

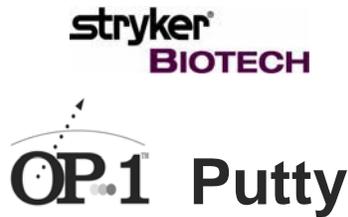
Section VII

Labeling

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CAUTION: Federal (USA) law restricts this device to sale by or on the order of a physician with appropriate training.

Description

OP-1[®] Putty is an osteoinductive and osteoconductive bone graft material. OP-1[®] Putty is supplied in two glass vials containing sterile powders for reconstitution:

- A large vial containing 1 g of powder comprised of 3.5 mg recombinant human Osteogenic Protein-1 (OP-1) in bovine bone type I collagen;
- A small vial containing 230 mg of carboxymethylcellulose sodium (CMC putty additive).

OP-1, the active substance, is also known as recombinant human Bone Morphogenetic Protein-7 (rhBMP-7), or eptoterminal alfa. It is an osteoinductive protein produced by a genetically engineered cell line. OP-1 is a dimeric protein consisting of two mature monomers linked via an interchain disulfide bond. The molecular weight ranges from 30 to 46 kDa, representing species with differing degrees of glycosylation and N-terminal truncation. The collagen matrix is osteoconductive and acts as a bioresorbable scaffold for anchorage-dependent cell proliferation and differentiation processes induced by the active substance. OP-1[®] Putty must be mixed and reconstituted with sterile saline according to the **Product Preparation Instructions**. The CMC putty additive imparts a consistency to the product which aids surgical implantation.

Indications

OP-1[®] Putty is indicated for posterolateral lumbar spinal fusion in patients with spondylolisthesis who have failed at least six months of conservative non-surgical treatment.

Contraindications

OP-1[®] Putty should not be used in patients with the following:

- A known hypersensitivity to rhBMP-7, bovine Type I collagen or carboxymethylcellulose;
- Active infection at the operative site or history of reoccurring infections;
- Active malignancy or in patients undergoing treatment for a malignancy;
- Pregnancy. 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 a clinical study assessing the safety and efficacy of OP-1[®] Putty, 194 out of 207 (94%) patients treated with OP-1[®] Putty and 18 out of 86 (21%) treated with autograft bone developed antibodies to rhBMP-7. Within the OP-1[®] Putty treatment group, 26% of the patients produced antibodies with neutralizing capacity versus 1% in the autograft group. The peak antibody response was seen 3 months following treatment. There were no patients with neutralizing antibodies 2 years following treatment. Studies in genetically altered mice indicate that BMP-7 is critical for fetal development and that lack of BMP activity, as might be induced by antibodies, may cause neonatal death or birth defects.
- Women of childbearing potential should be advised not to become pregnant for 2 years following treatment with OP-1 Putty.
- There are no data on the excretion of OP-1 in the breast milk of female patients who are nursing. Women should discontinue breast-feeding following treatment with OP-1[®] Putty.

Precautions

- One unit of OP-1[®] Putty must be used on each side of the spine. The maximum dose should not exceed 2 units.
- OP-1[®] Putty has no biomechanical strength.
- The safety and effectiveness of repeat applications have not been established.
- OP-1[®] Putty should be used with caution in patients with a history of underlying cardiac disease or with a predisposition to infectious conditions; close follow-up post-operatively is advised for these conditions.
- A two year rat bioassay, in which approximately 17.5-70 times the equivalent human dose of OP-1 in collagen 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, described as 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.
- OP-1 is important in the embryonic 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.
- Inadequate vascularity in the surrounding tissues may diminish the effectiveness of OP-1[®] Putty. Make every effort to surround the product with viable tissue.
- 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.
- For single use only. Do not re-use OP-1[®] Putty. Discard unused product.

- Do not use after the printed expiration date on the label.

Adverse Events

The safety of OP-1[®] Putty in spinal fusion patients was evaluated in two controlled clinical trials, a pilot study (S99-01US) and a pivotal study (S01-01US). See **Clinical Trial Results** section for descriptions of the studies. Adverse event data from the safety populations for both studies are presented in the following table.

Table 1: Treatment Emergent Adverse Events

Pivotal Study S01-01US: Treatment Emergent Adverse Events Reported in ≥ 1% of Patients

| System Organ Class/Preferred Term | OP-1 [®] Putty (N=208) | Autograft (N=87) |
|---|---------------------------------|------------------|
| Total | 201 (96.6) | 82 (94.3) |
| Blood and lymphatic system disorders | | |
| Anaemia | 10 (4.8) | 12 (13.8) |
| Anaemia postoperative | 0 (0.0) | 1 (1.1) |
| Thrombocytopenia | 0 (0.0) | 1 (1.1) |
| Cardiac disorders | | |
| Acute coronary syndrome | 2 (1.0) | 0 (0.0) |
| Atrial fibrillation | 5 (2.4) | 0 (0.0) |
| Cardiac failure congestive | 3 (1.4) | 0 (0.0) |
| Chest pain | 7 (3.4) | 3 (3.4) |
| Coronary artery disease | 2 (1.0) | 0 (0.0) |
| Myocardial infarction | 5 (2.4) | 1 (1.1) |
| Supraventricular tachycardia | 0 (0.0) | 1 (1.1) |
| Tachycardia | 3 (1.4) | 0 (0.0) |
| Ear and labyrinth disorders | | |
| Tinnitus | 1 (0.5) | 1 (1.1) |
| Vertigo | 3 (1.4) | 0 (0.0) |
| Eye disorders | | |
| Cataract | 2 (1.0) | 0 (0.0) |
| Conjunctival haemorrhage | 0 (0.0) | 1 (1.1) |
| Diplopia | 0 (0.0) | 1 (1.1) |
| Eye pruritus | 0 (0.0) | 1 (1.1) |
| Gastrointestinal disorders | | |
| Abdominal discomfort | 0 (0.0) | 1 (1.1) |
| Abdominal pain | 3 (1.4) | 0 (0.0) |
| Colitis | 1 (0.5) | 1 (1.1) |
| Colitis ischaemic | 0 (0.0) | 1 (1.1) |
| Constipation | 9 (4.3) | 3 (3.4) |
| Diarrhoea | 6 (2.9) | 0 (0.0) |
| Diverticulitis | 2 (1.0) | 0 (0.0) |
| Gastric ulcer | 2 (1.0) | 0 (0.0) |
| Gastroenteritis viral | 2 (1.0) | 0 (0.0) |
| Gastrointestinal haemorrhage | 2 (1.0) | 0 (0.0) |
| Gastrooesophageal reflux disease | 3 (1.4) | 1 (1.1) |
| Ileus | 3 (1.4) | 0 (0.0) |
| Nausea | 10 (4.8) | 3 (3.4) |
| Oesophagitis | 0 (0.0) | 1 (1.1) |

