

# **Synergo<sup>®</sup> SB-TS 101.1 Device**

Understanding Superficial Bladder Cancer, Synergo Therapy, and Treatment Options

## **Patient Information Guide**

### **Introduction**

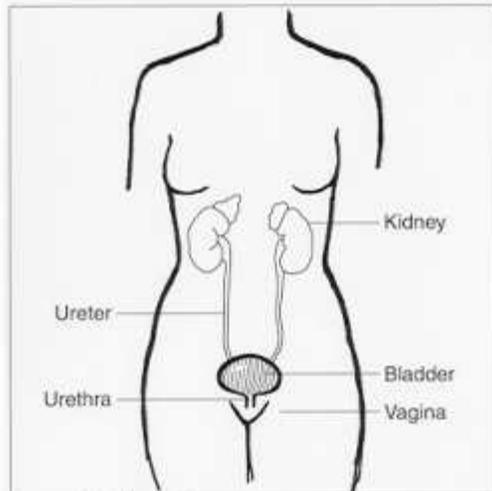
You have an important role to play in order to ensure that your procedure will be as successful as possible. Read all of this booklet, cooperate with your physician and be sure to do everything you need to do as part of the patient/medical team.

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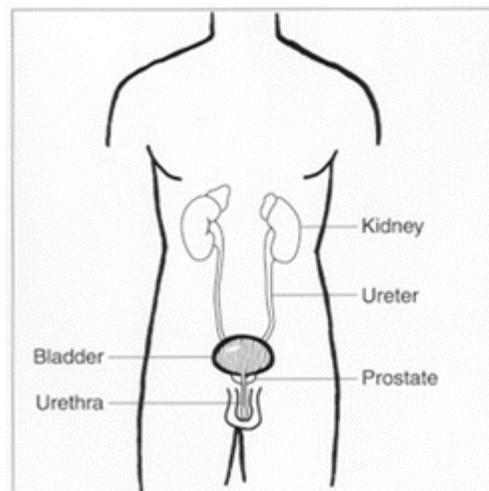
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### **The Urinary Bladder and Urinary System**

The bladder is a hollow organ in the lower [abdomen](#). It stores [urine](#), the liquid waste produced by the [kidneys](#). Urine passes from each kidney into the bladder through a tube called the [ureter](#). When the bladder is full, the muscles in the bladder wall tighten to perform urination. Urine leaves the bladder through another tube, the [urethra](#). An outer layer of muscle surrounds the inner lining of the bladder. The inner lining of the bladder is composed of several layers of transitional cells.



Female Urinary Tract



Male Urinary Tract

## Bladder Cancer

If you or a member of your family has been diagnosed with superficial bladder cancer (STCCB or superficial transitional cell carcinoma of the bladder), this booklet may answer some of your questions about this disease. If your doctor has recommended a surgical procedure called transurethral resection (TUR) followed by prophylactic treatment with intravesical instillations, this booklet will also answer some of your questions about this treatment.

## Superficial Bladder Cancer

There are different types of bladder cancer: superficial bladder cancer and invasive bladder cancer. About 90% of all bladder cancers are the “Transitional Cell Carcinoma” (TCC) type. This type of cancer starts in the epithelial cells (the internal lining) of the bladder wall. When the tumor is limited to this layer, it is called “superficial” urinary bladder cancer. Superficial bladder cancer tends to return (recur) after surgery and treatment. In most cases, the subsequent tumor is also a superficial bladder cancer. A tumor that penetrates into the muscular layer of the urinary bladder is called “invasive” urinary bladder cancer.

## What Causes Bladder Cancer?

No one knows the exact causes of bladder cancer. However, it is clear that this disease is not contagious. No one can “catch” cancer from another person.

## Risk Factors

People who get bladder cancer are more likely than other people to have certain risk factors. These risk factors include male gender (the male:female ratio is 3:1), smoking, irradiation of the pelvis, occupational exposure to chemical dyes (especially Aniline fabric dyes), white race, and increasing age.

