

UROPLASTY, INC.
MACROPLASTIQUE® IMPLANTS
INSTRUCTIONS FOR USE

SYMBOL DESCRIPTION

-  **Consult Instructions for Use**
 -  **Do not reuse**
 -  **Use by**
 -  **Sterilized using irradiation**
 -  **Store at room temperature**
 - REF** **Product reference number**
 - LOT** **Lot Number**
 -  **Latex-free**
- Rx Only** **Caution: Federal law (USA) restricts this device to sale by or on the order of a physician trained in diagnostic and therapeutic cystoscopy.**

PRODUCT DESCRIPTION

Macroplastique® Implants is a sterile, nonpyrogenic, latex-free, injectable tissue bulking agent comprised of flexible, soft textured implants of heat-vulcanized polydimethylsiloxane (a solid silicone elastomer) suspended in a bio-excretable polyvinylpyrrolidone (PVP) carrier gel. When implanted in the urethral wall between the mid-urethra and the bladder neck, the implants bulk tissue and create coaptation of the urethra.

Macroplastique is supplied sterile in a pre-filled polypropylene syringe containing approximately 2.5 ml of product. The Macroplastique product is implanted using an administration device and an endoscopic injection needle recommended by Uroplasty, Inc.

Macroplastique is a biocompatible, nonresorbable implant that allows tissue healing to occur. The synthetic implants remain in place at the implantation site as a result of the naturally occurring tissue response. The carrier gel is exchanged for tissue fluids containing host fibroblasts that subsequently deposit a collagen matrix around the individual implants, as well as around the periphery of the implanted material. After the exchange, the carrier gel is removed by the reticuloendothelial system and excreted unmetabolized from the body through the kidneys.

INDICATIONS FOR USE

Macroplastique is indicated for transurethral injection in the treatment of adult women diagnosed with stress urinary incontinence (SUI) primarily due to intrinsic sphincter deficiency (ISD).

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CONTRAINDICATIONS FOR USE

Macroplastique must not be used in patients with:

- Acute urogenital tract inflammation or infection.
- Fragile urethral mucosal lining (e.g., post radiation therapy, post-surgery to the bladder neck).

WARNINGS

- Do not inject Macroplastique into blood vessels. This may cause vascular occlusion or embolic phenomena.
- Avoid using Macroplastique in patients with non-viable tissue, e.g. history of significant pelvic irradiation, multiple pelvic surgeries, etc. Scar tissue and significantly compromised tissue will not coapt appropriately.
- Do not use within 12 weeks of a previous Macroplastique treatment or within 12 weeks of a previous sling placement. Reimplantation prior to 12 weeks may not allow enough time for the initial inflammatory response to subside.
- Macroplastique should not be used in patients with obstructive conditions, such as bladder neck or urethral strictures, until such conditions have been corrected. Use of Macroplastique in patients with uncorrected urinary obstruction may cause occlusion of the urethra.
- Overcorrection using Macroplastique may lead to urinary obstruction.
- Macroplastique should only be used by someone properly trained in diagnostic and therapeutic cystoscopy.

PRECAUTIONS

- Safety and effectiveness of periurethral injection of Macroplastique have not been established.
- Safety and effectiveness of Macroplastique in men have not been established.
- The long-term safety and effectiveness of Macroplastique treatment have not been established.
- The safety and effectiveness of Macroplastique have not been established in patients with any of the following conditions:
 - Urinary incontinence due to uncontrolled bladder instability or hyperreflexia,
 - Neuropathic bladder,
 - Prolapsed bladder,
 - Nocturnal enuresis (bed wetting),
 - Overflow incontinence,
 - Functional incontinence, or
 - Morbid obesity
- The safety and effectiveness of Macroplastique in patients who are pregnant or lactating have not been established.
- The effect of Macroplastique on subsequent pregnancy and delivery, and the impact of subsequent pregnancy on the effect of Macroplastique, is unknown. Therefore, the risks and benefits of the device in women of childbearing potential should be carefully assessed.
- The safety and effectiveness of more than one retreatment with Macroplastique, and retreatment administered less than 12 weeks after the initial treatment, are unknown.
- Patients should be counseled that a repeat Macroplastique injection procedure may be required to achieve dryness or a satisfactory level of improvement in incontinence.
- Dysuria, hematuria, and frequency of micturition are to be expected post-treatment. If any of these conditions persist past 48 hours, the patient should be instructed to contact the treating Physician immediately.
- Post-treatment retention may occur which may necessitate intermittent catheterization. If the patient remains unable to void freely, continued intermittent catheterization may be necessary.
- To reduce the risks of infection and bleeding, the usual precautions associated with cystoscopic procedures should be followed.

- There are risks associated with any implant procedure including, but not limited to, complications associated with anesthesia and patient tolerance to implanted foreign material.
- Macroplastique is supplied radiation sterilized in a sealed package and is for single use only. Do not reuse, reprocess, or resterilize.
- Do not use Macroplastique product if the integrity of the syringe or outer packaging has been damaged or compromised.

ADVERSE EVENTS

The Macroplastique clinical trial involved 186 Macroplastique treatments in 122 subjects. A total of 303 treatment related adverse events (including transient symptoms) in 96 patients were reported in the Macroplastique arm. In order to reduce potential bias, all genitourinary adverse events were analyzed as treatment related regardless of time period reported (i.e., a urinary tract infection occurring at either 1 month or 12 months post treatment was considered a treatment related adverse event). The severity of treatment related adverse events was noted as "serious" or "not serious"; there were no serious treatment related adverse events reported in the Macroplastique arm. There was one death of a Macroplastique patient due to respiratory failure secondary to cancer, which was determined to be not related to the treatment.

