This Patient Guide is designed to help you make an informed decision about treatment for your back pain and related problems. Your doctor has proposed surgery to relieve your back pain and related problems using the INFUSE® Bone Graft/LT-CAGE® Lumbar Tapered Fusion Device.

Your doctor has decided that you need spine surgery after carefully examining you, reviewing your history and X-rays and taking into account the results of other diagnostic studies and previous non-surgical treatments. Specifically, your doctor has determined that you would benefit from having spinal fusion surgery which fuses (connects) certain bones of your back together to prevent them from moving relative to each other.

**Your Lower Back**

- **Posterior (Back)**
- **Anterior (Front)**
- **Disc**
- **Ruptured Disc**
- **Vertebral Body**
- **Spinal Column**
- **Vertebral Body**
- **Disc Degeneration**
- **Reduced Height because of Degenerated Discs**
The bony vertebrae, which encircle and protect your spinal cord, are separated by shock-absorbing discs. The discs give your spine the flexibility to move. Nerves branching from the spinal cord pass through openings in the vertebra to other parts of your body. Several of these nerves form the sciatic nerve, which runs down your leg. Each disc has a spongy center (nucleus) surrounded by tough outer rings.

As discs lose their water content because of disease or age, they lose their height, bringing the vertebrae closer together. As a result, the nerve openings in your spine become more narrow and the discs don’t absorb the shocks as well, particularly when you are walking, running or jumping. Wear and tear, poor posture and incorrect body movements can also weaken the disc, causing disc degeneration. Disc degeneration may cause back and/or leg pain, as well as functional problems such as tingling or numbness in your legs or buttocks, or difficulty walking. Doctors call this degenerative disc disease (DDD).

**Device Description**

The INFUSE® Bone Graft/LT-CAGE® Lumbar Tapered Fusion Device was designed to aid in the treatment of DDD. It consists of two parts – a small, hollow, threaded, tapered metal cylinder (the LT-CAGE® Lumbar Tapered Fusion Device) and a bone graft substitute (the INFUSE® Bone Graft).

The LT-CAGE® Lumbar Tapered Fusion Device component is intended to restore the degenerated disc space to its original height, thereby relieving the pressure on your nerves. Two implants are placed side-by-side.
The INFUSE® Bone Graft component is used to fill the LT-CAGE® Lumbar Tapered Fusion Device. The INFUSE® Bone Graft consists of two parts – a solution containing rhBMP-2 (recombinant human Bone Morphogenetic Protein-2) and the ACS (absorbable collagen sponge). The protein is a manufactured (genetically engineered) version of a natural protein normally found in small quantities in the body. The purpose of the protein is to stimulate bone formation. During surgery, the protein solution is soaked into the ACS. The ACS acts as a scaffold for the formation of new bone that the protein stimulates. The ACS is a sponge manufactured from bovine (cow) Type I collagen. It is designed to resorb (disappear) over time.

Potential Benefit

A potential advantage to having spinal fusion surgery using the INFUSE® Bone Graft/LT-CAGE® Lumbar Tapered Fusion Device is that it removes the need to collect bone from your hip (iliac crest autograft) to fill the inside of the LT-CAGE® Lumbar Tapered Fusion Device. The use of autograft bone is the alternative procedure and involves a second or larger incision that may be painful and/or take longer to heal.

Indications for Use

The INFUSE® Bone Graft/LT-CAGE® Lumbar Tapered Fusion Device is indicated for spinal fusion procedures in skeletally mature patients for the treatment of DDD at one level from L2-S1 (the lower part of the back). DDD is defined as a disc that has deteriorated and causes back pain. The disc deterioration is confirmed by history and X-ray studies. In addition to the disc degeneration, there may also be a small amount of slippage of one disc relative to the next at the diseased spinal level (known as Grade 1 spondylolisthesis or Grade 1 retrolisthesis). Prior to this surgery, you should have been non-responsive to at least 6 months of non-operative therapy.

