

OP-1 PUTTY PACKAGE INSERT

HUMANITARIAN DEVICE. OP-1 Putty is authorized by Federal law for use as an alternative to autograft in compromised patients requiring revision posterolateral (intertransverse) lumbar spinal fusion, for whom autologous bone and bone marrow harvest are not feasible or are not expected to promote fusion. Examples of compromising factors include osteoporosis, smoking and diabetes. The effectiveness of OP-1 Putty for this use has not been demonstrated.

PRODUCT DESCRIPTION:

OP-1 Putty is an osteoinductive and osteoconductive bone graft material. OP-1 Putty consists of the recombinant human Osteogenic Protein (rhOP-1), Type 1 Bovine Bone Collagen Matrix (collagen matrix) and the Putty Additive carboxymethylcellulose sodium (CMC). OP-1 Putty is intended to be reconstituted with sterile saline (0.9%) solution.

OP-1 Putty is provided as two components:

- A large vial containing one gram sterile dry powder consisting of bovine collagen and OP-1.
- A small vial containing the Putty Additive (230 mg) consisting of a sterile dry powder comprised of carboxymethylcellulose (CMC).

Both components must be combined with sterile saline to produce the product.

STORAGE CONDITIONS:

Store OP-1 Putty at 2-8 °C.

SYMBOLS:



ATTENTION, SEE INSTRUCTIONS FOR USE



DO NOT REUSE



USE BY

R ONLY

CAUTION: Federal law restricts this device to sale by or on the order of a physician

REF

CATALOGUE NUMBER



LOT NUMBER



STERILE BY IRRADIATION

INDICATIONS:

OP-1 Putty is indicated for use as an alternative to autograft in compromised patients requiring revision posterolateral (intertransverse) lumbar spinal fusion, for whom autologous bone and bone marrow harvest are not feasible or are not expected to promote fusion. Examples of compromising factors include osteoporosis, smoking and diabetes.

CONTRAINDICATIONS:

- OP-1 Putty should not be used to treat patients who have a known hypersensitivity to any of the components of the product.
- OP-1 Putty should not be applied at or near the vicinity of a resected tumor or in patients with a history of malignancy.
- OP-1 Putty should not be administered to patients who are skeletally immature (<18 years of age or no radiographic evidence of closure of epiphyses).
- OP-1 Putty should not be administered to pregnant women. The potential effects of OP-1 treatment on the human fetus have not been evaluated. Studies in rats injected with high doses of OP-1 have shown that small amounts of OP-1 will cross the placental barrier.

WARNINGS:

- Women of childbearing potential should be advised that antibody formation to OP-1 and its influence on fetal development have not been assessed in recent studies. Antibodies to OP-1 were measured at pretreatment and 6 weeks and 6 months post treatment. Antibodies were detected in 23 out of 24 (96%) patients treated with OP-1 Putty. No antibodies were detected in patients treated with autograft. Neutralizing antibodies were detected in 7/24 (29%) patients treated with OP-1 Putty. For six out of the seven patients, neutralizing activity was detected at 6 weeks post treatment, but not at 6 months post treatment. For the seventh patient, neutralizing activity was detected only at 6 months post treatment. The clinical significance of these antibodies is not known. The effect of maternal antibodies to OP-1 on the unborn fetus is unknown, both when the antibodies are detected during the first year following treatment and later, when the antibodies may not be detectable. Studies in genetically altered mice indicate that OP-1 is critical for fetal development and that lack of OP-1 activity, as might be induced by antibody, may cause neonatal death or birth defects.
- Women of childbearing potential should be advised to avoid becoming pregnant for one year following treatment with OP-1 Putty.

- The maximum human dose should not exceed 2 vials.
- Localized ectopic or heterotopic bone formation may occur outside of the treatment site.
- OP-1 Putty has no biomechanical strength.

PRECAUTIONS:

- Clinical studies using OP-1 Putty were performed in patients requiring a primary spinal fusion. Except for an animal study evaluating the effect of OP-1 on revision spinal fusion surgery in the presence of nicotine, no data have been collected on the use of OP-1 Putty for revision spinal fusion surgery in compromised patients, *i.e.*, those who are smokers or have diabetes or osteoporosis.
- The safety or probable benefit of OP-1 Putty in patients with autoimmune disease has not been demonstrated.
- The effect of radiation therapy, chemotherapy, immunosuppressive or steroid therapy on the probable benefit of OP-1 Putty is not known.
- There are no data on the excretion of OP-1 in the breast milk of female patients who are nursing.
- OP-1 is important in the development of the kidney. Studies have not been performed to examine the effect of neutralizing antibodies to OP-1 in patients with impaired renal function.
- IMMUNOGENICITY: As with all therapeutic proteins, there is a potential for immune responses to be generated against components of the OP-1 Putty. In the degenerative spondylolisthesis pilot study, antibodies to OP-1 were measured at pretreatment and 6 weeks and 6 months post treatment. Antibodies were detected in 23 out of 24 (96%) patients treated with OP-1 Putty. No antibodies were detected in patients treated with autograft. Neutralizing antibodies were detected in 7/24 (29%) patients treated with OP-1 Putty. For six out of the seven patients, neutralizing activity was detected at 6 weeks post treatment, but not at 6 months post treatment. For the seventh patient, neutralizing activity was detected only at 6 months post treatment. The clinical significance of these antibodies is not known. The incidence of antibody detection is highly dependent on the sensitivity and specificity of the assay. Additionally, the incidence of antibody detection may be influenced by several factors including sample handling, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to OP-1 Putty with the incidence of antibodies to other products may be misleading.
- A two year rat bioassay, in which approximately 17.5-70 times the equivalent maximum human dose of 2 vials of OP-1 Implant, a component of OP-1 Putty, was placed under the skin, produced more cancer growths at the site of implantation of the OP-1 compared to rats that had no OP-1. It is believed that this may be due to the Oppenheimer Solid State Tumor Effect, the formation of tumors at the site of implantation of inert objects under the skin in rats. This effect has not been reported in humans. Additional studies are ongoing to examine the effect of OP-1 on the growth of pre-existing tumors.
- Take care to ensure that OP-1 Putty will be contained by viable tissue. Obtain adequate hemostasis before implanting OP-1 Putty to prevent the product from being displaced.
- Inadequate vascularity in the surrounding tissues may diminish the probable benefit of OP-1 Putty. Make every effort to surround the product with viable tissue.
- For single use only. Do not re-use OP-1 Putty. Discard unused product and use a new device for subsequent applications.
- Prior to use, inspect the packaging, vial and stopper for visible damage. If damage is visible, don't use the product. Retain the packaging and vial, and contact a Stryker Biotech representative.
- Do not use after the printed expiration date on the label.

ADVERSE EVENTS:

The following table was compiled from multi-center pilot and pivotal studies of OP-1 Putty in patients with degenerative spondylolisthesis requiring primary fusion of the affected spinal level. This table contains all of the reported events for the two groups that were reported to the studies as of October 17, 2003.

**Summary of Adverse Events for All Patients
in the Pilot and Pivotal Posterolateral Spinal Fusion Studies**

Body System	OP-1 (n=228)	Autograft (n=98)
Abnormal lab values	6 (3%)	8 (8%)
Blood and lymphatic system disorders	8 (4%)	14 (14%)
Cardiac disorders	9 (4%)	1 (1%)
Ear and labyrinth disorders	2 (1%)	1 (1%)
Eye disorders	2 (1%)	0 (0%)
Gastrointestinal disorders	30 (13%)	10 (10%)
General disorders and administration site condition	36 (16%)	18 (18%)
Immune system disorders	2 (1%)	2 (2%)
Infections and infestations	18 (8%)	8 (8%)
Injury, poisoning and procedural complications	44 (19%)	23 (24%)
Metabolism and nutrition disorders	6 (3%)	1 (1%)
Musculoskeletal and connective tissue disorders - other	50 (22%)	23 (24%)
Musculoskeletal and connective tissue disorders - joint inflammation	24 (11%)	6 (6%)
Musculoskeletal and connective tissue disorders - pseudarthrosis	12 (5%)	3 (3%)
Neoplasms benign, malignant and unspecified	2 (1%)	2 (2%)
Nervous system disorders - other	26 (11%)	10 (10%)
Nervous system disorders - TIA	4 (2%)	0 (0%)
Psychiatric system disorders	10 (4%)	3 (3%)
Renal and urinary disorders	13 (6%)	9 (9%)
Reproductive system and breast disorders	1 (0.4%)	1 (1%)
Respiratory, thoracic and mediastinal disorders	15 (7%)	4 (4%)
Skin and subcutaneous tissue disorders - other	8 (4%)	1 (1%)
Skin and subcutaneous tissue disorders - wound infection	15 (7%)	2 (2%)
Social Circumstances	1 (0.4%)	0 (0%)
Surgical and Medical Procedures	2 (1%)	0 (0%)
Vascular Disorders	17 (8%)	10 (10%)

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