In the randomized trial comparing Macroplastique to a control urethral bulking agent, the proportion of patients experiencing treatment related and/or genitourinary adverse events were similar across treatment groups with no significant differences found either overall or for any specific event. The incidence for the most prevalent treatment related adverse events reported in the multicenter evaluation is listed in Table 1.

Table 1: Number (%) of Subjects Reporting Treatment Related Adverse Events

Event Category	Macroplastique (n = 122)
Post-procedure catheterization (see paragraph below)	53 (43.4%)
Urinary tract infection (UTI) (including bladder infection)	31 (25.4%)
Urinary retention	26 (21.3%)
Dysuria	23 (18.9%)
Hematuria (including transient hematuria)	19 (15.6%)
Pain at implantation site	16 (13.1%)
Frequency	14 (11.5%)
Urgency	14 (11.5%)
Slowed urine stream	9 (7.4%)
Incomplete bladder emptying	7 (5.7%)
Urge incontinence	7 (5.7%)
Hesitancy	6 (4.9%)
Vaginal bleeding	4 (3.3%)
Yeast infection	4 (3.3%)
Bladder pain	3 (2.5%)
Increased/worsening nocturia	3 (2.5%)
Overactive bladder (OAB)	3 (2.5%)
Cystitis	3 (2.5%)
Number of Other Events ¹	29(N/A)

¹ "Other" treatment related adverse events in Macroplastique subjects, occurring at frequencies of < 2%, were as follows (listed alphabetically): abdominal pain, allergic reaction – control bulking agent skin test, bolus ruptured, change in urine stream, diarrhea, dizziness, filling defect, headache, increased AM urge incontinence, joint pain during urination, nausea, partial urethral closure, pelvic tenderness, perineal discomfort/pain, sleep disturbance, spotting between periods, tiredness, urethral erosion, uterine polyp, vaginal discharge, vaginal itching, visible product, and vulvar lesion.

Placement of an in/out catheter immediately post-procedure is commonly performed and was included in the clinical trial protocol as a way to drain the bladder at the end of the procedure. The duration of placement was brief and did not disrupt the newly placed bulking agent bolus. Five subjects (4 Macroplastique,

1 Control) were sent home with an indwelling catheter, which was removed the next day. An additional Macroplastique subject had a Foley catheter placed for 48 hours to address her retention. While the proportion of Macroplastique patients with in/out catheters was statistically higher when compared with Control, this event is not clinically significant, particularly since the protocol allowed for this practice.

Two cases of urethral erosion were observed in the Macroplastique arm. Neither case was reported due to patient complaint, but rather was observed during regular patient follow-up visit by study-related cystoscopy. One of the cases resolved spontaneously while the other case's resolution status was not specifically evaluated on follow-up cystoscopy and is listed as unknown. The patient in each case received subsequent reimplantation with Macroplastique.

Excluding transient symptoms reported during treatment, a total of 154 treatment related/genitourinary adverse events reported for Macroplastique subjects were analyzed for time-to-onset and resolution. This information was not typically reported for transient symptoms. Of these 154 events, 89 (57.8%) occurred within 30 days of the most recent treatment date, 35 (22.7%) occurred more than 30 days from the most recent treatment date and 30 (19.5%) had an unknown onset date. The resolution status at the time of database closure of the 154 treatment related events was as follows: 124 resolved (80.5%), 15 were reported as ongoing (9.7%) and 15 had unknown resolution status (9.7%). Of those reported as resolved, 73 resolved within 30 days of onset, 30 resolved after more than 30 days from onset and 21 had unknown onset dates/resolution dates. The 30 events reported as ongoing or unresolved at closure are: abdominal pain (1), bladder infection (1), bladder infection symptoms (1), change in urine stream (2), dysuria (2), filling defect (1), frequency (1), hesitancy (2), incomplete bladder emptying (2), overactive bladder (1), pelvic tenderness (1), spotting between periods (1), sleep disturbance (1), slowed urine stream (2), tenderness at implant site (1), transient hematuria (2), urethral erosion (1), urgency (3), urge incontinence (3), vaginal discharge (1).

Potential Adverse Events

Although not reported in the clinical study, potential adverse events which may occur include erythema, embolic phenomena, granuloma, migration, and vascular occlusion.

CLINICAL STUDY

Study Design

The Macroplastique clinical study was a prospective, multicenter, single-blind, randomized controlled trial. This study was designed to evaluate Macroplastique in a pivotal trial and was conducted to determine the safety and effectiveness of Macroplastique implants as a minimally invasive, transurethral endoscopic treatment of female stress urinary incontinence (SUI) primarily due to intrinsic sphincter deficiency (ISD).

To be eligible for enrollment, subjects were required to be adult women diagnosed with SUI primarily due to ISD, and to have viable mucosal lining and normal bladder capacity. Subjects with urinary tract infections, uncontrolled bladder instability, high post void residual urine volume, prolapse greater than stage II, confounding bladder pathology, as well as subjects who were pregnant or morbidly obese were excluded.

