ENTERYX™ PATIENT INFORMATION BROCHURE

Boston Scientific, Inc.

Enteryx™ Procedure for the Treatment of Symptoms of *Gastroesophageal Reflux Disease (GERD)*

This brochure is designed to help you and your doctor decide whether or not you should have the procedure to implant Enteryx™ for the treatment of your symptoms of *gastroesophageal reflux disease (GERD)*. Please read this entire brochure and discuss it thoroughly with your doctor, so that all of your questions have been answered before you agree to the

Boston Scientific, Inc.
551 Foster City Blvd., Suite G
Foster City, CA 94404
(650) 574-2867

Introduction

This brochure should help you decide whether or not to have the Enteryx procedure for the treatment of your symptoms of *gastroesophageal reflux disease* (*GERD*). Note: In this brochure, all *italicized* words are defined in the glossary at the back of the brochure.

Please read this brochure carefully and discuss the information with your doctor and his or her staff. Only your doctor can determine if you are a candidate for the Enteryx procedure. However, you are the only one who can decide whether this procedure is right for you. The information in this brochure should help you make your decision. You should discuss your decision with your doctor and make sure you have all your questions answered before having the procedure.

What is heartburn?

Your *esophagus* is the tube that carries food from your mouth to your stomach. In the lower part of your *esophagus*, near where it connects with your stomach, is a muscular ring called your *lower esophageal sphincter* (*LES*). The *LES* acts as a valve that allows food to pass into your stomach, but normally keeps stomach fluids and acid from going back up into your *esophagus*. If your stomach fluids and acid "back up" from your stomach into your *esophagus*, and irritate it, you may feel a burning sensation, called heartburn. Nearly half of Americans have some heartburn at least once a month. For some of those who have heartburn, it is severe or frequent enough to be called *gastroesophageal reflux disease* (*GERD*).

20

What are the symptoms of *GERD*?

GERD is backflow of acid from the stomach into the *esophagus* (reflux) that is frequent or severe enough to cause more significant problems and to be considered a disease or clinical condition. People who have *GERD* may have heartburn that is persistent, frequent, and severe enough to disrupt their daily activities. It may interrupt their sleep. Many people get heartburn sometimes, but they do not suffer the way acid *GERD* sufferers do. People with *GERD* have some or all of the following symptoms:

- Persistent heartburn (the most common symptom, a rising, burning sensation in the chest)
- Sour or bitter taste from regurgitation of stomach contents
- Difficult or painful swallowing
- Choking episodes at night
- Asthma
- Chronic sore throat
- Chronic cough
- Chest pain
- Laryngitis

Some people experience a worsening of symptoms after eating, or when bending over or lying down. Your doctor has determined through testing that your combination of symptoms is from *GERD* that requires treatment.

Besides the symptoms, can *GERD* cause other problems?

The fluids and acid that reflux into your esophagus can irritate and damage the lining, perhaps leading to inflammation (*esophagitis*) or ulcers. In severe cases, this damage can scar the *esophagus* lining and narrow it causing a *stricture* which may make it hard or painful to swallow. In severe cases this damage may lead to *Barrett's esophagus*, a condition where the lining of the esophagus changes and may over time lead to cancer of the esophagus. These findings are called "signs" of the disease since they can be seen.

What causes *GERD*?

In people who have *GERD*, the *LES* may relax more than it should and/or at the wrong times, allowing stomach fluids and acid to back up from the stomach into the *esophagus*. Unlike your stomach, your *esophagus* has little natural protection against these stomach fluids and acid. When these fluids and acid enter your *esophagus*, they cause heartburn or other *GERD* symptoms or signs.

What may make GERD worse?

Although some foods may make *GERD* symptoms worse, they are not the cause of *GERD*. Some of the most common aggravators include:

- Fatty foods
- Onion
- Coffee (decaf or regular)
- Citrus
- Peppermint
- Carbonated beverages
- Tomato
- Pepper/ spices
- Chocolate
- Alcohol

Several other conditions or activities can also make *GERD* symptoms more severe, such as:

- Smoking
- Lying down or sleeping after eating
- Obesity
- Pregnancy
- Taking certain medication such as calcium-channel blockers for high blood pressure

How does my doctor treat *GERD*?

Many people can get relief from *GERD* symptoms by changing their diet and/or using drugs. Drugs available to manage *GERD* symptoms slow the process the stomach uses to make acid and include *proton pump inhibitors* (*PPIs*), such as Prilosec® and Prevacid®, *H_2 receptor antagonists*, such as Pepcid®, Tagamet®, and Zantac®, and common antacids, such as Maalox® or Mylanta®. For those people who do not want to be on continual drug therapy, there are procedures for treating *GERD*, such as *anti-reflux surgery*. You should discuss the risks and benefits of the alternative *GERD* treatment options with your doctor.

