



Memorandum

P960020

Date • AUG 16 1996
From Director, Office of Device Evaluation (HFZ-400)
Center for Devices and Radiological Health (CDRH)
Subject Premarket Approval of UroMed Corp.'s Reliance® Urinary
Control Insert and Sizing Device - ACTION
To The Director, CDRH
ORA _____

ISSUE. Publication of a notice announcing approval of the subject PMA.

FACTS. Tab A contains a FEDERAL REGISTER notice announcing:

- (1) a premarket approval order for the above referenced medical device (Tab B); and
- (2) the availability of a summary of safety and effectiveness data for the device (Tab C).

RECOMMENDATION. I recommend that the notice be signed and published.

Susan Alpert
Susan Alpert, Ph.D., M.D.

Attachments
Tab A - Notice
Tab B - Order
Tab C - S & E Summary

DECISION

Approved _____ Disapproved _____ Date _____

Prepared by Rao Nimmagadda, CDRH, HFZ-470, August 6, 1996, 594-2194
Donald St.Pierre, CDRH, HFZ-470, August 6, 1996, 594-2194
Russell Pagano, CDRH, HFZ-470, August 6, 1996, 594-2194
Nicole Wolanski, CDRH, HFZ-470, August 6, 1996, 594-2194
Hector Herrera, CDRH, HFZ-470, August 6, 1996, 594-2080
John Baxley, CDRH, HFZ-470, August 15, 1996, 594-2194
Dan Schultz, CDRH, HFZ-470, August 15, 1996, 594-5072

1

DRAFT

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[DOCKET NO. _____]

UroMed Corp.; Premarket Approval of Reliance[®] Urinary Control Insert and Sizing Device

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing its approval of the application by UroMed Corp., Needham, MA, for premarket approval, under the Federal Food, Drug, and Cosmetic Act (the act), of the Reliance[®] Urinary Control Insert and Sizing Device. After reviewing the recommendation of the Gastroenterology and Urology Devices Advisory Panel, FDA's Center for Devices and Radiological Health (CDRH) notified the applicant, by letter on August 16, 1996, of the approval of the application.

DATES: Petitions for administrative review by (insert date 30 days after date of publication in the FEDERAL REGISTER).

ADDRESSES: Written requests for copies of the summary of safety and effectiveness data and petitions for administrative review, to the Dockets Management Branch (HFA-305), Food and Drug Administration, 12420 Parklawn Dr., Rm. 1-23, Rockville, MD 20857.

2

FOR FURTHER INFORMATION CONTACT:

Venkat Rao Nimmagadda, Ph.D.,
Center for Devices and Radiological Health (HFZ-470),
Food and Drug Administration,
9200 Corporate Blvd.,
Rockville, MD 20850,
301-594-2194.

SUPPLEMENTARY INFORMATION: On August 18, 1995, UroMed Corp., Needham, MA 02194, submitted to CDRH an application for premarket approval of the Reliance[®] Urinary Control Insert and Sizing Device. The device is a transurethral female urinary occlusion device and is intended for use in the management of stress urinary incontinence in adult women.

On July 25, 1996, the Gastroenterology and Urology Devices Advisory Panel, an FDA advisory committee, reviewed and recommended approval of the application.

On August 16, 1996, CDRH approved the application by a letter to the applicant from the Director of the Office of Device Evaluation, CDRH.

A summary of the safety and effectiveness data on which CDRH based its approval is on file in the Dockets Management Branch (address above) and is available from that office upon written request. Requests should be identified with the name of the device and the docket number found in brackets in the heading of this document.

Opportunity for Administrative Review

Section 515(d) (3) of the act, (21 U.S.C. 360e(d) (3)) authorizes any interested person to petition, under section 515(g) of the act, for administrative review of CDRH's decision to approve this application. A petitioner may request either a formal hearing under part 12 (21 CFR part 12) of FDA's administrative practices and procedures regulations or a review of the application and CDRH's action by an independent advisory committee of experts. A petition is to be in the form of a petition for reconsideration under 10.33(b) (21 CFR 10.33(b)). A petitioner shall identify the form of review requested (hearing or independent advisory committee) and shall submit with the petition supporting data and information showing that there is a genuine and substantial issue of material fact for resolution through administrative review. After reviewing the petition, FDA will decide whether to grant or deny the petition and will publish a notice of its decision in the FEDERAL REGISTER. If FDA grants the petition, the notice will state the issue to be reviewed, the form of the review to be used, the persons who may participate in the review, the time and place where the review will occur, and other details.



Petitioners may, at any time on or before (insert date 30 days after date of publication in the FEDERAL REGISTER), file with the Dockets Management Branch (address above) two copies of each petition and supporting data and information, identified with the name of the device and the docket number found in brackets in the heading of this document. Received petitions may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.

59

This notice is issued under the Federal Food, Drug, and Cosmetic Act (secs. 515(d), 520(h), (21 U.S.C. 360e(d), 360j(h))) and under authority delegated to the Commissioner of Food and Drugs (21 CFR 5.10) and redelegated to the Director, Center for Devices and Radiological Health (21 CFR 5.53).

Dated: _____.

6



Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

Ms. Joanne H. Moon
Vice President, Operations
UroMed Corporation
64 A Street
Needham, Massachusetts 02194

AUG 16 1996

Re: P960020
Reliance® Urinary Control Insert and Sizing Device
Filed: August 18, 1995
Amended: June 25 and August 14, 1996

Dear Ms. Moon:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your premarket approval application (PMA) for the Reliance® Urinary Control Insert and Sizing Device. This device is indicated for the management of stress urinary incontinence in adult women. We are pleased to inform you that the PMA is approved subject to the conditions described below and in the "Conditions of Approval" (enclosed). You may begin commercial distribution of the device upon receipt of this letter.