Your doctor may implant the device through an opening in your abdomen. This is known as the open anterior surgical approach. Another option is to use a laparoscope. This “scope” allows the surgeon to look into your abdomen through one small hole and perform the surgery through several other small holes. This is known as the laparoscopic anterior surgical approach.
Contraindications

The INFUSE® Bone Graft/LT-CAGE® Lumbar Tapered Fusion Device should not be used if:

» you are pregnant or suspect that you might be pregnant
» you are sensitive to titanium, titanium alloy, bovine (cow) Type I collagen or recombinant human Bone Morphogenetic Protein-2
» you have an infection near the area of the surgical incision
» you had a tumor removed from the area of the implantation site or currently have a tumor in that area
» you have or are currently being treated for cancer
» your bones have not stopped growing

Warnings and Precautions

This device has not been tested in pregnant women to determine if there is any effect on a developing fetus. This device has also not been studied in nursing mothers.

When tested in female rabbits that received the rhBMP-2, a component of the device, developed an immune response and later became pregnant, the following was seen:

» The antibodies developed by the mother were able to reach the developing rabbit fetus. The effect of these antibodies on the developing rabbit fetus is not currently known.
» Some bone formation abnormalities were observed in a small number of the rabbit fetuses tested. It is not known if these changes would disappear as the rabbit fetus continued to develop or at some time after birth.

This device should not be used immediately prior to or during pregnancy. Women of child-bearing potential should be advised not to get pregnant for one year following treatment with the device. Women of child bearing potential should be warned of potential risk to a fetus and should discuss other possible orthopedic treatments with their surgeon.

BMP-2 plays a critical role during fetal development in humans and other animals. It is not known whether a pregnant woman, previously exposed to BMP-2 by implantation with the device, might develop a second immune response to BMP-2 from the developing fetus with adverse effects for the woman or baby. In a rabbit pregnancy study to investigate this issue, no increase in anti-BMP-2 antibodies was observed.
In addition, this device has not been tested:

- to see if there are side effects by using it more than once in the same person
- in people with liver or kidney problems (this might be important because these organs are involved in removing any by-products of the device)
- in people with metabolic bone diseases, such as osteoporosis
- in people with autoimmune or immunosuppressive disease, such as lupus or HIV/AIDS
- in people with immune deficiency due to other treatments, such as radiation therapy, chemotherapy or steroid therapy

Sufficient numbers of patients 65 years and older have not been studied to determine whether they respond differently from younger people.

After this device is implanted using the anterior laparoscopic surgical approach, some males may experience retrograde ejaculation (a form of sexual dysfunction).

Although not seen in these studies performed by the manufacturer, there is a possibility that too much bone may form at the implantation site (exuberant bone formation), bone may form at a location away from the implantation site (ectopic bone formation) or the bone that is formed may be abnormal.

Some patients may have an allergic reaction to the INFUSE® Bone Graft component.

Please talk with your doctor about any of the above warnings and precautions.
Surgery

The INFUSE® Bone Graft/LT-CAGE® Lumbar Tapered Fusion Device can be implanted through an opening in your abdomen. This is known as the open anterior surgical approach. Another option is to use a laparoscope. This “scope” allows the surgeon to look into your abdomen through one small hole and perform the surgery through several other small holes. This is known as the laparoscopic anterior surgical approach. You should speak with your doctor about the risks and benefits of both techniques prior to surgery.

During your surgery, your doctor will remove portions of the degenerated disc and vertebral body to allow the implants to be inserted. Rather than taking bone (autograft) from your hip or from the area in which the implants will be inserted, the surgeon will utilize the INFUSE® Bone Graft to pack inside the hollow implants. Your surgeon will implant two LT-CAGE® Lumbar Tapered Fusion Devices side-by-side in your disc space.

There are alternative treatments to this surgery – both surgical and non-surgical. You should discuss these other options with your surgeon before you make your decision.
After Surgery

Ask your doctor about your specific recovery plan following surgery. It is important to follow your doctor’s instructions carefully to recover from surgery as quickly as possible and increase your chances of a successful outcome. Recovering from back pain and surgery is an ongoing process. How fast you recover depends on the type of surgery you had, your commitment to working closely with your physical therapist, and moving and exercising correctly, as recommended by your surgeon.

In most cases, immediately after surgery, your heart and lung function will continue to be monitored, a drainage tube may have been left in your wound and your doctor may prescribe medicines to control pain and nausea. The average hospital stay for patients in the study used to evaluate the INFUSE® Bone Graft/LT-CAGE® Lumbar Tapered Fusion Device was just over 1 day for the laparoscopic surgical approach and 3 days for the open surgical approach.