| System Organ Class/Preferred Term | OP-1[®] Putty (N=208) | Autograft (N=87) |
|---|---------------------------------------|-------------------------|
| Pancreatitis | 2 (1.0) | 0 (0.0) |
| Small intestinal obstruction | 0 (0.0) | 1 (1.1) |
| Vomiting | 5 (2.4) | 0 (0.0) |
| General disorders and administration site conditions | | |
| Adverse drug reaction | 2 (1.0) | 0 (0.0) |
| Asthenia | 4 (1.9) | 4 (4.6) |
| Chest pain | 2 (0.0) | 1 (1.1) |
| Discomfort | 0 (0.0) | 1 (1.1) |
| Fatigue | 3 (1.4) | 0 (0.0) |
| Hernia | 0 (0.0) | 1 (1.1) |
| Localised oedema | 0 (0.0) | 1 (1.1) |
| Oedema | 0 (0.0) | 1 (1.1) |
| Oedema peripheral | 5 (2.4) | 3 (3.4) |
| Pain | 2 (0.0) | 1 (1.1) |
| Pyrexia | 9 (4.3) | 4 (4.6) |
| Tenderness | 0 (0.0) | 1 (1.1) |
| Hepatobiliary disorders | | |
| Cholecystitis | 0 (0.0) | 1 (1.1) |
| Immune system disorders | | |
| Drug hypersensitivity | 2 (0.0) | 2 (2.3) |
| Infections and infestations | | |
| Bone infection | 0 (0.0) | 1 (1.1) |
| Cellulitis | 2 (0.0) | 3 (3.4) |
| Clostridium colitis | 4 (1.9) | 0 (0.0) |
| Ear infection | 2 (1.0) | 0 (0.0) |
| Herpes zoster | 6 (2.9) | 1 (1.1) |
| Infection | 12 (5.8) | 5 (5.7) |
| Labyrinthitis | 0 (0.0) | 1 (1.1) |
| Pneumonia | 6 (2.9) | 1 (1.1) |
| Sinusitis | 5 (2.4) | 1 (1.1) |
| Stitch abscess | 0 (0.0) | 1 (1.1) |
| Urinary tract infection | 11 (5.3) | 3 (3.4) |
| Viral infection | 1 (0.5) | 1 (1.1) |
| Injury, poisoning and procedural complications | | |
| Back injury | 3 (1.4) | 1 (1.1) |
| Cerebrospinal fluid leakage | 1 (0.5) | 1 (1.1) |
| Compression fracture | 2 (0.0) | 1 (1.1) |
| Donor site complication | 0 (0.0) | 8 (9.2) |
| Dural tear | 16 (7.7) | 7 (8.0) |
| Fall | 12 (5.8) | 8 (9.2) |
| Foot fracture | 3 (1.4) | 0 (0.0) |
| Hand fracture | 2 (1.0) | 0 (0.0) |
| Incision site complication | 0 (0.0) | 1 (1.1) |
| Injury | 2 (0.0) | 1 (1.1) |
| Joint dislocation | 0 (0.0) | 1 (1.1) |
| Limb injury | 0 (0.0) | 1 (1.1) |
| Lower limb fracture | 0 (0.0) | 1 (1.1) |
| Lumbar vertebral fracture | 3 (1.4) | 0 (0.0) |
| Meniscus lesion | 4 (1.9) | 1 (1.1) |
| Muscle strain | 0 (0.0) | 1 (1.1) |
| Nerve injury | 0 (0.0) | 1 (1.1) |
| Nerve root injury | 0 (0.0) | 1 (1.1) |
| Operative haemorrhage | 2 (0.0) | 1 (1.1) |

| System Organ Class/Preferred Term | OP-1[®] Putty (N=208) | Autograft (N=87) |
|--|---------------------------------------|-------------------------|
| Pelvic fracture | 0 (0.0) | 1 (1.1) |
| Post procedural complication | 3 (1.4) | 0 (0.0) |
| Postoperative heterotopic calcification | 3 (1.4) | 0 (0.0) |
| Procedural site reaction | 0 (0.0) | 1 (1.1) |
| Road traffic accident | 3 (1.4) | 1 (1.1) |
| Seroma | 2 (1.0) | 0 (0.0) |
| Spinal compression fracture | 4 (1.9) | 1 (1.1) |
| Spinal fracture | 0 (0.0) | 1 (1.1) |
| Stress fracture | 0 (0.0) | 1 (1.1) |
| Tibia fracture | 0 (0.0) | 1 (1.1) |
| Wound complication | 0 (0.0) | 1 (1.1) |
| Wound dehiscence | 3 (1.4) | 1 (1.1) |
| Wound secretion | 3 (1.4) | 3 (3.4) |
| Wrist fracture | 2 (1.0) | 0 (0.0) |
| Investigations | | |
| Alanine aminotransferase increased | 0 (0.0) | 1 (1.1) |
| Arterial bruit | 0 (0.0) | 1 (1.1) |
| Blood glucose increased | 2 (1.0) | 0 (0.0) |
| Blood potassium abnormal | 0 (0.0) | 1 (1.1) |
| Blood potassium increased | 0 (0.0) | 1 (1.1) |
| Blood pressure abnormal | 0 (0.0) | 1 (1.1) |
| Blood pressure decreased | 0 (0.0) | 1 (1.1) |
| Blood pressure increased | 1 (0.5) | 1 (1.1) |
| Electrocardiogram ST segment depression | 0 (0.0) | 1 (1.1) |
| Haematocrit decreased | 0 (0.0) | 3 (3.4) |
| Haemoglobin decreased | 2 (0.0) | 1 (1.1) |
| Weight decreased | 1 (0.5) | 1 (1.1) |
| White blood cell count increased | 0 (0.0) | 2 (2.3) |
| Metabolism and nutrition disorders | | |
| Cachexia | 0 (0.0) | 1 (1.1) |
| Dehydration | 3 (1.4) | 0 (0.0) |
| Diabetes mellitus non-insulin-dependent | 1 (0.5) | 1 (1.1) |
| Gout | 0 (0.0) | 1 (1.1) |
| Hypercholesterolemia | 2 (1.0) | 0 (0.0) |
| Hyperglycaemia | 1 (0.5) | 1 (1.1) |
| Hyperkalaemia | 0 (0.0) | 1 (1.1) |
| Hypokalemia | 2 (1.0) | 0 (0.0) |
| Hyponatraemia | 1 (0.5) | 1 (1.1) |
| Musculoskeletal and connective tissue disorders | | |
| Arthralgia | 39 (18.8) | 19 (21.8) |
| Arthritis | 9 (4.3) | 1 (1.1) |
| Arthropathy | 2 (0.0) | 1 (1.1) |
| Atlantoaxial instability | 3 (1.4) | 1 (1.1) |
| Back disorder | 0 (0.0) | 1 (1.1) |
| Back pain | 42 (20.2) | 21 (24.1) |
| Bunion | 0 (0.0) | 1 (1.1) |
| Bursitis | 14 (6.7) | 6 (6.9) |
| Buttock pain | 10 (4.8) | 1 (1.1) |
| Cervical spinal stenosis | 1 (0.5) | 1 (1.1) |
| Foot deformity | 0 (0.0) | 1 (1.1) |
| Fracture delayed union | 1 (0.5) | 2 (2.3) |
| Groin pain | 6 (2.9) | 2 (2.3) |

| System Organ Class/Preferred Term | OP-1[®] Putty (N=208) | Autograft (N=87) |
|--|---------------------------------------|-------------------------|
| Impingement syndrome | 0 (0.0) | 1 (1.1) |
| Intervertebral disc degeneration | 5 (2.4) | 2 (2.3) |
| Intervertebral disc disorder | 3 (1.4) | 2 (2.3) |
| Intervertebral disc protrusion | 4 (1.9) | 1 (1.1) |
| Limb discomfort | 2 (0.0) | 1 (1.1) |
| Lumbar spinal stenosis | 10 (4.8) | 1 (1.1) |
| Muscle disorder | 0 (0.0) | 1 (1.1) |
| Muscle spasms | 8 (3.8) | 3 (3.4) |
| Musculoskeletal discomfort | 3 (1.4) | 1 (1.1) |
| Musculoskeletal stiffness | 1 (0.5) | 1 (1.1) |
| Neck pain | 7 (3.4) | 3 (3.4) |
| Osteoarthritis | 14 (6.7) | 3 (3.4) |
| Pain in extremity | 52 (25.0) | 20 (23.0) |
| Pseudarthrosis | 23 (11.1) | 10 (11.5) |
| Rotator cuff syndrome | 1 (0.5) | 3 (3.4) |
| Shoulder pain | 8 (3.8) | 4 (4.6) |
| Spinal osteoarthritis | 2 (1.0) | 0 (0.0) |
| Spondylolisthesis | 1 (0.5) | 1 (1.1) |
| Spondylolisthesis acquired | 0 (0.0) | 2 (2.3) |
| Synovial cyst | 1 (0.5) | 2 (2.3) |
| Tendon disorder | 2 (1.0) | 0 (0.0) |
| Tendonitis | 2 (0.0) | 1 (1.1) |
| Vertebral column mass | 0 (0.0) | 1 (1.1) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | |
| Benign neoplasm | 1 (0.5) | 1 (1.1) |
| Cerebral haemangioma | 0 (0.0) | 1 (1.1) |
| Endometrial cancer metastatic | 0 (0.0) | 1 (1.1) |
| Hepatic mass | 0 (0.0) | 1 (1.1) |
| Lung neoplasm | 0 (0.0) | 1 (1.1) |
| Lung neoplasm malignant | 0 (0.0) | 1 (1.1) |
| Refractory anaemia with an excess of blasts | 0 (0.0) | 1 (1.1) |
| Renal cell carcinoma (stage unspecified) | 2 (1.0) | 0 (0.0) |
| Renal cyst | 3 (1.4) | 1 (1.1) |
| Small cell lung cancer stage unspecified | 1 (0.5) | 1 (1.1) |
| Nervous system disorders | | |
| Amnesia | 2 (1.0) | 0 (0.0) |
| Areflexia | 5 (2.4) | 3 (3.4) |
| Balance disorder | 0 (0.0) | 2 (2.3) |
| Burning sensation | 0 (0.0) | 1 (1.1) |
| Carpal tunnel syndrome | 1 (0.5) | 2 (2.3) |
| Cervicobrachial syndrome | 1 (0.5) | 2 (2.3) |
| Cubital tunnel syndrome | 0 (0.0) | 1 (1.1) |
| Dementia | 0 (0.0) | 1 (1.1) |
| Depressed level of consciousness | 1 (0.5) | 1 (1.1) |
| Diplegia | 0 (0.0) | 1 (1.1) |
| Dizziness | 2 (0.0) | 2 (2.3) |
| Dysaesthesia | 5 (2.4) | 2 (2.3) |
| Encephalopathy | 0 (0.0) | 1 (1.1) |
| Facial palsy | 2 (1.0) | 0 (0.0) |
| Headache | 5 (2.4) | 1 (1.1) |
| Hyperreflexia | 1 (0.5) | 1 (1.1) |
| Hypoaesthesia | 17 (8.2) | 4 (4.6) |