Two hundred sixty subjects were enrolled in the study, of which, two hundred forty-eight patients were randomized 1:1 and treated with either Macroplastique or a Control device (a commercially available absorbable urethral bulking agent). Two hundred forty-seven subjects were treated in accordance with their randomization.

Only one subsequent treatment was allowed. If performed, the second treatment took place within one month after patients' 3-month follow-up in both study arms.

Evaluation of study endpoints was performed 12 months after the patient's last treatment.

Primary Effectiveness Endpoint

Continence status was determined by evaluating patients prior to treatment through twelve months follow-up using the Stamey incontinence grading described as follows:

- Grade 0: Continent or dry
- Grade 1: Patient loses urine with sudden increases in abdominal pressure, but never in bed at night
- Grade 2: Patient's incontinence worsens with lesser degrees of stress, such as walking, standing erect from a sitting position, or sitting up in bed
- Grade 3: Patient has total incontinence and urine is lost without any relation to physical activity or position

The primary endpoint in the study was the percentage of patients demonstrating improvement of at least one Stamey Grade from baseline to 12 months after last treatment. The primary endpoint was analyzed using a non-inferiority hypothesis with a 15% delta for Macroplastique versus Control. Pad weight, dryness, and quality of life (I-QoL) were assessed as secondary endpoints at 12 months.

Safety Endpoint

All adverse events associated with the clinical study were summarized and classified according to severity, duration, and relationship to the device and/or the treatment. In order to minimize potential bias, all genitourinary adverse events were conservatively classified as treatment related.

Results

All study objectives were met in the Macroplastique trial. Tables 2 through 5 present data from the multicenter clinical trial for the Intent-to-Treat and Per Protocol patient populations. The Intent-to-Treat population includes all 260 subjects enrolled in the study (130 Macroplastique and 130 Control); the Per Protocol population excludes those subjects who were neither implanted nor followed and also excludes 1 subject treated contrary to her randomization for 122 Macroplastique and 125 Control subjects. Patients whose outcomes were unknown at 12 months are automatically analyzed as failures using both the Intent-to-Treat and Per Protocol analysis methods.

Table 2: Patient Baseline Information

PATIENT BASELINE INFORMATION	MACROPLASTIQUE	CONTROL
Mean age (range)	60.5 years (27-85)	61.6 years (34-90)
Mean duration of incontinence	11.3 years	11.0 years
Patients with baseline Stamey grade = 1	30%	39%
Patients with baseline Stamey grade = 2	68%	54%
Patients with baseline Stamey grade = 3	2%	7%
Baseline pad weight	28 grams	28 grams
Baseline I-QoL score	49.3	48.2

Table 3: Treatment Information

TREATMENT INFORMATION	MACROPLASTIQUE	CONTROL
Mean number of treatments per patient during study	1.5	1.6
Patients receiving a single treatment	47.5%	41.3%
Patients receiving two treatments	52.5%	58.7%
Mean initial volume injected per patient	4.6 ml	4.6 ml
Mean retreatment volume injected per patient	4.3 ml	4.5 ml
Mean total volume injected per patient	6.8 ml	7.2 ml

Analysis of the primary endpoint demonstrated that Macroplastique was statistically non-inferior to the Control bulking agent for the endpoint of improvement in Stamey Grade at 12 months, where 'non-inferior' is defined statistically as the study arm is not worse than the control arm (with a tolerable margin of 15%).

Table 4: Key Effectiveness Results at 12 Months (Intent-to-Treat)

	MACROPLASTIQUE	CONTROL
Stamey Grade		
Dry	34.6% (45/130)	23.8% (31/130)
Improvement of ≥ 1 grade	57.7% (75/130)	46.9% (61/130)
Same	19.2% (25/130)	24.6% (32/130)
Worse / Unable to assess*	23.1% (30/130)	28.5% (37/130)
Pad Weight		
$\geq 50\%$ improvement	60.0% (78/130)	53.1% (69/130)
0-49% improvement	6.9% (9/130)	7.7% (10/130)
Worse / Unable to assess*	33.1% (43/130)	39.2% (51/130)

* No 12-month data was available for the Unable to assess group; these subjects were analyzed as failures.

Table 5: Key Effectiveness Results at 12 Months (Per Protocol)

	MACROPLASTIQUE	CONTROL
Stamey Grade		
Dry	36.9% (45/122)	24.8% (31/125)
improvement of ≥ 1 grade	61.5% (75/122)	48.8% (60/125)
Same	20.5% (25/122)	25.6% (32/125)
Worse / Unable to assess*	18.0% (22/122)	26.4% (33/125)
Pad Weight		
$\geq 50\%$ improvement	63.9% (78/122)	54.4% (68/125)
0-49% improvement	7.4% (9/122)	8.0% (10/125)
Worse / Unable to assess*	28.7% (35/122)	37.6% (47/125)
Quality of Life (As Followed)		
Mean improvement in I-QoL	28.7	26.7

* No 12-month data was available for the Unable to assess group; these subjects were analyzed as failures.

Twenty-four month follow-up Stamey Grade data were available on 84 Macroplastique subjects. Of these 84 subjects, 63 had improvement in Stamey Grade at 24 months, 28 of whom were dry.

PHYSICIAN TRAINING

Macroplastique should only be used by someone properly trained in diagnostic and therapeutic cystoscopy.