A nurse will show you how to care for your wound before you are sent home and your doctor will discuss a program to gradually increase your activity. You may be required to wear a back brace for at least 1 month after surgery and you may be told to avoid repetitive bending, lifting, stooping, twisting and athletic activities until fusion has occurred. You may also be cautioned to avoid vibrations, like you might experience when driving a car, for a period of time after your surgery.

Contact your doctor immediately if:

» you get a fever
» the wound starts leaking fluids
» you have trouble swallowing or breathing
» you have trouble urinating
» you have new or increased back or leg pain or numbness

Your doctor will schedule office visits to check on how you are doing and see if anything else needs to be done. After surgery, your surgeon may refer you to a physical therapist who will teach you exercises to improve your strength and increase your mobility. The goal of physical therapy is to help you become active as soon as possible, using safe body movements that protect your back. This often includes abdominal strengthening exercises. You may also be taught different ways of standing, sitting, or lifting to avoid reinjuring your back.
Possible Complications

As with any surgery, spinal surgery is not without risk. A variety of complications related to the use of the INFUSE® Bone Graft/LT-CAGE® Lumbar Tapered Fusion Device can occur. These may occur singly or in combination. Some of these may be severe, affecting your outcome. You may also need to have additional surgery to correct these complications. Some of the possible complications include:

- allergic reaction to the implant materials;
- bending, breakage, loosening, and/or migration of the implants;
- bleeding, which may require a blood transfusion;
- bone fracture or failure to fuse;
- bone formation that is abnormal, excessive or in an unintended location;
- bowel, bladder or gastrointestinal problems;
- damage to nearby tissues;
- death;
- fetal development complications;
- infection;
- pain or discomfort;
- paralysis or other neurological problems;
- postoperative changes in spinal curvature, loss of correction or disc height;
- respiratory (breathing) problems;
- scar formation or other problems with the surgical incision;
- sexual dysfunction;
- side effects from anesthesia or the surgical approach;
- spinal cord or nerve damage;
- tears of the dura (a layer of tissue covering the spinal cord); or
- vascular problems other than bleeding.
Other Information

While this brochure has hopefully provided you with the information you need to make an informed decision about your treatment options, it is not intended to replace professional medical care or provide medical advice.

If you have any questions or need additional information about the INFUSE® Bone Graft/LT-CAGE® Lumbar Tapered Fusion Device, please call or see your doctor, who is the only one qualified to diagnose and treat your back. As with any surgical procedure, you should find a surgeon who is experienced in performing the specific surgery that you are considering.

Clinical Results

A total of 413 patients participated in a clinical study of the INFUSE® Bone Graft/LT-CAGE® Lumbar Tapered Fusion Device. The anterior open surgical approach was used for 143 patients and the anterior laparoscopic surgical approach was used for 134 patients. A group of 136 control patients were implanted with the LT-CAGE® Lumbar Tapered Fusion Device filled with bone taken from their hip, an alternative procedure.

The tables on the next page compare the success rates at 24 months after surgery for the three groups of patients:
Anterior open surgical approach groups (24 month evaluation)

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<thead>
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<th>Chance the investigational patients had a successful outcome</th>
<th>Chance the control patients had a successful outcome</th>
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<tbody>
<tr>
<td>Fusion</td>
<td>93%</td>
<td>88%</td>
</tr>
<tr>
<td>Pain and function</td>
<td>71%</td>
<td>71%</td>
</tr>
<tr>
<td>Neurologic status</td>
<td>81%</td>
<td>82%</td>
</tr>
<tr>
<td>Overall success</td>
<td>57%</td>
<td>57%</td>
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Anterior laparoscopic surgical approach groups (24 month evaluation)

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<th>Chance the investigational patients had a successful outcome</th>
<th>Chance the control patients had a successful outcome</th>
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<tr>
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<tr>
<td>Pain and function</td>
<td>83%</td>
<td>71%</td>
</tr>
<tr>
<td>Neurologic status</td>
<td>89%</td>
<td>82%</td>
</tr>
<tr>
<td>Overall success</td>
<td>68%</td>
<td>57%</td>
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The overall success rate describes the number of patients who had successful outcomes in fusion, pain and function and neurologic status. Also, to be considered an overall success, a patient could not have a serious complication associated with the device or have a second surgery because the first surgery was not successful.

Two years after their surgery, 82% of the investigational patients and 80% of the control patients said that it was definitely true or mostly true that they were satisfied with the results of their surgery.

