECTION PROCEDURE RELATED ADVERSE EVENTS		
Bruising	1 (1%)	30 (30%)
Edema	3 (3%)	17 (17%)
Discomfort	19 (19%)	15 (15%)
Erythema	0	3 (3%)
DEVICE-RELATED ADVERSE EVENTS		
Injection site subcutaneous papule	6 (6%)	13 (13%)

The duration of the adverse events in Table 2 was not collected. The most common device related adverse effect was the delayed occurrence of subcutaneous papules, which were confined to the injection site and were typically palpable, asymptomatic, and non-visible. The study protocols did not include evaluation of treatment for subcutaneous papules, therefore, no information is available on how the papules were treated. In the VEGA study, the average onset of subcutaneous papules was 7 months after initial injection (range 0.3 – 25 months). Subcutaneous papules resolved spontaneously in 6/26 patients (24%) during the study. No information of onset and duration of papules is available from the Chelsea & Westminster study.

Treatment related adverse events, not included in Table 1 & 2, observed in clinical studies with a frequency of less than 5% were: injection site tenderness, injection site lesion, injection site bleeding, injection site induration, injection site infection and fever.

The following adverse events, which were not observed in the clinical studies, were detected from post-marketing surveillance outside of the US and literature reports, and may or may not be associated with the use of **SCULPTRA**: visible nodules with or without inflammation or dyspigmentation, malaise, injection site abscess, allergic reaction, injection site atrophy, Quincke's edema, injection site fat atrophy, photosensitive reaction, fatigue, injection site granuloma, hypersensitivity reaction, skin rash, skin roughness, lack of effectiveness, injection site reaction, hypertrophy of skin, hair breakage, colitis not otherwise specified, brittle nails, application site discharge, angioedema, aching joints, ectropion, and telangiectasias.

CLINICAL STUDIES

Clinical data including skin thickness measurements and serial photographs were collected in four clinical studies.

Vega Study

This was a 96-week, open-label, uncontrolled, single-center study to determine the treatment effects of **SCULPTRA** on the signs of lipoatrophy of the face in 50 patients infected with human immunodeficiency virus. Patients had a mean age of 45 years (range 33-58), 84% were Caucasian and 98% were male. All patients had little or no adipose tissue in cheek area at baseline, indicating severe facial lipoatrophy (mean adipose thickness of 0.5 ± 0.7 mm, ranging from 0.0 to 2.1 mm).

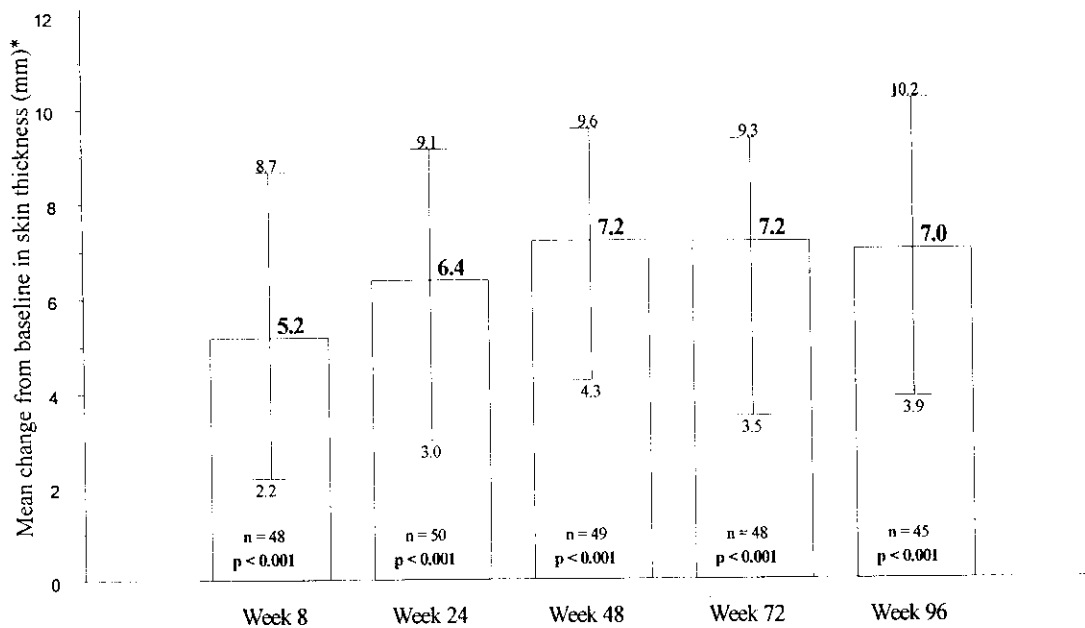
Treatment

Injection sessions were conducted at approximately two-week intervals, and the majority (86%) of the patients received four to five injection sessions. Generally, one vial of product was injected intradermally into multiple points of each cheek at each injection session. The quantity of injected product and number of injection sessions depended upon the severity of the facial depression.