| System Organ Class/Preferred Term | OP-1[®] Putty (N=208) | Autograft (N=87) |
|--|---------------------------------------|-------------------------|
| Hyporeflexia | 7 (3.4) | 1 (1.1) |
| Hypotonia | 3 (1.4) | 2 (2.3) |
| Loss of consciousness | 2 (1.0) | 0 (0.0) |
| Lumbar radiculopathy | 2 (0.0) | 4 (4.6) |
| Meralgia paraesthetica | 1 (0.5) | 1 (1.1) |
| Monoplegia | 0 (0.0) | 1 (1.1) |
| Nerve compression | 0 (0.0) | 2 (2.3) |
| Neurological symptom | 0 (0.0) | 1 (1.1) |
| Neuropathy peripheral | 1 (0.5) | 3 (3.4) |
| Paraesthesia | 6 (2.9) | 3 (3.4) |
| Peroneal nerve palsy | 2 (1.0) | 0 (0.0) |
| Post herpetic neuralgia | 0 (0.0) | 1 (1.1) |
| Radiculopathy | 2 (0.0) | 1 (1.1) |
| Reflexes abnormal | 3 (1.4) | 1 (1.1) |
| Restless legs syndrome | 1 (0.5) | 1 (1.1) |
| Sciatica | 1 (0.5) | 1 (1.1) |
| Sensory disturbance | 7 (3.4) | 1 (1.1) |
| Psychiatric disorders | | |
| Anxiety | 3 (1.4) | 0 (0.0) |
| Confusional state | 3 (1.4) | 4 (4.6) |
| Delirium | 3 (1.4) | 1 (1.1) |
| Depression | 3 (1.4) | 0 (0.0) |
| Disorientation | 0 (0.0) | 1 (1.1) |
| Mental status changes | 1 (0.5) | 1 (1.1) |
| Renal and urinary disorders | | |
| Dysuria | 3 (1.4) | 0 (0.0) |
| Haematuria | 0 (0.0) | 1 (1.1) |
| Micturition urgency | 1 (0.5) | 1 (1.1) |
| Pollakiuria | 2 (1.0) | 0 (0.0) |
| Renal failure | 1 (0.5) | 1 (1.1) |
| Urethral stricture | 2 (1.0) | 0 (0.0) |
| Urinary incontinence | 2 (0.0) | 1 (1.1) |
| Urinary retention | 14 (6.7) | 7 (8.0) |
| Reproductive system and breast disorders | | |
| Prostatic disorder | 0 (0.0) | 1 (1.1) |
| Uterine prolapse | 1 (0.5) | 1 (1.1) |
| Respiratory, thoracic and mediastinal disorders | | |
| Asthma | 0 (0.0) | 1 (1.1) |
| Atelectasis | 1 (0.5) | 1 (1.1) |
| Bronchitis | 4 (1.9) | 1 (1.1) |
| Chest pain | 2 (1.0) | 0 (0.0) |
| Dysphonia | 0 (0.0) | 1 (1.1) |
| Dyspnoea | 3 (1.4) | 0 (0.0) |
| Hiccups | 0 (0.0) | 1 (1.1) |
| Hypoxia | 5 (2.4) | 3 (3.4) |
| Pulmonary embolism | 4 (1.9) | 1 (1.1) |
| Respiratory depression | 0 (0.0) | 1 (1.1) |
| Upper respiratory infection | 2 (1.0) | 0 (0.0) |
| Wheezing | 4 (1.9) | 0 (0.0) |
| Skin and subcutaneous tissue disorders | | |
| Blister | 2 (1.0) | 0 (0.0) |
| Drug eruption | 0 (0.0) | 1 (1.1) |
| Excoriation | 2 (1.0) | 0 (0.0) |

| System Organ Class/Preferred Term | OP-1[®] Putty (N=208) | Autograft (N=87) |
|--|---------------------------------------|-------------------------|
| Pruritis | 2 (1.0) | 0 (0.0) |
| Rash | 6 (2.9) | 2 (2.3) |
| Rash maculo-papular | 0 (0.0) | 1 (1.1) |
| Vascular disorders | | |
| Aortic aneurysm | 2 (1.0) | 0 (0.0) |
| Cerebrovascular accident | 3 (1.4) | 1 (1.1) |
| Deep vein thrombosis | 3 (1.4) | 1 (1.1) |
| Haematoma | 2 (0.0) | 5 (5.7) |
| Hypertension | 3 (1.4) | 2 (2.3) |
| Hypotension | 4 (1.9) | 1 (1.1) |
| Peripheral vascular disorder | 2 (1.0) | 0 (0.0) |
| Phlebitis superficial | 0 (0.0) | 1 (1.1) |
| Transient ischaemic attack | 4 (1.9) | 0 (0.0) |
| Vascular occlusion | 0 (0.0) | 1 (1.1) |

Pilot Study S99-01US: Treatment Emergent Adverse Events

| System Organ Class/Preferred Term | OP-1[®] Putty (N=24) | OP-1[®] Putty & Autograft (N=12) | Autograft (N=12) |
|---|--------------------------------------|--|-------------------------|
| Blood and lymphatic system disorders | | | |
| Anaemia | 1 (4.2) | 0 (0.0) | 1 (8.3) |
| Secondary anaemia | 0 (0.0) | 0 (0.0) | 1 (8.3) |
| Cardiac disorders | | | |
| Aortic valve disease | 1 (4.2) | 0 (0.0) | 0 (0.0) |
| Coronary artery disease | 0 (0.0) | 1 (8.3) | 0 (0.0) |
| Pulmonary oedema | 0 (0.0) | 1 (8.3) | 0 (0.0) |
| Tachycardia | 1 (4.2) | 0 (0.0) | 0 (0.0) |
| Ear and labyrinth disorders | | | |
| Otorrhoea | 1 (4.2) | 0 (0.0) | 0 (0.0) |
| Eye disorders | | | |
| Cataract unilateral | 1 (4.2) | 0 (0.0) | 0 (0.0) |
| Eye disorder NOS | 1 (4.2) | 0 (0.0) | 0 (0.0) |
| Gastrointestinal disorders | | | |
| Abdominal pain | 0 (0.0) | 0 (0.0) | 1 (8.3) |
| Diarrhoea | 0 (0.0) | 1 (8.3) | 0 (0.0) |
| Ileus paralytic | 0 (0.0) | 1 (8.3) | 1 (8.3) |
| Intestinal functional disorder | 2 (8.3) | 0 (0.0) | 0 (0.0) |
| Nausea | 0 (0.0) | 0 (0.0) | 1 (8.3) |
| Volvulus of bowel | 0 (0.0) | 1 (8.3) | 0 (0.0) |
| Vomiting | 0 (0.0) | 1 (8.3) | 0 (0.0) |
| General disorders and administration site conditions | | | |
| Chest pain | 1 (4.2) | 0 (0.0) | 1 (8.3) |
| Gait disturbance | 0 (0.0) | 1 (8.3) | 0 (0.0) |
| Injection site bruising | 0 (0.0) | 1 (8.3) | 0 (0.0) |
| Pain | 1 (4.2) | 2 (16.7) | 1 (8.3) |
| Hepatobiliary disorders | | | |
| Gall bladder disorder | 1 (4.2) | 0 (0.0) | 0 (0.0) |
| Infections and infestations | | | |