Cancer of the urinary bladder is the fourth most common type of cancer among men, and the eighth most common among women.

## **Symptoms of Bladder Cancer**

The symptoms of urinary bladder cancer are not always noticeable, but they usually include:

- Presence of visible blood in the urine (hematuria). Blood in the urine is usually painless.
- Blood traces in laboratory tests of urine.
- Urgency (inability to postpone urination) and frequency (urinating often).
- Discomfort during urination.

These symptoms may also be caused by other diseases such as: urinary tract infection, urinary bladder stones, benign tumors, and other problems. Only a physician can interpret the meaning of these symptoms. Therefore, if you have any of these symptoms, you should see a doctor.

## **How is Bladder Cancer Diagnosed?**

You may have experienced symptoms that caused you to seek your doctor's attention. In order to identify the cause of the symptoms, the doctor asks questions about your health and performs a physical examination. In addition, urine samples are sent to a laboratory to check for blood and cancer cells. A bladder cystoscopy may be required.

## **What is Bladder Cystoscopy?**

This procedure enables the doctor to see inside the urinary bladder. This examination is performed with a fiber optic instrument called a cystoscope. During this procedure, it is possible to take tissue samples (biopsies) of the bladder wall for examination under the microscope by a pathologist.

## **Performing a Biopsy and Other Examinations**

If during cystoscopy, a certain area inside your bladder looks suspicious for being abnormal, a tissue sample (biopsy) is usually necessary to determine the nature of this tissue. The sample is then sent to a pathologist, for evaluation. If the tissue is diagnosed as cancer, then the tumor grade and the extent to which it has penetrated the bladder wall (stage) are determined. The physician may refer the patient for additional medical examinations including CT, MRI, ultrasound, and x-rays of the urinary tract (IVP).

## **Can Bladder Cancer Be Treated?**

Most patients with bladder cancer receive a combination of therapy that includes surgery or other means of tumor removal. Sometimes this is followed by drug therapy to reduce the chance of recurrence.

The doctor recommends the type of treatment based on the tumor's characteristics and the patient's condition. If there are several treatment options, the decision will be taken jointly by the doctor and the patient.

## **Transurethral Resection of Bladder Tumors**

Surgery is a common form of treatment for bladder cancer. The most common procedure for superficial bladder cancer is called TURBT, Trans-Urethral Resection of Bladder Tumors. This procedure surgically removes all tumors (under partial or general anesthesia). This procedure is performed through the urethra, with no need to open the abdomen.

## **Other Treatment Options**

If a recurrent single small tumor is present, it is possible to fulgurate (destroy) its root by laser or electrical current during the cystoscopy (TUF). If there are numerous superficial tumors, the doctor may need to perform a series of TURBTs or an extensive surgical operation to partially or completely remove the urinary bladder (cystectomy). In case of penetration into the muscle tissue (“invasive” cancer), a complete radical removal of the bladder is often required and another route for draining urine from the body is created.

## **When Bladder Cancer Returns (Recurrence of Bladder Cancer)**

Despite surgery and additional treatments used, the percentage of tumor recurrence and disease progression has been high among certain patient sub-groups. Superficial bladder cancer tends to occur again and again.

## **Preventive Treatment (Prophylactic Instillations)**

After having diagnosed the type of tumor and evaluated the chances of its recurrence, a treatment is usually administered to reduce the likelihood of recurrence by flushing the bladder with various chemically or biologically active materials (bladder instillations). Flushing with chemotherapeutic materials is intended to destroy cancer cells that were not removed during the operation or that have a high malignant potential. Biological flushing materials, such as BCG (a weakened cow tuberculosis bacteria: Bacillus Calmette-Guerin) and others, are intended to create an immune response in the urinary bladder lining that would destroy cancer cells.