PATIENT COUNSELING

Uroplasty relies on the physician to advise the patient of all potential risks and benefits associated with the Macroplastique implant procedure. Patient should be fully apprised of the indications, contraindications, warnings, precautions, expected clinical outcomes, adverse events, and methods of implantation. The patient should be advised that bulking agent therapy with Macroplastique is a course of treatment that may require more than one injection procedure to achieve dryness

or a desired level of improvement in incontinence. Patients should be counseled to report adverse events to the treating physician and physicians are advised to report adverse events to Uroplasty. The Macroplastique Patient Brochure may be beneficial in providing additional information to the patient.

TREATMENT WITH MACROPLASTIQUE

A complete medical history and urological examination should be obtained to determine whether the patient is an appropriate candidate for treatment with Macroplastique.

INSTRUCTIONS FOR USE

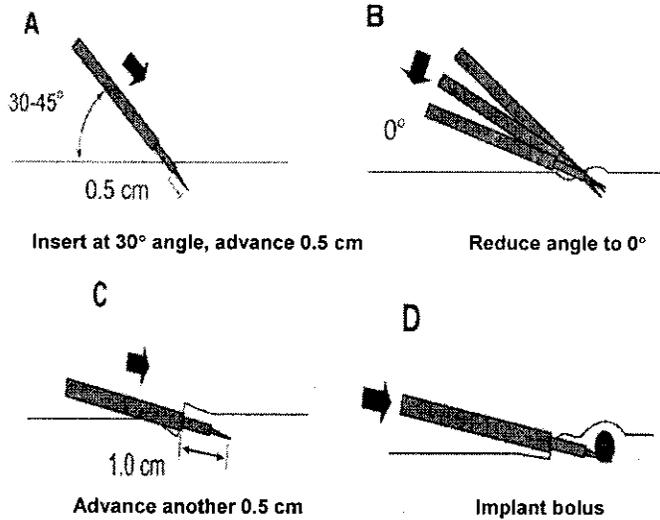
Patient Pretreatment

1. Perform appropriate pretreatment evaluation to ensure the absence of urinary tract infection.
2. Broad-spectrum antibiotics should be administered prior to implantation consistent with current surgical implant procedures (i.e., levofloxacin, ciprofloxacin). Physicians are cautioned not to allow antibiotics to interfere with pretreatment microbiological cultures.
3. Using standard procedure, prepare the patient for cystoscopy and inject a local anesthetic into the urethra. Fill the bladder to approximately 50% of its capacity with sterile water or sterile saline.

Macroplastique Implantation Procedure

1. Macroplastique is implanted transurethraly through a cystoscope with a minimum 7 Fr. working channel to accommodate the endoscopic needle recommended by Uroplasty, Inc. (e.g., Uroplasty Rigid Endoscopic Needle, Catalog Number: MRN-518).
2. Place the syringe collar over the Macroplastique syringe flanges, then firmly grasp the collar and lock the syringe/collar assembly securely onto the rotating hub of the Administration Device.
3. Firmly twist and fasten the Uroplasty endoscopic needle hub onto the luer lock tip of the syringe to achieve a tight connection. Remove the protective sleeve from the needle.
4. Prime the needle with Macroplastique by engaging the Administration Device. To stop the flow, depress the release mechanism located on top of the Administration Device.
5. Insert the cystoscope into the urethra and advance the needle through the working channel of the scope to visualize the needle tip.
6. Retract the needle tip and scope back into the urethra 1.5 to 2.0 cm distal from the bladder neck.
7. Advance the needle with the bevel facing the center of the urethra.
8. In all positions, use the tissue tunneling technique (Figures A-D) and wait approximately 30 seconds before withdrawing the needle from the tissue to limit product loss from the implantation site.

Figures A-D: Tissue Tunneling Technique



9. Locate the 6 o'clock position within the urethral lumen and tilt the scope to a 30-45° angle (Figure A). Insert the needle tip into the urethral tissue at this angle, and then advance the needle 0.5 cm in depth. Angle the scope to 0°, parallel with the urethra, (Figure B) and advance the needle another 0.5 cm to create a tissue tunnel (Figure C).

Recommended Treatment Locations & Volumes			
6 o'clock	10 o'clock	2 o'clock	Total Volume
≤ 2.5 ml	≤ 1.25 ml	≤ 1.25 ml	5 ml

10. Implant a small amount of Macroplastique to confirm correct needle placement within the mucosa (Figure D). If the needle is properly placed, a bleb (tissue bulking) in the urethral mucosa should immediately be visible with the cystoscope. If it does not appear, withdraw and reposition the needle more superficially. Then, inject again.
11. Implant product slowly. Wait a few seconds between each pull of the Administration Device lever.
12. Repeat the implantation procedure at the 2 o'clock and 10 o'clock positions to achieve urethral coaptation.
13. Depending on the patient's history of previous incontinence surgery (i.e., bladder neck suspension, sling procedures, etc.), the Macroplastique implantation sites and injected volume may be adjusted according to the morphology of the bladder neck and urethra to achieve urethral coaptation.
14. Use caution and avoid passing the cystoscope over the implantation site, which could potentially disrupt product placement.
15. Use a small intermittent catheter (8-12 Fr.) to drain the bladder when necessary.

Needles and treatment syringes may be potential biohazards. After use, handle accordingly and dispose of all materials in accordance with accepted medical practice and all applicable local, state and federal laws and regulations.