What is Enteryx and how does the procedure work?

The Enteryx procedure may be an alternative treatment to long-term drug use or *anti-reflux surgery* for *GERD*. The Enteryx procedure is a minimally invasive treatment option, performed on an outpatient basis. Enteryx is a liquid polymeric material that is injected into the muscle of the *lower esophageal sphincter* (*LES*), through an *endoscope* (a tube used to look at

the *esophagus* and stomach) – Figures 1 and 2 depict the placement of the endoscope and the injection of Enteryx into the LES. Enteryx forms a soft, spongy permanent implant in the sphincter muscle. Enteryx is intended to reduce the symptoms of GERD by helping the *LES* keep stomach fluids and acids from backing up into the *esophagus*. It does not affect the stomach's ability to produce acid or other digestive fluids.

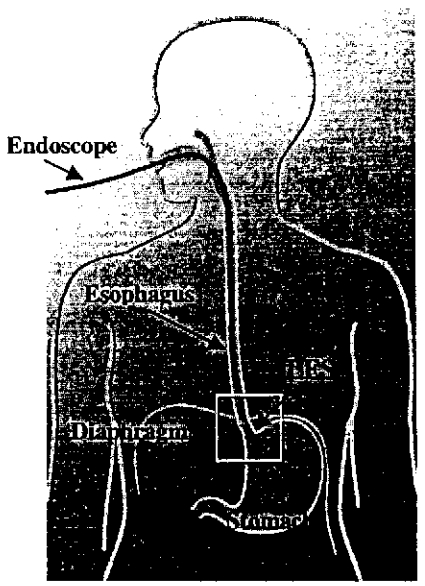

Figure 1

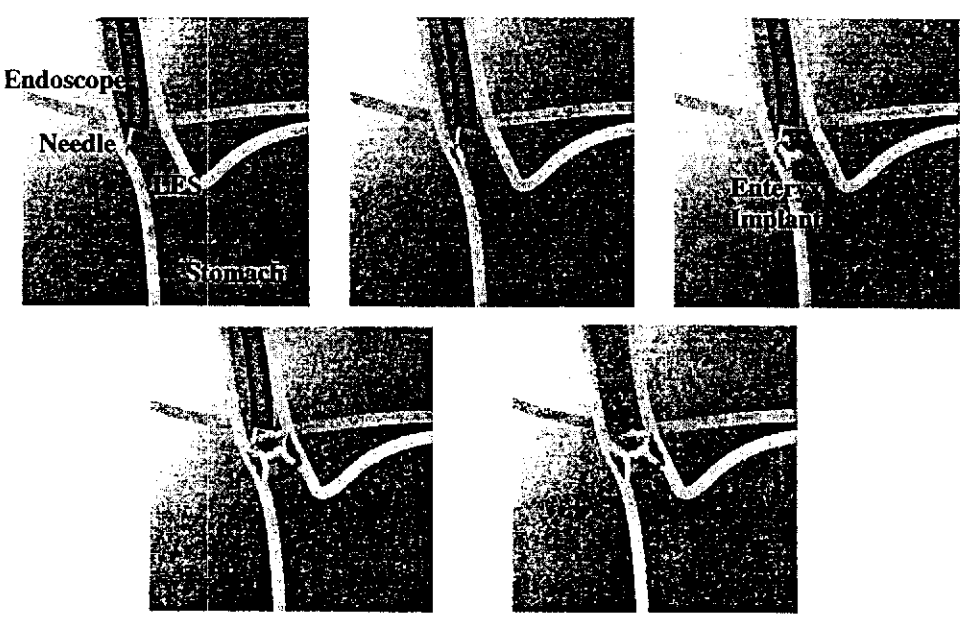

Figure 2

Is everyone a good candidate for Enteryx?

No. You should consider having this procedure done only if you have been diagnosed by a doctor as having persistent symptoms of *gastroesophageal reflux disease* (*GERD*) and you have needed the regular use of PPI medications. If these conditions apply, and your symptoms have responded well to one of the medications, then you may be a candidate for the procedure.

You should not have the procedure done if you have *varices* (distended veins) in the *esophagus*, particularly related to a condition called *portal hypertension* which is usually caused by chronic liver disease. If you are unsure whether you have these conditions or not, you should have your doctor evaluate you thoroughly.