## **How is Preventive Treatment Performed?**

A catheter is inserted into the urinary bladder through the urethra. Flushing of the bladder with chemotherapeutic materials or immunotherapeutic drugs is then performed. The drug is introduced into the bladder cavity for a certain period of time and expelled at the end of the procedure. This procedure is repeated one or more times a week for several weeks and then one or more times a month for several months.

## **What is Synergo Therapy and How Does It Work?**

Synergo therapy involves local heating (hyperthermia) of the internal bladder wall while flushing the bladder at the same time with a chemotherapy drug called Mitomycin C. Mitomycin C is an antibiotic that has antitumor activity. The combination of local heat and Mitomycin C has been shown to reduce the recurrence of superficial bladder cancer better than using Mitomycin C alone.

The Synergo consists of two parts:

- A console unit that the doctor uses to control and monitor treatment parameters such as the amount of heating applied to the bladder walls, the flow rate of the circulating drug, the bladder wall temperature during treatment and others.
- A Synergo Kit including Mitomycin C and a catheter-tubing line set. The catheter is inserted into the bladder through the urethra. This catheter contains an element, which heats the bladder. The catheter is connected via the tubing line set to a circulation unit, which circulates the Mitomycin C into and out of the bladder at the same time.

The Synergo console unit monitors the treatment so that the required bladder temperature is maintained throughout the treatment.



*Figure A – Synergo Device*

Hundreds of patients have been treated with Synergo technology and the treatments have shown impressive results. The Synergo treatment has significantly reduced post-surgery tumor recurrence ratios. The recurrence rate dropped from 58% to 17% in a two-year follow-up, and from 65% to 26% in a five-year follow-up compared to treatment with chemotherapy alone.

### **When Should Synergo Therapy Not Be Used (Contra-indications)?**

- Your doctor cannot safely treat you with Synergo if you are incapable of feeling pain in the bladder area. If you have had surgery or radiation therapy near your bladder

before or if you are put to sleep (general anesthesia) for this procedure, you may have less ability to sense pain and this procedure would not be safe for you.

- Your doctor cannot safely treat you if you have an implanted or carry-on electronic device such as a cardiac pacemaker, a cardioverter defibrillator, or a neurostimulator (including electronic incontinence devices) because these devices may not operate properly during the procedure. These devices would need to be temporarily turned off during the treatment, if possible.
- Your doctor cannot safely treat you if you have metal pins or implants near your bladder, stomach, lower trunk, back, hips, upper leg bone (femur), or knees. These implants may heat up during this procedure.
- Your doctor cannot safely treat you if you have an infection in the bladder, narrowing of the urinary canal (urethral stricture), connection between the urinary canal and other body areas unrelated to the urinary system (fistula), if your bladder was partially removed during surgery, if you ever received pelvic radiation, or if your bladder volume is too small to maintain the solution.
- Your doctor cannot safely treat you if you have fever, or if your body temperature is not between 35.5 and 37.5°C before treatment.
- This treatment is not suitable for you if this is your first episode of the disease and you have a single tumor in your bladder, defined as TaG1 or; if you have a tumor stage greater than T1 (i.e. T2, T3 or T4).
- Your doctor cannot safely treat you if you have demonstrated sensitivity or are allergic to Mitomycin C. See drug insert supplied with the Synergo Kit for Mitomycin C contraindications.

### **What Are the Risks and Potential Benefits of Treatment with Synergo?**

Synergo technology has been checked and shown to be safe in a number of clinical studies. The adverse events of the treatment are usually mild and temporary. These adverse events include local pain, temporarily passing blood in the urine, a burning sensation during urination, and urgency and frequency of urination. You may have an allergic reaction to the chemotherapeutic drug – Mitomycin C.

The adverse events are usually mild, well tolerated, and disappear within 48-72 hours after the treatment. These adverse events are not dangerous to you.

Your bladder or urinary canal may shrink. In a clinical trial, two patients (out of 42 patients) had long-term adverse effects (reduced bladder volume).