Results

The mean increases from baseline in skin thickness are presented in Figure 1 below.

FIGURE 1: MEAN INCREASES ABOVE BASELINE IN SKIN THICKNESS (MM) OBSERVED IN THE VEGA STUDY



Bars represent maximum and minimum values; The p-value is based on the paired t-test.

* Baseline = 3.0 ± 0.6 mm

All patients experienced increases in skin thickness in the treatment area (minimum increase of 2.2 mm noted at Week 8 visit). Statistically significant increases above baseline values of mean skin thickness were noted at all time points (Weeks 8, 24, 48, 72 and 96) during the study. Increases in mean skin thickness changes above baseline persisted for up to 2 years.

Chelsea & Westminster (C&W) Study

This was a 24-week, open-label, single-center, uncontrolled study in 30 human immunodeficiency virus positive patients with facial lipoatrophy. Patients were placed into groups of 12 or 24 weeks of follow-up. Patients had a mean age of 41 (range 32-60), 72% were Caucasian and 93% were male.

Treatment

All patients received a fixed treatment regimen of three injection sessions conducted at two-week intervals. Each vial of SCULPTRA was reconstituted with 2 mLs of SWFI and 1 mL of 2% lidocaine to give a total volume of 3 mL. Up to 3 mL of the reconstituted product was injected bilaterally into multiple points into the cheek and nasolabial areas.

Results

Baseline skin thickness in the treatment areas ranged from 2.1 to 2.7 mm and are presented in the Table 3 below.

**TABLE 3:
RANGE OF MEAN INCREASES IN SKIN THICKNESS FROM BASELINE**

	12 WEEKS AFTER 1ST TREATMENT N=27*	24 WEEKS AFTER 1ST TREATMENT N=14*
Cheek Areas	3.9 – 5.7 mm	4.9 mm
Nasolabial Areas	3.9 – 6.0 mm	4.9 – 5.3 mm

Baselines ranged from 2.1 to 2.7 mm; all changes were significant (p<0.001).

* Number of patients varies dependent upon which group they were placed.

Significant changes from Baseline (p<0.001) in mean skin thickness were observed in the areas treated (left and right nasolabial and cheeks) with SCULPTRA in all patients. A mean increase in skin thickness of approximately 4-6 mm was observed twelve weeks after the initiation of treatment for all treated patients.

APEX 002 and Blue Pacific Studies

Data were obtained from two, single-center, open-label, 12-month investigator-initiated studies in human immunodeficiency virus positive patients with facial lipoatrophy. Ninety-nine patients

between 31 and 65 years of age were enrolled in each study. The majority of patients were Caucasian males.

Treatment

Patients were treated with **SCULPTRA** injections at an interval of approximately 3 to 6 weeks and received up to 6 injection sessions.

Results

The results from these studies are shown in Table 2 and were provided for safety information only.

INDIVIDUALIZATION OF TREATMENT (see also Patient Treatment)

The quantity of **SCULPTRA** and the number of injection sessions will vary by patient. Treatment for severe facial fat loss typically requires the injection of one vial of **SCULPTRA** per cheek area per injection session. A typical treatment course for severe facial fat loss involves 3-6 injection sessions, with the sessions separated by two or more weeks. Full effects of the treatment course are evident within weeks to months. The patient should be reevaluated no sooner than two weeks after each injection session to determine if additional correction is needed. Patients should be advised that supplemental injection sessions may be required to maintain an optimal treatment effect.

HOW SUPPLIED

SCULPTRA is supplied as a sterile freeze-dried preparation for injection in a clear glass vial, which is sealed by a penetrable stopper, covered by an aluminum seal with a flip-off cap. Each carton of **SCULPTRA** contains two vials.

COMPOSITION OF SCULPTRA

The final composition of **SCULPTRA** consists of poly-L-lactic acid, sodium carboxymethylcellulose (USP), non-pyrogenic mannitol (USP), sterile water for injection (USP).