| System Organ Class/Preferred Term | OP-1[®] Putty (N=24) | OP-1[®] Putty & Autograft (N=12) | Autograft (N=12) |
|--|--------------------------------------|--|-------------------------|
| Herpes viral infection | 0 (0.0) | 1 (8.3) | 0 (0.0) |
| Onychomycosis | 1 (4.2) | 0 (0.0) | 0 (0.0) |
| Pneumonia | 0 (0.0) | 1 (8.3) | 0 (0.0) |
| Post-operative wound infection | 4 (16.7) | 0 (0.0) | 0 (0.0) |
| Urinary tract infection | 1 (4.2) | 1 (8.3) | 1 (8.3) |
| Injury, poisoning and procedural complications | | | |
| Accidental injury | 1 (4.2) | 0 (0.0) | 0 (0.0) |
| Anaemia postoperative | 3 (12.5) | 0 (0.0) | 1 (8.3) |
| Blister | 1 (4.2) | 0 (0.0) | 0 (0.0) |
| Donor site complication | 0 (0.0) | 2 (16.7) | 5 (41.7) |
| Dural tear | 1 (4.2) | 1 (8.3) | 1 (8.3) |
| Fall | 3 (12.5) | 0 (0.0) | 0 (0.0) |
| Haemorrhage | 0 (0.0) | 1 (8.3) | 0 (0.0) |
| Injury | 0 (0.0) | 1 (8.3) | 0 (0.0) |
| Joint injury | 1 (4.2) | 0 (0.0) | 0 (0.0) |
| Post-procedural haemorrhage | 0 (0.0) | 1 (8.3) | 0 (0.0) |
| Post-procedure haematoma | 1 (4.2) | 0 (0.0) | 0 (0.0) |
| Pseudarthrosis | 10 (41.7) | 3 (25.0) | 0 (0.0) |
| Road traffic accident | 1 (4.2) | 0 (0.0) | 2 (16.7) |
| Thoracic vertebral fracture | 0 (0.0) | 0 (0.0) | 1 (8.3) |
| Urinary retention postoperative | 1 (4.2) | 1 (8.3) | 1 (8.3) |
| Wound complication | 1 (4.2) | 0 (0.0) | 0 (0.0) |
| Investigations | | | |
| Blood pressure decreased | 1 (4.2) | 0 (0.0) | 0 (0.0) |
| Body temperature increased | 0 (0.0) | 0 (0.0) | 1 (8.3) |
| Colonoscopy normal | 0 (0.0) | 1 (8.3) | 0 (0.0) |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | 7 (19.2) | 5 (41.7) | 0 (0.0) |
| Arthritis | 1 (4.2) | 1 (8.3) | 0 (0.0) |
| Back pain | 8 (33.3) | 7 (58.3) | 7 (58.3) |
| Bone pain | 0 (0.0) | 1 (8.3) | 0 (0.0) |
| Bursitis | 0 (0.0) | 1 (8.3) | 0 (0.0) |
| Fibromyalgia | 0 (0.0) | 1 (8.3) | 0 (0.0) |
| Groin pain | 0 (0.0) | 1 (8.3) | 0 (0.0) |
| Joint range of motion decreased | 0 (0.0) | 1 (8.3) | 0 (0.0) |
| Lumbar spinal stenosis | 1 (4.2) | 1 (8.3) | 0 (0.0) |
| Neck pain | 0 (0.0) | 1 (8.3) | 3 (25.0) |
| Neck stiffness | 0 (0.0) | 0 (0.0) | 1 (8.3) |
| Oedema peripheral | 1 (4.2) | 0 (0.0) | 0 (0.0) |
| Osteoarthritis | 1 (4.2) | 0 (0.0) | 0 (0.0) |
| Pain in extremity | 5 (20.8) | 3 (25.0) | 3 (25.0) |
| Pain in limb | 1 (4.2) | 1 (8.3) | 0 (0.0) |
| Spinal osteoarthritis | 1 (4.2) | 0 (0.0) | 0 (0.0) |
| Spondylolisthesis | 0 (0.0) | 1 (8.3) | 0 (0.0) |
| Synovial cyst | 0 (0.0) | 1 (8.3) | 0 (0.0) |
| Tendonitis | 0 (0.0) | 0 (0.0) | 1 (8.3) |
| Upper limb fracture | 0 (0.0) | 1 (8.3) | 0 (0.0) |
| Neoplasms Benign, Malignant And Unspecified (incl Cysts And Polyps) | | | |
| Bladder cancer | 0 (0.0) | 1 (8.3) | 0 (0.0) |
| Breast cancer | 1 (4.2) | 0 (0.0) | 0 (0.0) |

| System Organ Class/Preferred Term | OP-1[®] Putty (N=24) | OP-1[®] Putty & Autograft (N=12) | Autograft (N=12) |
|--|--------------------------------------|--|-------------------------|
| Colon cancer | 0 (0.0) | 1 (8.3) | 0 (0.0) |
| Lung neoplasm malignant | 1 (4.2) | 0 (0.0) | 0 (0.0) |
| Malignant melanoma | 0 (0.0) | 1 (8.3) | 0 (0.0) |
| Prostate cancer | 1 (4.2) | 0 (0.0) | 1 (8.3) |
| Nervous system disorders | | | |
| Hypoaesthesia | 1 (4.2) | 0 (0.0) | 0 (0.0) |
| Muscle contractions involuntary | 1 (4.2) | 0 (0.0) | 0 (0.0) |
| Neurological disorder | 0 (0.0) | 1 (8.3) | 2 (16.7) |
| Transient ischemic attack | 0 (0.0) | 0 (0.0) | 1 (8.3) |
| Vertigo | 1 (4.2) | 0 (0.0) | 0 (0.0) |
| Renal and urinary disorders | | | |
| Urinary incontinence | 1 (4.2) | 0 (0.0) | 0 (0.0) |
| Respiratory, thoracic and mediastinal disorders | | | |
| Pleural effusion | 1 (4.2) | 0 (0.0) | 0 (0.0) |
| Skin and subcutaneous tissue disorders | | | |
| Rash | 1 (4.2) | 0 (0.0) | 0 (0.0) |
| Rash pruritic | 1 (4.2) | 0 (0.0) | 0 (0.0) |
| Surgical and medical procedures | | | |
| Breast cosmetic surgery | 1 (4.2) | 0 (0.0) | 0 (0.0) |
| Hip arthroplasty | 1 (4.2) | 0 (0.0) | 1 (8.3) |
| Knee arthroplasty | 1 (4.2) | 0 (0.0) | 0 (0.0) |
| Vascular disorders | | | |
| Haemangioma | 0 (0.0) | 1 (8.3) | 0 (0.0) |
| Hypertension | 0 (0.0) | 1 (8.3) | 0 (0.0) |
| Hypotension | 0 (0.0) | 0 (0.0) | 1 (8.3) |
| Peripheral vascular disorder | 1 (4.2) | 0 (0.0) | 0 (0.0) |
| Pulmonary embolism | 0 (0.0) | 0 (0.0) | 1 (8.3) |
| Renal artery disorder | 1 (4.2) | 0 (0.0) | 0 (0.0) |

Post-marketing Experience:

OP-1[®] Putty has been authorized for commercial sale under HDE H020008 since April 7, 2004. The limitations of post-marketing adverse event reporting preclude the ability to establish a true causal relationship between the administration of OP-1 and the onset of the adverse events. The following post-marketing adverse events have been reported (identified by **System Organ Class** and preferred term) by more than one (1) patient:

Cardiac disorders: myocardial infarction (2)

General disorders and administration site conditions: asthenia (3), inflammation (4), local swelling (2), postoperative fever (3), wound secretion (2)

Injury, poisoning and procedural complications: incision site complication (3), medical device complication (2)

Musculoskeletal and connective tissue disorders: back pain (7), muscle spasms (3), pain in extremity (2), post procedural discomfort (3)

Nervous system disorders: hyperaesthesia (2), hypoaesthesia (4), sensory disturbance (2)

Clinical Trial Results

Pilot Study S99-01US was a controlled, randomized, multicenter, pilot clinical study to evaluate the safety and efficacy of OP-1[®] Putty for lumbar spinal fusion, both alone and as an adjunct to autogenous bone graft (autograft) in patients with single level (L3-S1) degenerative lumbar spondylolisthesis (Grade 1 or 2) with spinal stenosis. The initial protocol specified 2 treatment groups: an investigational arm of OP-1[®] Putty and autograft, and a control arm of autograft alone. A protocol revision added a new investigational arm of treatment with OP-1[®] Putty alone, and eliminated enrollment in the OP-1[®] Putty and autograft arm. At all times patients were randomized in a 2:1 manner to the OP-1[®] Putty-containing treatment arm versus the autograft treatment arm.

Patients underwent standard surgical procedures for lumbar spinal posterior decompression with concomitant posterolateral intertransverse process arthrodesis using OP-1[®] Putty alone, OP-1[®] Putty with autograft, or with autograft alone, as specified by randomization. Patients were evaluated postoperatively at 6 weeks, and 3, 6, 9, 12, and 24 months, and annually thereafter until the last patient in the Pivotal study (S01-01US) achieved 2-year follow-up.

The primary efficacy variable was overall success, a composite measure consisting of radiographic demonstration of spinal fusion (presence of bridging bone and $\leq 5^\circ$ angular motion and ≤ 2 mm translational motion), improvement of at least 20% on the Oswestry Disability Index (ODI), and absence of retreatment. Table 2 presents the Overall Success Rates through 48 months.

Table 2 Pilot Study: Overall Success Rate (Intent-to-Treat Population)

| | OP-1 [®] Putty Alone | | OP-1 [®] Putty/Autograft | | Autograft Alone | |
|-----------|-------------------------------|-------------------------|-----------------------------------|-------------------------|-----------------|-------------------------|
| | Pts. (N) | Number (%) of Successes | Pts. (N) | Number (%) of Successes | Pts. (N) | Number (%) of Successes |
| 12 Months | 21 | 11 (52.4) | 10 | 5 (50.0) | 9 | 4 (44.4) |
| 24 Months | 18 | 10 (55.6) | 9 | 4 (44.4) | 9 | 3 (33.3) |
| 36 Months | 18 | 9 (50.0) | 8 | 3 (37.5) | 5 | 1 (20.0) |
| 48 Months | 16 | 10 (62.5) | 7 | 3 (42.9) | 6 | 2 (33.3) |

Note: Missing data were not imputed.

The Pivotal Study (S01-01US) was a controlled, prospective, randomized, multicenter, pivotal clinical trial, in which patients with degenerative lumbar spondylolisthesis (Grade I/II) with spinal stenosis received decompression and spinal fusion treatment. Patients were randomized 2:1 to receive either OP-1[®] Putty or to autogenous bone graft (autograft). Patient pain/function levels were evaluated preoperatively and at 6 weeks, 3 months, 6 months, 9 months, 1 year, 2 years, and annually thereafter until the last patient achieved at least 2 years of

follow-up. Adverse events, device-related or not, were evaluated over the course of the clinical trial. Clinical, radiographic, and safety outcomes were assessed at each evaluation time point. Primary efficacy was determined based upon results at 24 months post-operatively. Serum samples were analyzed for anti-OP-1 antibodies preoperatively (baseline) and at the 6-week and 3-, 6-, 12-, and 24-month follow-up visits. Samples that were positive in an ELISA screen were further tested to determine antibody titer and neutralizing capacity.

The primary efficacy endpoint was the 24-month overall success rate for the modified intent-to-treat (mITT) population. A patient was considered an “overall success” by meeting criteria of pain, function, absence of surgical retreatment, absence of serious device-related adverse events, neurological function, and radiographic status. Additional outcome parameters included visual analog back and leg pain scale, general health survey, donor site pain (control group only), medication use, and procedure and hospitalization data. The primary radiographic outcome parameter consisted of evaluations of translation and angulation motion and presence of new bone.

Components of success

Overall success was a composite measure with the following 5 components:

- Improvement of at least 20% in the Oswestry Disability Index (ODI) from baseline
- Absence of retreatment
- Absence of treatment-emergent serious adverse events
- Absence of a decrease in neurological status (assessing muscle strength, reflexes, sensory and straight leg raise), unless attributable to a concurrent medical condition or to the surgical procedure by a blinded Independent Neurological Reviewer (muscle strength, reflexes, sensory assessments, and straight leg raise pain)
- Radiographic demonstration of spinal fusion, which was also a composite measure comprising the following:
 - Presence of bone formation
 - Angulation of $\leq 5^\circ$ on flexion/extension radiographs of the affected level
 - Translational movement of ≤ 3 mm on flexion/extension radiographs of the affected level

Efficacy endpoints

Table 3 presents Overall Success and its components at 24 months:

Table 3 Pivotal Study: Success Outcomes at 24 Months Follow-up (mITT Population)

| Outcome | OP-1 [®] Putty | Autograft | P Value for Non-Inferiority |
|-----------------------------------|-------------------------|-----------|-----------------------------|
| Overall Success ^a | 38.7% | 49.4% | 0.331 ^b |
| Oswestry Disability Index | 80.4% | 85.5% | 0.178 ^c |
| Absence of Retreatment | 92.3% | 88.6% | 0.001 ^c |
| Absence of Treatment-related SAEs | 88.7% | 91.4% | 0.038 ^c |
| Neurological Success | 100% | 93.9% | <0.001 ^c |
| Radiographic Success ^a | 53.0% | 68.9% | 0.622 ^b |

^a Calculated with imputation of missing data

^b P Value is based on one-sided 2-sample test for non-inferiority in the angular scale with a non-inferiority margin of 0.14 (radians); estimates and standard errors are based on logistic regression and multiple imputation.

^c P Value is based on one-sided two-sample t-test for non-inferiority with an equivalence limit of 0.10.

OP-1[®] Putty was statistically non-inferior to autograft with regard to neurological success and absence of retreatments or treatment-related SAEs. Despite the favorable outcomes on all clinical parameters (ODI, neurological success and absence of retreatments or treatment-related SAEs), OP-1[®] Putty treatment was not shown to be non-inferior to autograft with respect to Overall Success rate, the primary endpoint in the pivotal study. This was found to be due principally to the results of the Overall Radiographic Success, in particular presence of bone on plain film. Table 4 presents the summary of radiographic success components, including a *post hoc* analysis of presence of bone on CT at 9 months. CT was a more sensitive indicator of presence of bone in this population.

Table 4 Pivotal Study: Summary of Radiographic Success Components (mITT Population)

| Component | Timepoint | OP-1 [®] Putty | Autograft | P Value Non-inferiority ¹ |
|--|-----------|-------------------------|---------------|--------------------------------------|
| | | Successes (%) | Successes (%) | |
| Translational Success | 24 Months | 93.6 | 96.3 | 0.004 |
| Angulation Success | 24 Months | 76.6 | 79.3 | 0.087 |
| Presence of Bone on plain film | 24 Months | 61.7 | 83.1 | 0.990 |
| Presence of Bone on CT (<i>post hoc</i>) | 9 Months | 84.9% | 98.6% | 0.929 |

(1) P Value is based on one-sided 2-sample t-test for non-inferiority with an equivalence limit of 0.10.

Table 5 presents the rates of translational and angulation success at 24 and 36 months. Treatment with OP-1[®] Putty resulted in a high proportion of patients achieving successful and sustained dynamic radiographic outcomes of stability at 24 and 36 months, and is clinically comparable to autograft treatment.

