

## **COSMODERM™/COSMOPLAST™ COLLAGEN REPLACEMENT THERAPY®**

CosmoDerm and CosmoPlast are dermal fillers approved for the correction of facial wrinkles, acne scars and other soft tissue contour deficiencies, as well as for the restoration of the lip border. The collagen in CosmoDerm/CosmoPlast is purified from human dermal tissue that is grown under controlled conditions. Based on a clinical study conducted by Inamed Aesthetics, a pre-treatment skin test is not required. All medical procedures are subject to certain risks. Although treatments with CosmoDerm/CosmoPlast have been found to be a safe, non-surgical option for many skin contour problems, you should be aware of the safety issues and restrictions associated with their use. Although you should review these points with your physician, we have summarized them as follows:

CosmoDerm/CosmoPlast collagen implants must not be used in people with a history of serious allergic (anaphylactic) reactions or a known allergy to lidocaine (a local anesthetic). Though unlikely, it is possible for the needle to be accidentally placed through a blood vessel during injection, which could result in temporary discoloration of the treated area, or in tissue death leading to a scab and/or scar formation. Injectable collagen, like other substances that are injected, could be accidentally injected into a blood vessel. Although this possibility is remote, it could result in a blockage of the blood flow and loss of circulation in nearby areas. Blood flow blockage resulting in permanent loss of vision in one eye has been reported once since bovine product introduction in 1981. Local necrosis (tissue damage) is a rare event, which has been observed following bovine collagen implantation. Most necroses reported through post-marketing surveillance of bovine dermal collagen have occurred after injection into the glabellar region of the face (between the eyebrows).

Some physicians have reported the occurrence of connective tissue diseases such as rheumatoid arthritis, systemic lupus erythematosus, polymyositis (PM), and dermatomyositis (DM) after bovine collagen injections in people with no previous history of these disorders. Conflicting studies have been published in scientific journals regarding the association between PM/DM and injectable bovine collagen. A connection between bovine collagen injections and the onset of PM/DM, or the other connective tissue diseases listed, has not been established. The frequency and degree of such reactions after human collagen injections have not been determined.

An increased frequency of the potential to develop an allergic response to various collagens has been found in people with systemic connective tissue diseases, such as rheumatoid arthritis, juvenile rheumatoid arthritis, and progressive systemic sclerosis (scleroderma). A person with any one of these diseases may thus have an increased risk of experiencing an allergic response to the collagen injection. Additionally, one might notice that the effect of the collagen treatment might not last as long. The frequency and severity of such reactions with human collagen injections has not been determined.

Based on experience with bovine collagen implants, use of CosmoDerm 1 should be limited to 30 mL over a 1-year period. Use of CosmoDerm 2 should be limited to 15 mL over a 1-year period. Likewise, the use of CosmoPlast should also be limited to 30 mL over a 1-year period. The combination of CosmoDerm 1 and CosmoDerm 2, or of CosmoDerm in conjunction with CosmoPlast should be limited to 30 mL over a 1-year period. Safety of injecting greater amounts on an annual basis has not been established.

The safety of CosmoDerm/CosmoPlast use in people with a known allergy to bovine collagen has not been studied. Injectable collagen should be used with caution in people who have asthma, hay fever, eczema, or have a history of multiple allergies. People with these conditions may have a greater potential for exhibiting an allergic reaction. As with all procedures involving an injection, CosmoDerm/CosmoPlast collagen implantation carries a risk of infection. Also, previous facial herpes simplex at the site of injection may recur if aggravated by the injection. Active inflammatory skin conditions (e.g., cysts, pimples, rashes, or hives), or in areas where infection is present, require that treatment is postponed until the skin condition is under control. The safety of treatment during pregnancy or in infants and children has not been studied. CosmoDerm/CosmoPlast should be used with caution if you are taking medication that affects your immune system. If you are using substances that reduce blood clotting, such as aspirin or ibuprofen, you may, as with any injection, experience increased bruising or bleeding at injection sites. The safety and effectiveness of CosmoDerm/CosmoPlast implantation for use in lip augmentation has not been established.

There have been infrequent reports of the injected collagen being visible in the skin, in the form of a small raised or white area at the treatment site. This may persist from a few weeks to several months. Also, some areas (e.g., compressed scars) may resist precise placement of the material, which can result in a slight elevation beside the defect. Temporary puffiness around the treatment site should be expected, especially with CosmoDerm implant. You may also notice temporary blushing, slight bruising, and tenderness around the site with the use of either CosmoDerm or CosmoPlast. This should resolve in a few days. Any redness and/or visible swelling that persists for more than a few days should be brought to the attention of your physician.

In a study to evaluate any potential allergic responses to CosmoDerm/CosmoPlast, 428 patients were injected with CosmoDerm 1 into the forearm and followed for 2 months. Reported adverse events with >2 occurrences are as follows: Cold symptoms (4.1%); Flu-like symptoms (2.0%); Urinary tract infections (1.0%). Each of the following was reported 0.7% of the time: bronchitis, strep throat, sinus infection; acid dyspepsia or reflux, back ache/pain/spasm, ear infection, fevers, high blood pressure, insomnia, and sore throat were each reported 0.5% of the time. One subject reported redness and pain one week after the first injection. This was confirmed by the investigator as redness, tenderness, firmness and swelling at the injection site. These symptoms spontaneously resolved after 10 days without treatment or further sequelae. Further testing suggested that these symptoms were not an allergic response to the implant.

Touch-up injections are usually needed to maintain optimal correction. Because both CosmoDerm/CosmoPlast collagen are similar to other components of your skin, they will be altered by the same ongoing mechanical forces such as smiling or other muscle activity and biochemical processes (e.g., aging and active acne) that caused the original skin depressions. Based on clinical experience with bovine collagen, it has been reported that the body may deposit its own collagen at the site of collagen implantation. You should also note that inadequate correction/duration of correction, lumpiness, and other unsatisfactory results have been reported with bovine collagen.

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