Post-Implantation

Confirm that a patient's voiding function is satisfactory before she leaves the clinic. If the patient is unable to spontaneously void following the procedure, pass an intermittent catheter (8-12 Fr.) to relieve any symptoms of delayed voiding. If necessary, instruct the patient in the technique of clean intermittent self-catheterization.

Upon discharge, prescribe a broad-spectrum antibiotic (i.e., levofloxacin, ciprofloxacin, etc.), and provide analgesia to manage any possible post-treatment discomfort.

Counsel the patient to report adverse events to the treating physician. Physicians should report serious device-related adverse events to Uroplasty, Inc.

Subsequent Treatment

Some patients may require additional treatments to enhance their improvement or achieve dryness. It is recommended to delay further Macroplastique treatment for 12 weeks to allow tissue healing to occur.

For subsequent treatment, implant distal to the initial Macroplastique placement and follow the prescribed tunneling procedure and recommended treatment locations and volumes as described above.

STORAGE CONDITIONS

Carefully examine the sterile packaging and contents prior to use to confirm neither has been damaged in shipment. If damaged, do not use and immediately return damaged product to Uroplasty, Inc.

Store at room temperature (59-86°F; 15-30°C). See product labeling for expiration date.

WARRANTY

Uroplasty warrants that reasonable care has been used to design and manufacture this product. Product will be replaced if Uroplasty determines its material or workmanship is defective. This is Uroplasty's only warranty, and it excludes all other warranties (including those implied by operation of law). Uroplasty is not responsible for matters within the control of the user or others, such as product handling and storage, patient selection and diagnosis and treatment procedures.

This Limited Warranty is limited to its express terms. In particular:

(1) Except as expressly provided by this Limited Warranty, UROPLASTY IS NOT RESPONSIBLE FOR ANY DIRECT, INCIDENTAL OR CONSEQUENTIAL DAMAGES BASED ON ANY DEFECT, FAILURE OR MALFUNCTION OF THE PRODUCT, WHETHER THE CLAIM IS BASED ON WARRANTY, CONTRACT, TORT OR OTHERWISE.

(2) This Limited Warranty is made only to the purchaser of the Product. AS TO ALL OTHERS, UROPLASTY MAKES NO WARRANTY, EXPRESS OR IMPLIED, INCLUDING, BUT NOT LIMITED TO, ANY IMPLIED WARRANTY OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE WHETHER ARISING FROM STATUTE, COMMON LAW, CUSTOM OR OTHERWISE. THIS LIMITED WARRANTY SHALL BE THE EXCLUSIVE REMEDY AVAILABLE TO ANY PERSON.

Any implied warranties of merchantability or fitness are specifically excluded. Statements and descriptions in marketing literature, while generally describing product, do not constitute any warranties.

Disclaimer of Warranties

Uroplasty excludes all warranties and responsibilities for:

- Improper use of or tampering with the product, and/or
- Failure to follow instructions provided in this insert

Manufactured by: Uroplasty, Inc.
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Contigen and Bard are registered trademarks.

U.S. Patent Numbers 5,258,028; 5,571,182. United Kingdom Patent Number 2,227,176;
German Patent Number D3941023; Japanese Patent Number 2694372; Dutch Patent
Number 193399C. Other product applications and instrumentation are covered by additional
worldwide patents. U.S. and additional foreign patents pending.

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**A minimally invasive alternative for the treatment of stress urinary
incontinence**

**MACROPLASTIQUE®
IMPLANTS**

{Additional graphics (cover art) may be added to this brochure in future versions.}

This brochure is designed to help you decide whether or not to have a Macroplastique urethral bulking procedure for the treatment of stress urinary incontinence. Please read this entire brochure and discuss it with your doctor. Your doctor will answer any questions you have prior to your making a decision about treatment.

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Glossary

Adverse Event: Complication that may result from a procedure.

Bladder: Balloon-like organ in the lower abdomen where urine is stored.

Bulking Agent(s): Natural or man-made material injected into the body to support tissues.

Catheter: A small tube placed into the body through which fluids pass.

Catheterization: The use of or insertion of a catheter.

Contraindication: A statement in the product information that the product should not be used when a certain condition exists. For example, *Macroplastique* is contraindicated for patients who currently have a urinary tract infection.

Clinical Trial: Uroplasty's research study of women with incontinence and treated with *Macroplastique* or control bulking agent.

Cross-linked Polydimethylsiloxane (PDMS): The solid, medical grade silicone elastomer material used to make *Macroplastique Implants*.

Cystoscope: A small optical instrument used by the doctor to view the urinary organs (the urethra and bladder).

Incontinence: A condition where a person is unable to control the release of bodily fluids.

Intrinsic Sphincter Deficiency (ISD): A condition where the group of circular muscles surrounding the bladder neck weakens and can no longer close properly to hold urine.

Macroplastique Implants: Urethral bulking agent made with silicone elastomer implants.

Precautions: A statement in the product information that alerts the physician to take measures to avoid a problem.

Saline: Salt water.

Silicone Elastomer: A rubber-like material.

Stamey Grade: A diagnostic measure used by physicians to rate the severity of stress urinary incontinence.

Stress Urinary Incontinence (SUI): The accidental leakage of urine during exercise, or during normal, everyday activities such as coughing, sneezing, laughing, or during other body movements that put pressure on the bladder. SUI is the most common type of urinary incontinence in younger and middle-age women. In some cases, it is related to childbirth. It may also begin around the time of menopause.