You are having this procedure to reduce the chance that your cancer will return. By using this treatment, you will likely have a better chance that your cancer will not return, compared to using only chemotherapy. In the clinical trial, the cancer returned within 2 years in about a sixth of the patients who had the Synergo treatment. By contrast, the cancer returned within two years in over half of the patients who had chemotherapy alone.

### **Other Treatment Options**

Other options for the treatment of superficial bladder cancer include:

- No preventive measures following surgical removal of tumors.
- Intravesical instillations of chemotherapeutic drugs such as Mitomycin C or Thiotepa.
- Biological therapy such as BCG.
- Systemic (whole body) chemotherapy (rarely used)
- Radiation therapy (rarely used).

### **Preparing for Synergo Therapy**

On the day of your procedure:

- Reduce the amount of water and beverages that you drink.
- Avoid drinks, foods, and medicines that make you urinate more (diuretics) such as tea, coffee, cola with caffeine, beer, other alcoholic drinks, and watermelon. If you drink too much or consume diuretics, the increased urine production may lower the efficiency of the chemotherapeutic drug.

Tell your doctor if you have or have had any of the following:

- A defibrillator or neurostimulator because these devices may not act properly during the procedure.
- Any other surgery or radiation treatment because they may make this treatment more difficult or hazardous.
- Any prostheses, such as joint replacements or pins, because they may overheat during this procedure.
- Any intolerance (allergy or sensitivity) to Mitomycin C.

### **How is Treatment with Synergo Performed?**

Trained medical personnel perform the treatment in an outpatient clinic where the Synergo is located. You will be prepared for the treatment while you are lying on your back. The tip of your urinary canal will be cleaned. Using an anesthetic gel, the lubricated Synergo catheter will be inserted through the urinary canal (urethra) into your bladder. You will lie on your back during the entire session, which lasts about an hour. Each treatment is composed of two 30-minute cycles using a fresh Mitomycin C solution for each cycle.

*Catheter inserted through the urethra*

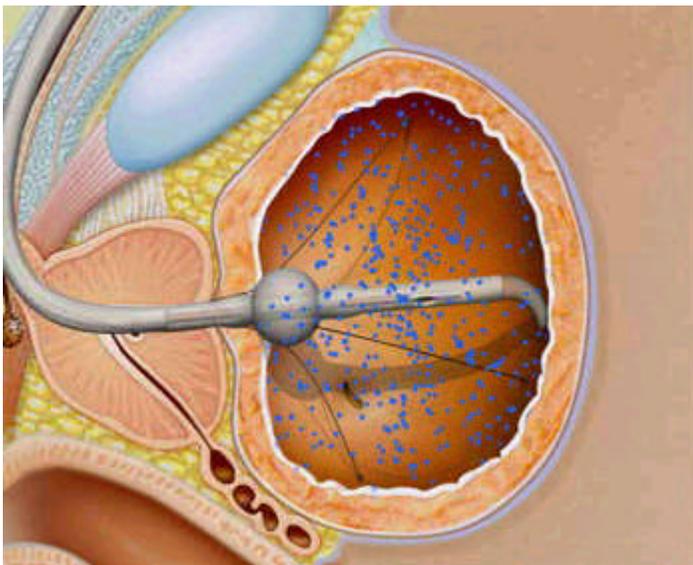


The Synergo catheter performs three main functions:

- Uniform heating of the bladder wall by means of a small antenna emitting radio-frequency (microwave) radiation.
- Temperature monitoring by sensitive thermocouples at several places on the bladder wall.
- Circulation of the cooled chemotherapeutic drug into and out of the bladder.

*Catheter situated in the bladder*

*Heat and chemotherapy are uniformly distributed*



Synergo treatment may cause local pain or discomfort, temporary bleeding, or a burning sensation along the urethra. These symptoms are mild and usually go away after treatment. Analgesic therapy during Synergo treatment is recommended to relieve these symptoms.