All the patients in the study had blood collected to see if they generated antibodies (had an allergic reaction) to specific parts of the device – rhBMP-2 and bovine Type I collagen – as well as to human Type I collagen. Three patients had a response to rhBMP-2, 66 patients had a response to bovine Type I collagen and none had a response to human Type I collagen. When these results were compared to whether or not these patients had a successful outcome, no connection was seen between the antibody response and outcome.

A total of 145 investigational subjects were evaluated out to 6 years (72 months) after the initial surgery in a post-approval study. The patient population was obtained from participants in both the open and laparoscopic arms of the clinical trial. Control subjects were not followed in the post-approval study. Using the same criteria from the clinical study, the table below summarizes the success rates at 4 and 6 years after the initial surgery.

Success rates in investigational patients

<table>
<thead>
<tr>
<th></th>
<th>4-Year Evaluation</th>
<th>6-Year Evaluation</th>
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<tbody>
<tr>
<td>Fusion</td>
<td>98%</td>
<td>99%</td>
</tr>
<tr>
<td>Pain and function</td>
<td>82%</td>
<td>79%</td>
</tr>
<tr>
<td>Neurologic status</td>
<td>73%</td>
<td>81%</td>
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<tr>
<td>Overall success</td>
<td>61%</td>
<td>60%</td>
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BRIEF SUMMARY OF INDICATIONS, CONTRAINDICATIONS, AND WARNINGS FOR:

INFUSE® BONE GRAFT/LT-CAGE® LUMBAR TAPERED FUSION DEVICE
INFUSE® BONE GRAFT/INTER FIX™ THREADED FUSION DEVICE
INFUSE® BONE GRAFT/INTER FIX™ RP THREADED FUSION DEVICE

The INFUSE® Bone Graft/Medtronic Titanium Threaded Interbody Fusion Device is indicated for spinal fusion procedures in skeletally mature patients with degenerative disc disease (DDD) at one level from L2-S1, who may also have up to Grade I spondylolisthesis or Grade 1 retrolisthesis at the involved level. The INFUSE® Bone Graft LT-CAGE® Lumbar Tapered Fusion Device is to be implanted via an anterior open or an anterior laparoscopic approach. INFUSE® Bone Graft with either the INTER FIX™ or INTER FIX™ RP Threaded Fusion Device is to be implanted via an anterior open approach.

The INFUSE® Bone Graft/Medtronic Titanium Threaded Interbody Fusion Device consists of two components containing three parts—a metallic spinal fusion cage, a recombinant human bone morphogenetic protein and a carrier/scaffold for the bone morphogenetic protein and resulting bone. These components must be used as a system for the prescribed indication described above. The bone morphogenetic protein solution component must not be used without the carrier/scaffold component or with a carrier/scaffold component different from the one described in this document. The INFUSE® Bone Graft component must not be used without the Medtronic Titanium Threaded Interbody Fusion Device component.

NOTE: The INTER FIX™ Threaded Fusion Device and the INTER FIX™ RP Threaded Fusion Device may be used together to treat a spinal level. LT-CAGE® Lumbar Tapered Fusion Device implants are not to be used in conjunction with either the INTER FIX™ or INTER FIX™ RP implants to treat a spinal level.

The INFUSE® Bone Graft/Medtronic Titanium Threaded Interbody Fusion Device is contraindicated for patients with a known hypersensitivity to recombinant human Bone Morphogenetic Protein-2, bovine Type I collagen or to other components of the formulation and should not be used in the vicinity of a resected or extant tumor; in patients with any active malignancy or patients undergoing treatment for a malignancy; in patients who are skeletally immature; in pregnant women; or in patients with an active infection at the operative site or with an allergy to titanium or titanium alloy.

There are no adequate and well-controlled studies in human pregnant women. In an experimental rabbit study, rhBMP-2 has been shown to elicit antibodies that are capable of crossing the placenta. Women of child-bearing potential should be warned by their surgeon of potential risk to a fetus and informed of other possible orthopedic treatments. The safety and effectiveness of this device has not been established in nursing mothers. Women of child-bearing potential should be advised to not become pregnant for one year following treatment with this device.

Please see the package insert for the complete list of indications, warnings, precautions, adverse events, clinical results, definition of DDD, and other important medical information. The package insert also matches the sizes of those sized devices that are indicated for use with the appropriate INFUSE® Bone Graft kit.

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