You should thoroughly discuss the risks and benefits of the procedure if you have any of the following conditions because no one knows whether Enteryx is safe and effective in patients who have any of these conditions:

- *Barrett's epithelium* of the *esophagus*
- Severe inflammation of the *esophagus* (*esophagitis*)
- Narrowings of the *esophagus* (*strictures*)
- Poor muscle contractions of the *esophagus* (dysmotility)
- Cancer of the *esophagus* or stomach
- Large *hiatal hernia*
- *Scleroderma*
- GERD symptoms that are not relieved by *PPI* drugs
- Pregnancy

Patients who expect perfect results may be poor candidates. As with any procedure, the Enteryx procedure does not guarantee perfect results.

24

Will I need to do anything special before the procedure?

Your doctor may ask you to have some tests to evaluate your *esophagus* and how it works prior to having the procedure. Your doctor will most likely ask you to not eat anything after midnight on the day of the procedure, so that your stomach will be empty for the procedure. He or she may also give you antibiotics before the procedure if you have some medical conditions or have some types of artificial implants, such as mechanical heart valves.

Will I be asleep for the procedure?
Your doctor will discuss the choice of sedation with you. The most common form of sedation for an upper endoscopy is called "intravenous (I.V.) conscious sedation" which usually is a mixture of drugs that calm you and lessen your pain.

What will take place during the procedure?

After you have received the sedation, your doctor will place an *endoscope* down into your *esophagus*. The endoscope allows your doctor to see the lining of your *esophagus* and stomach. Your doctor will then find the place for injection. Your doctor will insert a small tube (catheter) with a needle on its end through the endoscope to the place where the injection is needed. Your doctor injects Enteryx material through the catheter and needle. Your doctor will use a special piece of x-ray equipment (fluoroscope) to see where the Enteryx is injected. The procedure typically takes less than one hour. After the procedure is completed, you will be monitored in a recovery room.

Will I go home the same day as the treatment?

The Enteryx procedure is intended to be performed on an outpatient basis so that you can go home the same day. If you receive sedation, you will need to arrange for someone to drive you home.

Will I have any discomfort or problems after the procedure?

A clinical study was performed in the U.S. and abroad on 85 patients who received treatment with Enteryx. Most patients in the clinical study had at least one side effect of the treatment.

About 9 of every 10 patients who had the treatment had chest pain behind the breastbone after the procedure. In about half of these cases, the pain disappeared in a week. Some, however, had pain for more than 2 weeks. Most of the patients in the study needed pain medications, either over-the-counter or prescription strength to treat their pain.

About 1 in every 5 patients (20%) had a hard time swallowing after the procedure, starting right away or several days later. In about half of those patients, their symptoms went away within 2 weeks. If you have a hard time

swallowing after the procedure, you may have to have another procedure to stretch the bottom of your *esophagus* (called dilation) to make it easier for you to swallow.

About 1 in 10 patients (10%) had a fever after the procedure. All fevers went away in less than 3 days. You may need antibiotics if you have a fever.

About 1 in 10 patients (10%) had a sore throat after the procedure. In most cases, this resolved within 1 week.

About 1 in every 16 patients (6-7%) had more gas (bloating, belching, flatulence) after the procedure. In most cases, this resolved within 2 weeks.

Some patients had nausea (with or without vomiting) as well as a garlic body-odor after the procedure but these signs and symptoms went away quickly.

You may have other side effects from this procedure. There are several that may happen with procedures like this one, even though they were not noticed in the 85 patients in this study:

- bleeding
- open sores in the *esophagus* (ulceration)
- material eroding through the *esophagus* wall (erosion)
- creation of a hole through the *esophagus* wall (perforation)
- creation of an abnormal tract from the *esophagus* to another organ (fistula)
- infection or inflammation in the chest cavity (mediastinitis)

What will I need to do during the days right after the procedure?

Your doctor will most likely have you continue taking your GERD drugs for several days after the procedure. Your doctor will likely ask you to start with soft food and expand your diet slowly as you see you can tolerate foods. Your doctor may give you drugs for pain and to treat infections.

Will I need to take any drugs for my reflux after the procedure?

The Enteryx procedure is intended to reduce or eliminate your dependence on GERD medications. However, some patients may still have to take drugs. In the clinical study, patients were assessed one year after the treatment. About 2 of every 3 patients (67%) were no longer taking any of

their *PPI* drugs and about 3 of every 4 (77%) of the patients were either off all of their *PPI*s or had reduced their daily requirements by at least one-half. About 1 of 4 patients (26%) who were able to reduce or eliminate their *PPI* use were taking over-the-counter antacids (e.g., Maalox®) or H_2 blockers (e.g., Pepcid®, Zantac®) intermittently. This is about the same number of patients who were taking supplementary over-the-counter antacids or H_2 blockers before the Enteryx procedure (22%). How much of their drugs they took after one year is unknown.