### **How Long Does the Treatment Take?**

Each treatment lasts about one hour. You will not be hospitalized because the treatments are performed on an ambulatory (walk in – walk out) basis. After treatment, you can resume your daily activities. The complete series of treatments requires 8 sessions once a week followed by 4 sessions once a month. Altogether the Synergo treatment takes about 6 months.

### **What Happens After The Synergo Procedure?**

It is very important to follow the post-procedure instructions and arrive for your follow-up visits.

### **Post-Procedure Instructions**

Be sure to follow the instructions of your doctor and report any adverse events to your physician as soon as possible. Drink normal amounts of liquids. Rinse your hands and genitals with soap and water after you urinate for the first two days after the procedure. This will help avoid infection and keep urine containing Mitomycin C from irritating your skin.

### **Follow-up Visits**

Be sure to go to all of your appointments.

After treatment for urinary bladder cancer, you will require close medical monitoring. Routine cystoscopies and other tests may be required. Follow-up care is needed in order to identify any recurrence of the disease as early as possible. Initially, the frequency of follow-up visits is high (every three months). Later, the visits may become less frequent. Between checkups, you should report any health problems as soon as they appear. The follow-up visits are very important, and you must do your best to comply with the recommended schedule.

### **Lifestyle Changes**

You should avoid excessive fluid intake before each treatment session. During the two days after each session, wash hands and genitals after urination, and use a condom during sexual intercourse.

Refrain from smoking and drink an adequate amount of water

### **Summary**

To ensure that your procedure will be successful you should read this booklet carefully, cooperate with your physician, and do everything you need to do as part of the patient/medical team. If you have any questions, contact your physician to discuss them. We want you to get the most benefit from your treatment and join the thousands of people who had superficial bladder cancer but are now leading healthy, productive lives.

For more information about patient education, visit our website:

[www.medical-enterprises.com](http://www.medical-enterprises.com)

## **Glossary**

Ambulatory – walk in, walk out basis (non hospitalization)

Analgesic – pain relief medication

BCG – live weakened tuberculosis bacteria that activates the immune system

Benign – not cancerous

Bladder – the organ that holds urine

Biopsy – tissue sampling for microscopic examination

Cancer – abnormal cell division that spreads without control

Carcinoma – malignant tumor, cancer

Catheter – a tube used to put fluids into or take fluids out of the body

Chemotherapy – medication used to destroy cancer cells

Contraindications – situations when a treatment should not be used

Clinical trial – a research study that involves people

CT – a series of detailed pictures of areas inside the body (Computerized Tomography)

Cystectomy – surgical removal of the bladder

Cystoscopy – a method of viewing the bladder using fiber optic technology

Diagnosis – reason for symptoms

Fulguration – destruction of tissue using an electric current or laser

Grade – indicates how closely a cancer resembles normal tissue of the same type, and the cancer's probable rate of growth

Hyperthermia – heating

Instillation - flushing

Intravesical – inside the bladder

Invasive - penetrating

IVP – an x-ray of the urinary system taken after injecting a dye into your vein

Malignant – cancerous

Mitomycin C – a drug used to destroy cancer cells

MRI – a procedure that uses a magnet to create pictures of areas inside the body

Pathologist – a doctor who identifies disease by studying cells and tissues under a microscope

Progression – worsening of cancer stage

Prophylactic - preventive

Recurrence – when cancer comes back after removal

Resection - removal

Risk factor – something that increases the chance of developing a disease

Adverse events – problems that may occur when undergoing treatment

Stage – the extent of the cancer

Superficial – on the inner lining, non-invasive into the muscle

Surgery – an operation

Transitional cells – cells lining certain organs such as the bladder, ureter, kidney and urethra

Transurethral resection – surgical procedure performed through the urethra

Tumor – an abnormal growth of tissue

Ultrasound - a procedure that uses sound waves to create pictures of areas inside the body

Ureter – the tube that carries urine from the kidneys to the bladder

Urethra – the tube that carries urine from the bladder outside the body