Urethra: The tube that carries urine from the bladder to outside the body for elimination.

Urethral Bulking: The injection of material (bulking agent) into the tissues surrounding the urethra to help the urethra close to avoid accidental urine leakage. Urethral bulking does not close the urethra totally; the urethra can still open normally to allow for urination.

Urethral Hypermobility: A condition where the urethra is not sufficiently supported by the pelvic floor muscles resulting in stress urinary incontinence.

Urinary Incontinence: The accidental leakage of urine.

Urinary / Urethral Sphincter: A ring of muscles in the urethra that help keep the urethra closed and can be opened voluntarily to allow urination. In one type of SUI, the urethral sphincter does not close adequately, and allows urine to leak accidentally during physical activities.

Urinary Tract: The organs and pathways involved in the passing of urine.

Voiding: Eliminating urine from the body.

Water-soluble gel, Polyvinylpyrrolidone (PVP): The liquid that can be absorbed by the body in which **Macroplastique Implants** are mixed.

If you see a term in bold, it will be defined in the glossary.

Introduction

If you worry about occasional **bladder** leakage, a condition called **urinary incontinence**, you are not alone. Millions of women worry about **bladder** leakage -- a frustrating and often embarrassing condition that can affect a woman's lifestyle, relationships, and emotional well-being.

This brochure is provided as an overview of **Macroplastique® Implants** and **stress urinary incontinence**. It is not intended to replace discussions with your

doctor. Please be sure to discuss this information and any questions you may have with your doctor.

Approximately 13 million people in the United States are affected by **stress urinary incontinence (SUI)**. Of the 13 million, 85% are women. While SUI occurs more frequently in older women, SUI affects women of all ages and is not necessarily a result of getting older. More importantly, **incontinence** is treatable and is usually curable. You don't have to live with the effects of **incontinence**.

Frequently Asked Questions

What is stress urinary incontinence?

Stress urinary incontinence (SUI) is the most common type of **urinary incontinence**. SUI is the sudden, accidental loss of urine that occurs during normal, everyday activities. You may have SUI if you leak urine when you sneeze, cough or laugh, when you stand up, when you exercise, or when you lift items.

There are other types of **urinary incontinence**. Your doctor will be able to determine if your leakage problems are the result of SUI after learning your medical history and conducting a physical examination. Your doctor may perform special tests to evaluate your **bladder** and urethral function.

What causes stress urinary incontinence?

SUI occurs when the **urethra**, the tube that carries urine from the **bladder** to outside the body, does not remain closed until it is time to urinate. Even an activity such as standing up may result in accidental loss of urine. There are two main causes of SUI:

1. The **urinary sphincter**, a group of muscles surrounding the **urethra**, weakens and can no longer close properly to hold urine. This condition is called **Intrinsic Sphincter Deficiency** (also known as ISD). Approximately 2 million people have SUI due to ISD. **Macroplastique** is used to treat SUI primarily due to ISD.
2. The pelvic floor muscles weaken and are unable to provide sufficient support to the **urethra**. In this case, any increased pressure to the **bladder**, such as coughing, may cause the **urethra** to lose its seal and allow urine to escape.

Various factors may contribute to the weakening of the pelvic floor muscles including: pregnancy and childbirth, chronic heavy lifting or straining, obesity, menopause, or estrogen deficiency.

What are common treatment options?

Pelvic muscle strengthening: Pelvic floor exercises, commonly referred to as Kegel exercises, will most likely be one of the first treatment options recommended by your doctor. Depending on the severity of your SUI, Kegel exercises may not be sufficient to improve your symptoms. Kegel exercises may be combined with:

- Pelvic muscle stimulation – mild electrical stimulation to help automate the process of performing Kegel exercises. Stimulation is generally applied using a home-use device.
- Biofeedback – a process using signals of sight or sound to assist targeting the right muscle during pelvic muscle exercises.

Medications: Some types of **urinary incontinence** may be treated with drugs that affect the **bladder** and **urethra** muscles, and help prevent leakage. Hormone therapy, such as estrogen creams, may also be effective in helping to improve pelvic floor muscle function.

Bulking agents: **Bulking agents**, like *Macroplastique Implants*, may be used to treat SUI, specifically when the cause is **intrinsic sphincter deficiency**. Treatment with a **bulking agent** involves injecting a material into the tissues surrounding the **urethra** to help increase the thickness (the “bulk”) of the **urethra**, thereby improving urethral closure to avoid accidental leakage. **Urethral bulking** does not close the **urethra** totally; the **urethra** can still open normally to allow for urination.

Surgery: Surgery is often used to treat SUI, especially when the cause is a weakened pelvic floor. A common surgery to provide support for the **urethra** is a sling procedure. During this surgery, a narrow strip of a permanent material, a “sling,” is placed below the **urethra** to support the **urethra** and to maintain its seal.