Table 5 Pivotal Study: Translational and Angulation Success at 24 and 36 Months (mITT Population)

| Component | Timepoint | OP-1 [®] Putty | Autograft | P Value Non-inferiority ¹ |
|-----------------------|-----------|-------------------------|---------------|--------------------------------------|
| | | Successes (%) | Successes (%) | |
| Translational Success | 24 Months | 93.6 | 96.3 | 0.004 |
| | 36 Months | 93.3 | 78.6 | 0.022 |
| Angulation Success | 24 Months | 76.6 | 79.3 | 0.087 |
| | 36 Months | 87.5 | 71.4 | 0.029 |

(1) P Value is based on one-sided 2-sample t-test for non-inferiority with an equivalence limit of 0.10.

The non-radiographic clinical endpoints are shown in Table 6. Overall Clinical Success is a composite outcome, which includes ODI success, absence of retreatment, absence of serious treatment-related AEs, and neurological success. OP-1[®] Putty was statistically non-inferior to autograft with regard to this composite endpoint (71.2% in the OP-1[®] Putty group, and 69.0% in the autograft group, *P*=0.029 *post hoc* analysis).

Table 6: Pivotal Study: Clinical Success

| Outcome | OP-1 Putty | Autograft | P Value Non-Inferiority ¹ |
|--|------------|-----------|--------------------------------------|
| ODI Success | 80.4% | 85.5% | 0.178 |
| Absence of Retreatment | 92.3% | 88.6% | 0.001 |
| Absence of Serious Treatment-related AEs | 88.7% | 91.4% | 0.038 |
| Neurological Success | 100% | 93.9% | <0.001 |
| Overall Clinical Success (<i>post hoc</i> analysis) | 71.2% | 69.0% | 0.029 |

¹ P Value is based on one-sided two-sample t-test for non-inferiority with an equivalence limit of 0.10.

Safety findings

OP-1[®] Putty treatment was generally safe and well-tolerated in the posterolateral lumbar fusion population. As shown in Table 7, the safety of OP-1[®] Putty treatment in PLF was similar to that of autograft treatment with respect to the proportion of patients experiencing:

- Treatment-emergent AEs
- Severe AEs
- Treatment-related AEs
- SAEs
- Neoplasm
- Death

Table 7 Pivotal Study: Treatment-Emergent Adverse Events (Safety Population)

| Parameter | OP-1 [®] Putty (N=208) | | Autograft (N=87) | |
|---|------------------------------------|--------------|------------------------------------|--------------|
| | Number (%) of Patients with Events | 95% CI | Number (%) of Patients with Events | 95% CI |
| Any AE | 201 (96.6) | (93.2, 98.6) | 82 (94.3) | (87.1, 98.1) |
| Severe AE | 43 (20.7) | (15.4, 26.8) | 17 (19.5) | (11.8, 29.4) |
| Treatment-related AE | 54 (26.0) | (20.1, 32.5) | 23 (26.4) | (17.6, 37.0) |
| Serious AE | 104 (50.0) | (43.0, 57.0) | 43 (49.4) | (38.5, 60.4) |
| Serious and Unanticipated AE | 5 (2.4) | (0.8, 5.5) | 0 (0.0) | (0.0, 4.2) |
| Treatment-related Serious AE | 25 (12.0) | (7.9, 17.2) | 6 (6.9) | (2.6, 14.4) |
| Neoplasms Benign, Malignant And Unspecified (incl Cysts And Polyps) | 12 (5.8) | (3.0, 9.9) | 8 (9.2) | (4.1, 17.3) |
| Death | 7 (3.4) | (1.4, 6.8) | 4 (4.6) | (1.3, 11.4) |

- No clinically significant laboratory changes were associated with OP-1[®] Putty treatment.

- There was no apparent association of neutralizing antibodies and the development of immunologically-related AEs or SAEs of any kind.
- The presence of neutralizing antibodies was not statistically correlated with success outcomes.
- The risk of post-operative AEs related to the lumbar spine was clinically equivalent for OP-1[®] Putty and autograft treatments.
- There was a higher reported rate of AEs in the Cardiac and Infections and Infestations SOCs in the OP-1[®] Putty treated group. In the autograft group there was a higher reported rate in Blood and Lymphatic Disorders and Injury SOCs.

Special Populations

OP-1[®] Putty has not been studied in children.

Product Preparation Instructions

One unit of OP-1[®] Putty (1 vial of OP-1 protein in collagen, and 1 vial of CMC putty additive) is used on each side of the spine. The patient will receive a total of 7 mg OP-1 per bilateral posterolateral fusion. A unit is prepared as follows:

1. Remove each blister package from the outer carton.
2. Using aseptic technique, remove each vial from the sterile blister package.
3. Lift the plastic flip-off tops and remove the metal crimps from each vial.
4. Align your thumbs with the internal gap of the stopper and pry up the edge of the stopper. After the vacuum is broken, remove the stopper from each vial while holding the vial upright to prevent product loss.
5. Aseptically transfer the contents of the putty additive vial and the vial containing OP-1 into a sterile mixing bowl.
6. Utilizing a sterile syringe, add 2.5 cc of sterile 0.9% saline for injection to the mixing bowl.
7. Gently stir the contents with a sterile spatula to produce a product with a putty-like consistency.
8. Use OP-1[®] Putty promptly following reconstitution.
9. Use the same procedure to prepare OP-1[®] Putty for the contralateral side of the spine.

Dosage and Administration

Two units of OP-1[®] Putty are used for spinal fusion (one unit for each side of the spine) for a total dose of 7 mg OP-1. For detailed administration instructions, see the brochure entitled, "OP-1[®] Putty Surgical Technique". The bone must be debrided and decorticated so that the OP-1[®] Putty will directly contact viable tissue. Adequate hemostasis must be provided to ensure that the material stays at the surgical site. Irrigate the site as necessary prior to implantation of OP-1[®] Putty. Where practical, surgical manipulations to the site should be completed prior to device implantation. Place the OP-1[®] Putty in the lateral gutters, bridging the dorsal surfaces of the transverse processes. Pack OP-1[®] Putty into the desired area to its maximum capacity. Close the soft tissues around OP-1[®] Putty

immediately after implantation. Closure is critical for containment and maintenance of the device in the area of fusion. Do not place a drain at the fusion site; a drain may only be used subcutaneously. After closure of the soft tissue around the fusion site, irrigate the field if necessary to remove any stray particles of product.

How Supplied

The components of OP-1[®] Putty are packaged in two vials for reconstitution, each in separate blister packages, and stored together in one shelf box. The 2 oz vial contains 3.5 mg OP-1 protein in 1 g bovine type 1 collagen. The 10 mL vial contains 230 mg CMC. The contents of both vials and the blister packages are sterile. Two OP-1[®] Putty units are used per patient for spinal fusion. Sterile saline for injection (0.9%) and a sterile bowl and spatula are necessary for product preparation, but are not supplied with the product. Self-adhesive labels indicating the lot numbers of each device are provided for attachment to the patient's chart following surgery.

Storage Conditions

Store OP-1[®] Putty refrigerated, 2 to 8 °C . Keep product in outer carton until time of use.