NHRIC 8313-1106-02

INSTRUCTIONS FOR USE

Reconstitution

The following supplies are used with **SCULPTRA** but are to be provided by the end-user:

- Sterile Water for Injection (SWFI), USP
- Single-use 5 mL sterile syringe
- Single-use 1-3 mL (depending on physician/practitioner preference) sterile syringes (at least 2)
- 18 G sterile needles (at least 2)
- 26 G sterile needles (several should be available)
- Antiseptic

SCULPTRA is reconstituted in the following way:

1. Remove the flip-off cap from the vial and clean the penetrable stopper of the vial with an antiseptic. If the vial, seal, or flip-off cap are damaged, do not use, and call Aventis Pharmaceuticals Inc. at 1-800-633-1610.
2. Attach an 18 G sterile needle to a sterile single-use 5 mL syringe.
3. Draw 3-5 mLs of SWFI into the 5mL syringe.
4. Introduce the 18 G sterile needle into the stopper of the vial and slowly add all SWFI into the vial.
5. **Let the vial stand for at least 2 hours to ensure complete hydration; do not shake during this period.** **SCULPTRA** can be stored at room temperature up to 30°C (86°F) during and after hydration. Refrigeration is not required.
6. After waiting at least 2 hours, agitate the vial until a uniform translucent suspension is obtained. A single vial swirling agitator may be used. Product should be agitated immediately prior to use. The reconstituted product is usable within 72 hours of reconstitution. Discard any material remaining after use or after 72 hours following reconstitution.
7. Clean the penetrable stopper of the vial with an antiseptic, and use a new 18 G sterile needle to withdraw an appropriate amount of the suspension (typically 1 mL) into a single-use 1-3 mL sterile syringe. Do not store the reconstituted product in the syringe.
8. Replace the 18 G needle with a 26 G sterile needle before injecting the product into the deep dermis or subcutaneous layer. Do not inject **SCULPTRA** using needles of an internal diameter smaller than 26 G.
9. To withdraw remaining contents of the vial, repeat steps 6 through 8.

Patient Treatment

1. **Patient Assessment.** Before treatment with **SCULPTRA**, the patient should be informed completely of the indications, contraindications, warnings, precautions for use, possible side effects and mode of administration of **SCULPTRA**. A complete medical history should be taken to determine if the treatment is appropriate. Patients should be informed that more than one injection session is typically necessary to achieve the desired results.
2. **Patient Preparation.** As with all injectable products, universal precautions must be observed when there is a potential for contact with patient body fluids. The injection session must be conducted with aseptic technique.

3. **The needle for injections.** SCULPTRA should be injected using a 26 G sterile needle. Do not inject with needles smaller than 26 G and do not bend the needle. Agitate the product in the syringe as needed to maintain a uniform suspension throughout the procedure. Before injecting, expel some drops of the product from the prepared syringe with 26 G needle attached to eliminate air and to check for needle blockage. If the 26 G needle becomes occluded or dull during a injection session replacement may be necessary. Draw a small amount of air into the syringe between needle changes to assist in removing clogged particles.
4. **The dermal plane.** SCULPTRA should be injected into the deep dermis or subcutaneous layer. In order to control the injection depth of SCULPTRA, stretch/pull the skin opposite to the direction of the injection to create a firm injection surface. The 26 G sterile needle, bevel up, should be introduced into the skin at an angle of approximately 30-40 degrees, until the desired skin depth is reached. A change in tissue resistance is evident when the needle traverses the dermal-subcutaneous junction. If the needle is inserted at too shallow an angle [i.e., into the mid or superficial (papillary) dermis] the bevel of the needle may be visible through the skin. If product is injected too superficially it will be evident as immediate or slightly delayed blanching in the injected area. If this occurs, the needle should be removed and the treatment area gently massaged.
5. **Injecting: Threading or Tunneling**
 - a. **Technique.** When the appropriate dermal plane is reached, the needle angle should be lowered to advance the needle in that dermal plane. Prior to depositing SCULPTRA in the skin, a reflux maneuver should be performed to assure that a blood vessel has not been entered. Using the threading or tunneling technique, a thin trail of SCULPTRA should then be deposited in the tissue plane as the needle is withdrawn. To avoid deposition in the superficial skin, deposition should be stopped before the needle bevel is visible in the skin.
 - b. **Volume per injection.** The volume of SCULPTRA should be limited to approximately 0.1 mL – 0.2 mL per each individual injection. Note that in areas such as the cheek, approximately 20 injections may be required to cover the targeted area.
 - c. **Volume per treatment area.** The volume of product injected per treatment area will vary depending on the surface area to be treated. Treatment of an entire cheek typically requires injection of one vial of SCULPTRA per cheek per injection session. Multiple injections (typically administered in a grid or cross-hatched pattern) may be required to cover the targeted area. The total number of injections and thus total volume of SCULPTRA injected will vary based on the surface area to be corrected, not on the depth or severity of the deficiency to be corrected.