Will the procedure stop the reflux of acid or digestive juices into my *esophagus*?

Although you may have fewer and less severe symptoms and need fewer drugs, you may continue to reflux acid into your *esophagus*. In the clinical trial, a test was performed one year after treatment to assess how much acid refluxed into the *esophagus*. Although the esophagi of most patients were less exposed to stomach fluids and acid, compared to before Enteryx implantation when they were on no medications, nearly two-thirds of patients (60%) still had abnormal reflux.

Will inflammation that was already affecting the lining of my *esophagus* heal?

Maybe. Although your symptoms and requirements for PPI drugs may improve, stomach fluids and acid may continue to reflux into your *esophagus*, thus preventing the healing of inflammation. In the clinical study, some patients had low-grade inflammation in their *esophagus* prior to being treated with the Enteryx procedure. In about half (40-45%) of these cases, the inflammation looked like it was gone at 12 months. Some patients, however, developed inflammation after treatment. So a third (35-40%) of patients had some form of low-grade inflammation in their *esophagus* at 12 months. This is about the same number of patients who had some form of low-grade inflammation while on PPI medications prior to the Enteryx procedure (35 – 40%).

Can the Enteryx be removed?

No. Once your doctor injects Enteryx into the muscle of your lower *esophagus*, he or she cannot remove it.

Since Enteryx cannot be removed, does that mean that all of it stays where my doctor injects it?

Possibly not. In the clinical trial, after a year, about half (55%) of patients had all, or nearly all, Enteryx where the doctor injected it. About a third (20-30%) of patients had only about half of the injected material left where the doctor injected it.

If some patients did not have all of the material when later checked, where did it go?

The material most likely shed (sloughed) into the intestinal tract and passed out of the rectum.

Will I need more than one procedure to get the desired results and if so, how many and how often?

We do not know how long the result of a single Enteryx treatment will last. Your symptoms may increase or return sometime and you may need to restart your PPI drugs. You and your physician may determine, based on your symptoms, that you should have another treatment. We do not know whether Enteryx is safe and effective in this situation. You should discuss this with your physician before having any more Enteryx injections.

Will the Enteryx interfere with any surgery I may later have involving my *esophagus*?

We do not know whether a treatment with Enteryx will interfere with a future surgery of the *esophagus* or stomach. However, 4 of the clinical trial patients went on to have successful surgery for GERD.

What if I have other questions?

If you still have questions or concerns after you read this brochure, discuss them with your doctor before you agree to have this procedure. For more information about Enteryx you may call 1-800-813-7271.

GLOSSARY

Anti-reflux surgery: surgical procedure to reinforce the valve between the *esophagus* and the stomach.

Barrett's *esophagus*: the transformation of normal esophageal cells into abnormal cells. In some cases this can lead to cancer of the esophagus.

Endoscope: a flexible tube and optical system for observing the inside of the esophagus and stomach.

Esophagus: the muscular tube that carries swallowed foods and liquids from the mouth to the stomach.

Esophagitis: inflammation or irritation to the lining of the esophagus. It is often caused by reflux of acid and other digestive fluids from the stomach.

Gastroesophageal reflux disease (GERD): backflow of acid from the stomach into the *esophagus* (reflux) that is frequent or severe enough to cause more significant problems and to be considered a disease or clinical condition.

H_2 receptor antagonists: a type of drug to manage the symptoms of GERD by decreasing or eliminating the production of gastric acid. Examples include Pepcid® and Zantac®.

Hiatal hernia: the protrusion of the stomach upward into the chest cavity.

Heartburn: a burning sensation in the retrosternal area caused by reflux of acid contents of the stomach into the lower *esophagus*.

Lower esophageal sphincter (LES): a valve located at the junction of the *esophagus* and stomach that relaxes to permit passage of food, and contracts to prevent backup of stomach contents.

Portal hypertension: increased blood pressure in the vein draining into the liver, often caused by chronic liver disease or cirrhosis.

Proton pump inhibitors (PPIs): a type of drug to manage the symptoms of GERD by decreasing or eliminating the production of gastric acid. Examples include Prilosec® and Prevacid®

Scleroderma: a chronic, autoimmune disease of the connective tissue often affecting the skin, joint, kidneys, and lungs in addition to the esophagus.

Stricture: a narrowing within the *esophagus*

Varices: dilated blood vessels within the wall of the stomach or *esophagus*. These are often the result of portal hypertension (see above).