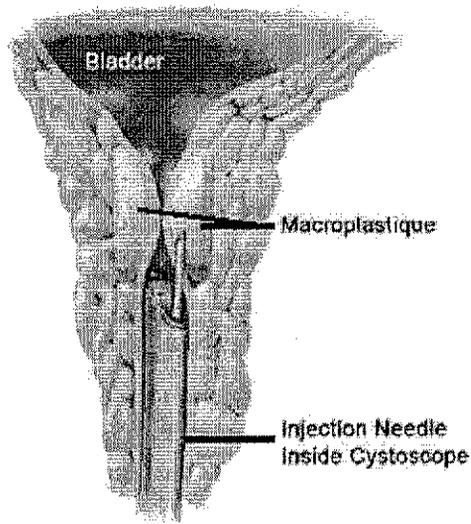
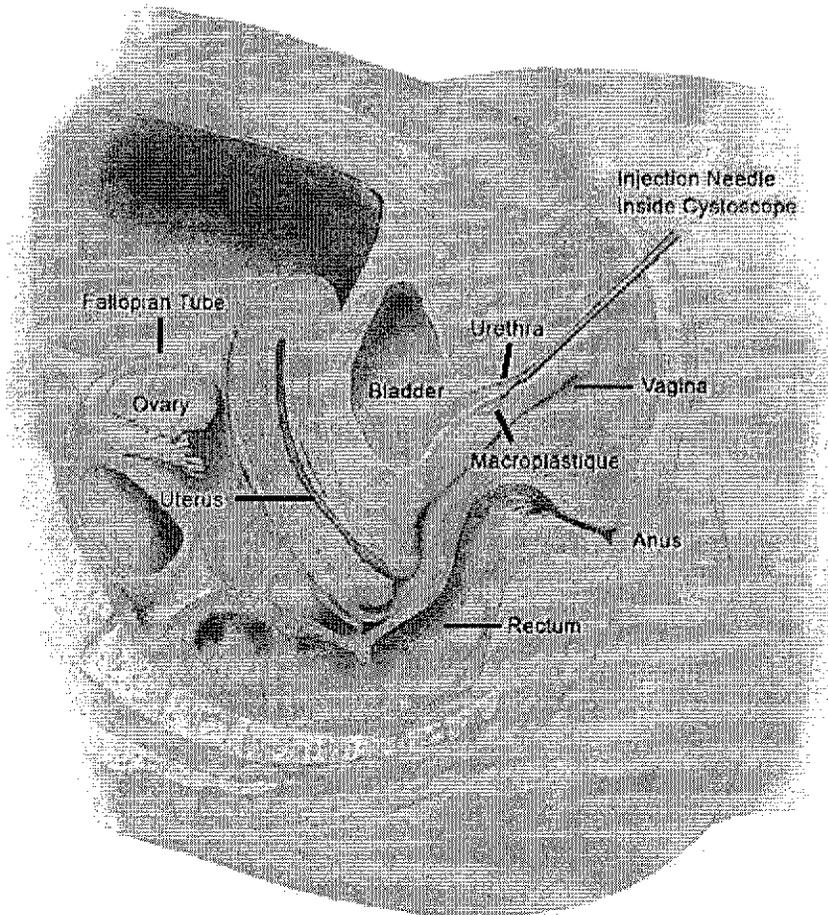
All treatment options are associated with **contraindications**, **precautions**, and **adverse events**. You can discuss the variety of treatments available with your doctor.

What is *Macroplastique*?

Macroplastique is an injectable soft-tissue **urethral bulking agent** for treating **stress urinary incontinence** primarily due to **intrinsic sphincter deficiency**. ***Macroplastique*** is made up of two parts – the **water-soluble gel** (**polyvinylpyrrolidone**) that is absorbed and removed from the body in urine and the man-made, rubber-like, **silicone elastomer** implant material (**cross-linked polydimethylsiloxane**) that is permanent and not absorbed by the body. It is this permanent material that causes the bulking effect around the **urethra** after implantation.

How does *Macroplastique* work?

Macroplastique is injected into the tissues surrounding the **urethra**. The increased “bulk” allows the **urethra** to close more effectively and prevents urine from leaking. Refer to the drawings below to see where ***Macroplastique*** is injected.



Is *Macroplastique* right for me?

Your doctor will perform tests to determine what type of **incontinence** you have and the cause for your **incontinence**. You and your doctor will then decide on the treatment that is most suitable for you.

Macroplastique may be right for you, even if other **incontinence** treatments such as a sling procedure have failed.

Are there times when *Macroplastique* should not be used?

You cannot be treated with ***Macroplastique*** if you have an infection or inflammation of the kidney, **bladder** or **urinary tract**, or vagina. Your doctor will test your urine to ensure you do not have a **urinary tract** infection because the ***Macroplastique*** injection cannot be performed until an infection has been treated. Also, ***Macroplastique*** cannot be injected if the tissue around your **urethra** does not look healthy to the doctor.

This treatment has not been evaluated in pregnant women or women who had a child within the past year.

How is the *Macroplastique* treatment performed?

The procedure to inject ***Macroplastique*** can be performed in your doctor's office or in an outpatient clinic or hospital in approximately 30 minutes. Prior to the procedure, the doctor will give you an antibiotic to reduce the risk of infection. Upon the start of the procedure, the doctor will give you local anesthetic in the tissues near your **bladder** to reduce discomfort.

A small optical instrument (**cystoscope**), placed in the **urethra**, is used during the procedure to allow your doctor to view your **urethra** and **bladder** while injecting ***Macroplastique*** into the surrounding urethral tissue. Your doctor will also fill your **bladder** to halfway with water or **saline** to better view the implantation area. The optical instrument is removed after the injection and your treatment is complete.

What can I expect after the procedure?