Manufactured by:

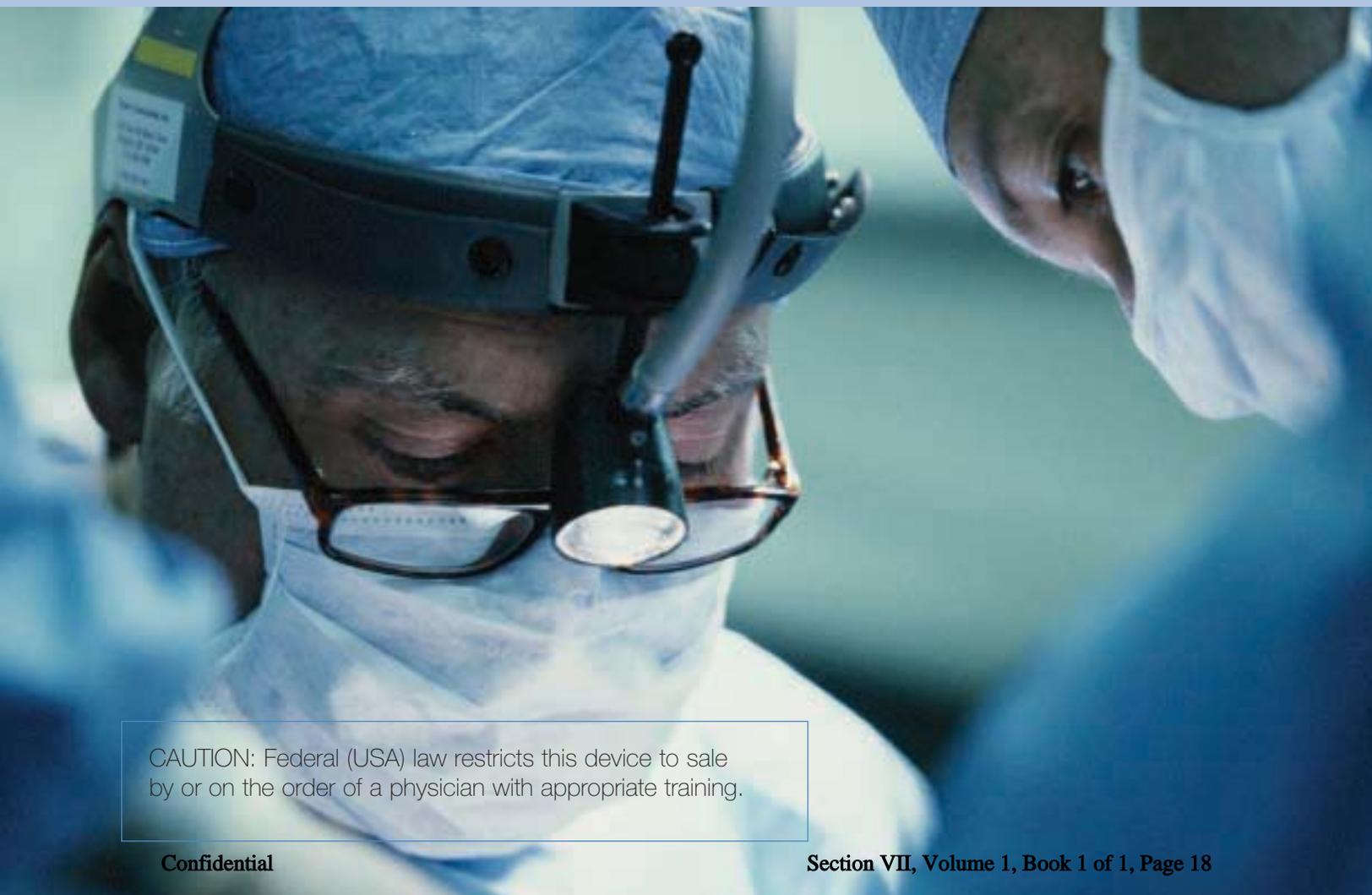
Stryker Biotech
35 South Street
Hopkinton, MA 01748 USA
Phone (508) 416-5200
www.op1.com

A division of Stryker Corporation
2725 Fairfield Road
Kalamazoo, MI 49003

9JUN06

OP-1[®] Putty

Surgical Technique



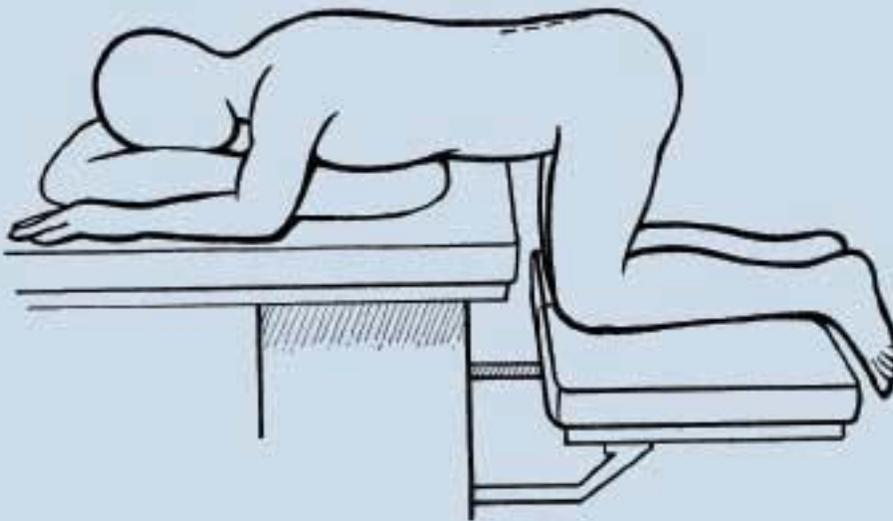
CAUTION: Federal (USA) law restricts this device to sale by or on the order of a physician with appropriate training.

Please adhere to the following order:

Step 1

Patient Positioning

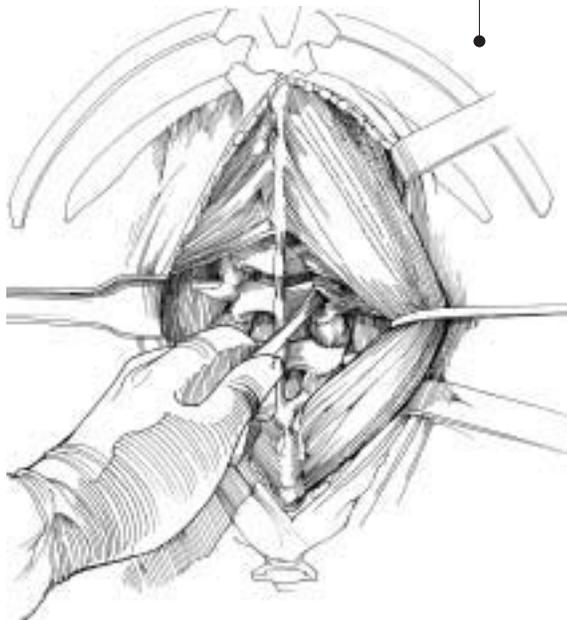
Place patient in prone position using an appropriate spine table that allows maintenance of normal spine lordosis.



Step 2

Exposure and Bone Preparation

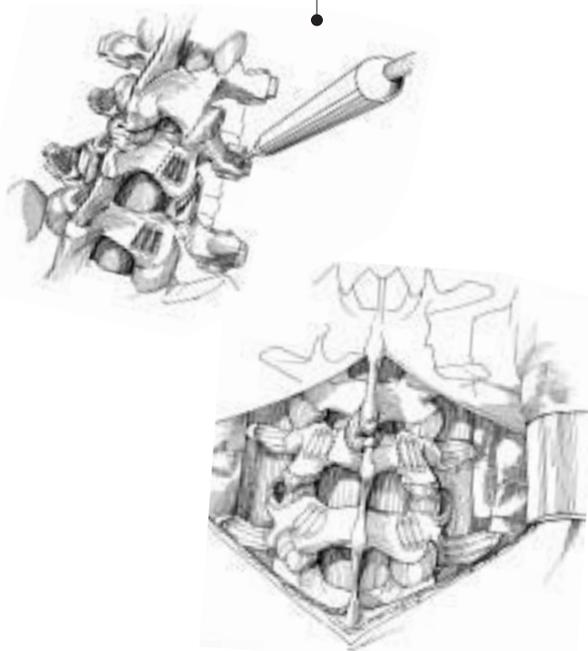
Make a single midline incision in both the skin and the lumbodorsal fascia. Strip the paraspinal muscles subperiosteally and retract laterally. Denude the facet joints and transverse processes of all soft tissue.