6. **Injecting: Depot**

- a. **Technique**. The depot technique is most appropriate for injections into areas of thin skin at the level of the upper zygoma or temples. When using this technique, **SCULPTRA** is injected as a small bolus. For the upper zygoma it is injected under the orbicularis oculimuscle. For the temples, it is injected in the temporal fascia.
 - b. **Volume per injection**. The volume of **SCULPTRA** should be reduced to approximately 0.05 mL/injection. Following each injection, the area should be massaged.
7. **Massage during the injection session**. The treatment areas should be periodically massaged during the injection session to evenly distribute the product.
8. **Degree of correction**. The depressed area should never be overcorrected (overfilled) in an injection session. Limited correction of the treatment area allows for the gradual improvement of the depressed area over several weeks as the treatment effect occurs. Typically, patients will experience some degree of edema associated with the injection procedure itself, which will give the appearance of a full correction by the end of the injection session (within about 30 minutes). The patient should be informed that the injection-related edema typically resolves in several hours to a few days, resulting in the ‘reappearance’ of the original contour deficiency.
9. **Post-treatment care**. Immediately following an injection session with **SCULPTRA**, redness, swelling, and/or bruising may be noted in the treatment area. Refer to **ADVERSE EVENTS** for details. After the injection session, an ice pack (avoiding any direct contact of the ice with the skin) should be applied to the treatment area in order to reduce swelling. It is important to thoroughly massage the treatment area to evenly distribute the product. The patient should periodically massage the treatment area for several days after the injection session to promote a natural-looking correction.
10. **Treat, Wait, Assess**. During the first injection session with **SCULPTRA**, only a limited correction should be made. Do not overcorrect (overfill). The patient should be evaluated no sooner than two weeks after the injection session to determine if additional correction is needed. The original skin depression may initially reappear, but the depression should gradually improve within several weeks as the treatment effect of **SCULPTRA** occurs. The patient should be advised of the potential need for additional injection sessions at the first consultation.

PATIENT INSTRUCTIONS

It is recommended that the following information be shared with patients:

- To report any adverse reactions, call Aventis Pharmaceuticals Inc. at 1-800-633-1610.
- Within the first 24 hours, an ice pack (avoiding any direct contact of the ice with the skin) should be applied to the treatment area to reduce swelling. **SCULPTRA** may cause

redness, swelling, or bruising when first injected into the skin, typically resolving in hours to one week. Hematoma may also occur, typically resolving in hours to about two weeks. Worsening or prolonged symptoms or signs should be reported to the health care provider. The original skin depression may initially reappear, but the depression should gradually improve within several weeks as the treatment effect of **SCULPTRA** occurs. The health care provider will assess the need for additional **SCULPTRA** injection sessions after two or more weeks.

- Massage the treatment area daily, for several days following any injection session.
- Treatment with **SCULPTRA** can result in small papules in the treatment area. These subcutaneous papules are typically not visible and asymptomatic and may be noticed only upon pressing on the treatment area. However, visible nodules, sometimes with redness or color change to the skin, have been reported. Patients should report any side effects to their health care provider.
- Make-up may be applied a few hours post-treatment if no complications are present (e.g. open wounds, bleeding, redness and swelling).
- Patients should minimize exposure of the treatment area to excessive sun and UV lamp exposure until any initial swelling and redness has resolved.

STORAGE

SCULPTRA can be stored at room temperature, up to 30°C (86°F). **DO NOT FREEZE.**

Refrigeration is not required.

STERILITY

Each vial of **SCULPTRA** is packaged for single-use only. Do not resterilize.

IF THE VIAL, SEAL, OR THE FLIP-OFF CAP ARE DAMAGED, DO NOT USE AND CONTACT AVENTIS PHARMACEUTICALS INC. AT 1-800-633-1610.

Rx only.

ANY SIDE EFFECTS OR PRODUCT COMPLAINTS SHOULD BE REPORTED TO:

Aventis Pharmaceuticals Inc.

Bridgewater, NJ USA

1-800-633-1610

Pat. No. US 6,716,251

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