Most women can expect:

- To stay at the treatment facility until the numbness from the anesthetic is gone and they can urinate on their own. If you have difficulty urinating after the procedure, a **catheter** may be inserted until you urinate normally.
- To receive a prescription for antibiotics to prevent infection. It is important to take this antibiotic to reduce the risk of a **urinary tract** infection.
- To resume their normal daily activities and return to work within a few days.

Your doctor will provide you with more specific instructions about your own recovery and if any restrictions on normal activities are recommended.

What are the treatment benefits?

The benefit of **Macroplastique** treatment is that you could be free from unwanted urinary leakage (dry) or have fewer episodes of urinary leakage. Other commercially available **bulking agents** may be absorbed into the body; **Macroplastique** is made of a **water-soluble gel** that is removed from the body leaving behind the permanent **silicone elastomer** implants.

Macroplastique has been available to treat this condition worldwide since 1991. The majority of women treated with **Macroplastique** report a cure or improvement in their symptoms, with many seeing that improvement as soon as they leave the doctor's office, hospital or clinic. A successful treatment is a decrease in the amount and frequency of urine leakage due to **stress urinary incontinence**.

Uroplasty conducted a **clinical trial** with **Macroplastique** at twelve medical centers in the U.S. and Canada. One hundred twenty two (122) female patients received **Macroplastique Implants** and were followed for 12 months after the initial treatment. In the study, 75 out of 122 **Macroplastique** patients (61.5%) were improved at 12 months based on a physician's scoring system (**Stamey Grade**). Of the 75 improved patients, 45 (36.8% of the original 122 patients) were dry using the same scoring system.

For 22 of the 122 **Macroplastique** patients in the trial (18%), their SUI was worse or was unknown after 12 months. When the patient's condition was unknown, data was not available and Uroplasty does not know if these patients' symptoms improved, remained the same, or became worse.

What are the risks I should know about?

As with any treatment, there are risks involved. It is important to discuss risks and side effects with your doctor before undergoing any type of medical treatment.

Risks following a **Macroplastique** treatment include pain related to the procedure (which can be controlled with pain medication), a small amount of blood in your urine, having to use the bathroom more often or more urgently, delayed **voiding**, painful urination, and/or **urinary tract** infection. There is also a potential risk related to receiving anesthesia during the treatment.

If after 48 hours you have urination that is difficult, frequent, or painful, or there is blood in your urine, contact your doctor immediately. These may be signs of other more serious problems.

An additional risk is that you may experience no benefit from **Macroplastique** treatment. This could happen if **Macroplastique** is placed too deeply in the tissue, thereby creating poor bulking around the **urethra**. Also, if you have a different type of **incontinence** (i.e., urge **incontinence**) or your **incontinence** condition worsens (i.e., due to **urethral hypermobility**), **Macroplastique** may not be an effective treatment for you.

In the **clinical trial**, 122 patients were treated with **Macroplastique** and followed for 12 months after the last treatment. The most common side effects (**adverse events**) reported are listed below.

Adverse Event	Number of Patients
Post-operative catheterization*	43 in 100
Urinary tract / bladder infection (0 – 365 days post treatment)	25 in 100
Urinary retention	21 in 100
Painful urination (Dysuria)	19 in 100
Blood in urine (Hematuria / Transient hematuria)	19 in 100
Pain at implantation site	16 in 100
Frequency	12 in 100
Strong desire to urinate, but no incontinence episodes (Urgency)	12 in 100
Slowed urine stream	7 in 100
Incomplete bladder emptying	6 in 100
Urge incontinence	6 in 100
Hesitancy	5 in 100

* Instructions to the doctors allowed them to perform **catheterizations** as a routine part of the procedure.

Many of the side effects reported in the clinical study occurred within 7 days after treatment and resolved within 30 days. You should talk to your doctor about these side effects and how they can be resolved.

Will I need more than one treatment?

In the **clinical trial**, about half of the patients requested an additional treatment to either further improve or cure their **incontinence**. Uroplasty recommends patients wait 12 weeks between treatments to allow healing and accurately see the full effect of the first treatment. Talk to your doctor about an additional treatment if you continue to experience urine leakage.

What are the long-term results?

The long-term results with **Macroplastique** have not been established. Eighty-four women participated in the **Macroplastique clinical trial** for 2 years. Using the same physician's scoring system reported at 12 months (**Stamey Grade**), 63 out of these 84 women were improved at 2 years. However, too many women did not attend their 2-year exam to assess improvement at 2 years. Therefore, the actual improvement rate beyond 12 months is unknown.

If your symptoms do not improve or if symptoms return after treatment with **Macroplastique**, there are other options available. You may require further treatment for **stress urinary incontinence** or you may have an additional form of **incontinence** or other urology or gynecology problem that needs to be diagnosed and treated. For example, many women have mixed **incontinence**, such as a

combination of SUI and urge **incontinence**, where urge **incontinence** is a sudden and uncontrollable urge to urinate. If this were the case, your doctor would work with you to determine an appropriate treatment option for your urge **incontinence**. Treatment with **Macroplastique** does not prevent you from receiving other types of **incontinence** treatments – either for SUI or another form of **incontinence**.

MORE INFORMATION ABOUT INCONTINENCE:

National Association for Continence
1-800-BLADDER or 1-843-377-0900
www.nafc.org

The Simon Foundation for Continence
1-800-23-SIMON or 1-847-864-3913
www.simonfoundation.org

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