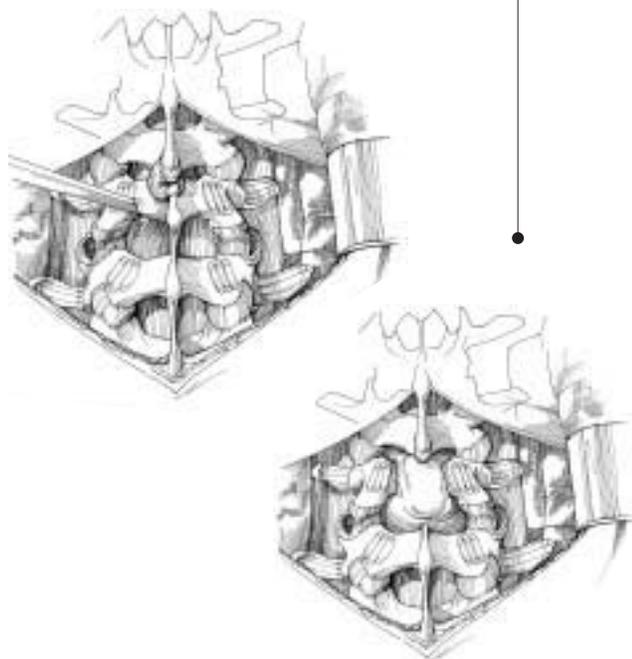


Step 3

Decortication

Decorticate all cortical surfaces, including the dorsal, lateral, superior, and inferior surfaces of the transverse processes and the dorsal and lateral aspects of the pars interarticularis from the most proximal vertebra, to the most distal vertebra to be included in the fusion. It is recommended to pack off the lateral gutters with sponges, preferably soaked with epinephrine, to promote hemostasis.





Step 4

Decompression* (if necessary)

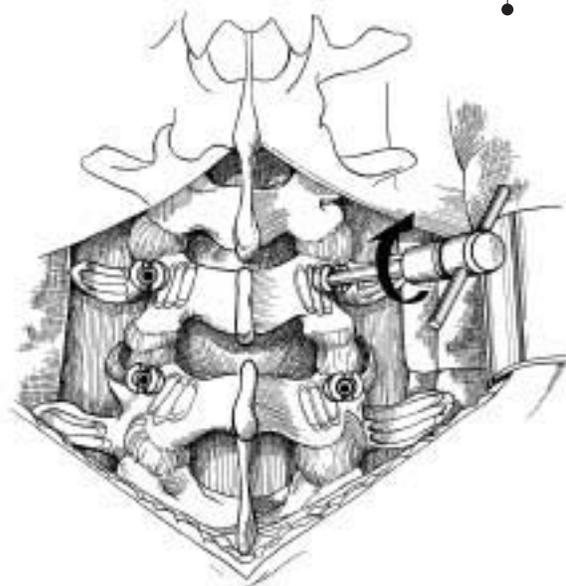
Perform a decompression of the stenotic portions of the posterior spine. The decompression may involve a whole or partial laminectomy and may include one or more levels.

Step 5

Inserting Instrumentation (pedicle screws) (if necessary)

Using the preferred surgical technique, insert pedicle screws carefully. (Pedicle screws can be inserted before decompression). If possible the fixation should also be added at this time. If it is determined that the fixation interferes with the ability to place the OP-1 Putty, the fixation should be placed after implantation of the OP-1 Putty.

***Decompression may be performed after decortication or after insertion of instrumentation.**



Step 6
Preparation of OP-1 Putty

One OP-1 Putty device should be used on each side of the spine. Remove OP-1 Implant and putty additive from tray and place onto sterile field.



1



2



3



4



5



1) Pry and remove the metal bands from the OP-1 Implant vial and the Putty Additive vial.

WARNING: Care should be taken to remove the metal bands carefully since the edges are sharp and may damage or puncture gloves.

2) Open both vials by aligning your thumb with the internal gap of the stopper and pry up the edge of the stopper. After the vacuum seal is broken, remove the stopper from each vial.

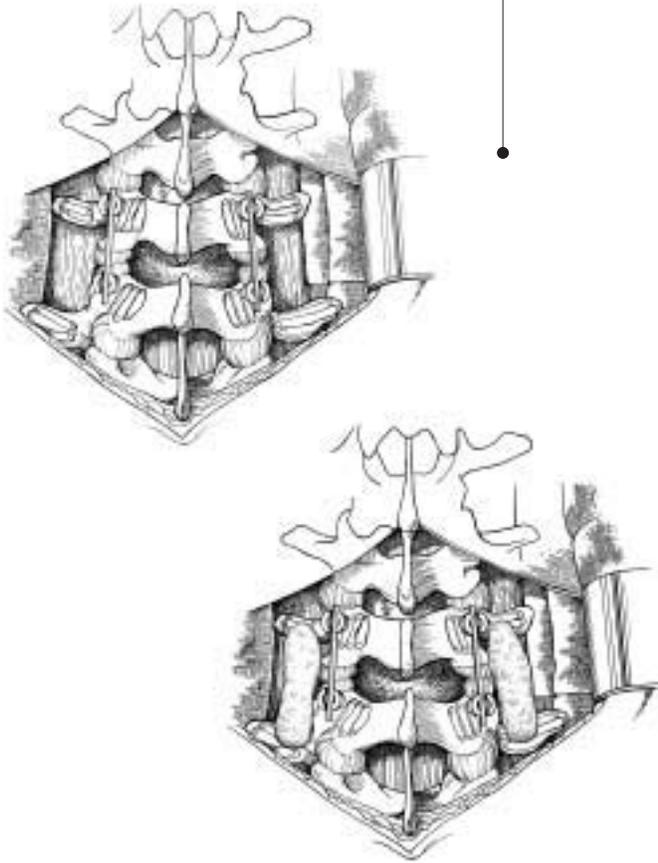
3) Pour OP-1 Implant into a sterile bowl. WARNING: Do not insert a needle through the stopper. Puncture of the stopper with a needle may result in particles of stopper material contaminating the device.

Add the contents of the Putty Additive vial to the bowl containing OP-1 Implant under sterile technique.

4) Utilize a sterile syringe to add 2.5 cc of sterile saline (0.9%) solution to the bowl containing OP-1 Implant and Putty Additive slowly and carefully.

5) Gently stir the contents of the vial with a sterile spatula to aid mixing. CAUTION: Do not shake vial to mix dry powder and solution. Agitation of vial may cause loss of device.

The same procedure should be used to prepare OP-1 Putty for the contralateral side of the spine.



Step 7

Placement of OP-1 Putty

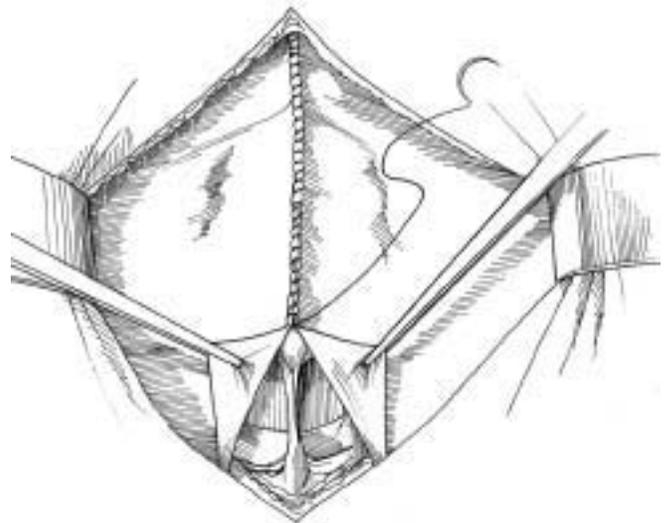
CAUTION: Surgical manipulations, irrigations or suction to the site should be completed prior to device implantation.

- One vial should be used per side.
- Remove packed sponges.
- Provide adequate haemostasis to ensure the OP-1 Putty stays at the surgical site. Irrigate the surgical site as necessary prior to implanting the OP-1 Putty.
- Place the OP-1 Putty in the decorticated lateral gutters, bridging the dorsal surfaces of the transverse processes.
- Pack the OP-1 Putty into the desired area to its maximum capacity.
- Ensure that the OP-1 Putty directly contacts viable tissue.

Step 8

Closing

Close the soft tissues around the OP-1 Putty immediately after implantation. Closure is critical for containment and maintenance of OP-1 Putty. Do not place a drain at the fusion; a drain may only be used subcutaneously.





Joint Replacements

Trauma

Spine

Micro Implants

Orthobiologics

Instruments

Interventional Pain

Navigation

Endoscopy

Communications

Patient Handling Equipment

EMS Equipment

Stryker Biotech
35 South Street
Hopkinton, MA 01748 USA
Phone 866-GRO-BONE

www.stryker.com