The sale, distribution, and use of this device are restricted to prescription use in accordance with 21 CFR 801.109 within the meaning of section 520(e) of the Federal Food, Drug, and Cosmetic Act (the act) under the authority of section 515(d)(1)(B)(ii) of the act. FDA has also determined that to ensure the safe and effective use of the device that the device is further restricted within the meaning of section 520(e) under the authority of section 515(d)(1)(B)(ii), (1) insofar as the labeling specify that the device should be prescribed by a physician trained in the management of urinary incontinence and (2) insofar as the sale, distribution, and use must not violate sections 502(q) and (r) of the act.

In addition to the postapproval requirements in the enclosure, the postapproval reports must include the following information:

An evaluation of the long-term (i.e., 5-year) effects of the device on a minimum of 150 patients. This postapproval study should assess urethral integrity and provide a detailed analysis of urinary tract infections, including bacteriologic analysis of urinary pathogens.

Expiration dating for this device has been established and approved at 2 years. This is to advise you that the protocol you used to establish this expiration dating is considered an approved protocol for the purpose of extending the expiration dating as provided by 21 CFR 814.39(a)(8).

CDRH will publish a notice of its decision to approve your PMA in the FEDERAL REGISTER. The notice will state that a summary of the safety and effectiveness data upon which the approval is based is available to the public upon request. Within 30 days of publication of the notice of approval in the FEDERAL REGISTER, any interested person may seek review of this decision by requesting an

9

opportunity for administrative review, either through a hearing or review by an independent advisory committee, under section 515(g) of the act.

Failure to comply with the conditions of approval invalidates this approval order. Commercial distribution of a device that is not in compliance with these conditions is a violation of the act.

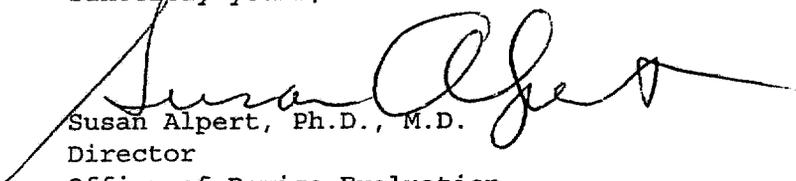
You are reminded that, as soon as possible and before commercial distribution of your device, you must submit an amendment to this PMA submission with copies of all approved labeling in final printed form.

All required documents should be submitted in triplicate, unless otherwise specified, to the address below and should reference the above PMA number to facilitate processing.

PMA Document Mail Center (HFZ-401)
Center for Devices and Radiological Health
Food and Drug Administration
9200 Corporate Blvd.
Rockville, Maryland 20850

If you have any questions concerning this approval order, please contact Rao Nimmagadda, Ph.D., at (301) 594-2194.

Sincerely yours,



Susan Alpert, Ph.D., M.D.
Director
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

8

**SUMMARY OF SAFETY AND EFFECTIVENESS DATA: RELIANCE®
URINARY CONTROL INSERT AND SIZING DEVICE**

I. GENERAL INFORMATION

DEVICE GENERAL NAME: Transurethral Female Urinary
Occlusion Device

DEVICE TRADE NAME: Reliance® Urinary Control Insert
& Sizing Device

APPLICANT: UroMed Corporation
64 A Street
Needham, Massachusetts 02194

PREMARKET APPROVAL
APPLICATION (PMA) NUMBER: P960020

DATE OF NOTICE OF APPROVAL TO
APPLICANT: August 16, 1996

REGULATORY HISTORY:

Clinical data supporting the safety and effectiveness of the UroMed Reliance® Urinary Control Insert device was initially collected as part of a non-significant risk study. During an interim analysis of the data, one of the institutional review boards (IRB) determined that the study should be reclassified as a significant risk clinical trial. FDA agreed with the IRB determination and informed UroMed on July 1, 1994, that an Investigational Device Exemptions (IDE) application was required. UroMed was subsequently granted approval for their IDE G940135 on January 13, 1995. This approval limited the investigation to 10 institutions and 255 subjects. The company, on the advise of FDA then proceeded along the 510(k) regulatory pathway until analysis of the data indicated that, due to the many unique features of this device, a suitable predicate could not be found and therefore substantial equivalence to a legally marketed device could not be determined. Extensive discussions were held between FDA and UroMed regarding the aforementioned concerns. These discussions ultimately led to a letter from the agency dated June 6, 1996, informing UroMed that the 510(k) was being converted to a PMA. In the letter dated June 7, 1996, UroMed acknowledged the 510(k) conversion to a PMA (P960020), and the scheduling of Gastroenterology-Urology Advisory Panel meeting on July 25, 1996, to discuss this PMA.

II. INDICATIONS FOR USE

The Reliance® Urinary Control Insert is intended for use in the management of stress urinary incontinence in adult women.

III. DEVICE DESCRIPTION

The Reliance® Urinary Control Insert is a sterile, single use, balloon-tipped catheter that is inserted into the urethra by the user after appropriate training by a physician or a health care provider. The Reliance® Urinary Control Insert device consists of the following components: a catheter shaft, a meatal plate (tab), and a balloon molded from various types of thermoplastic elastomers; a braided nylon deflation string coated with a nylon resin; a nylon ball valve; an internal device lubricant; and a syringe applicator (3 cc B-D syringe).

The user performs self-catheterization to insert the device into the urethra using the syringe to inflate the balloon (the syringe is reused). The Reliance® Urinary Control Insert is held in place by the balloon and meatal plate. To void, the user pulls on the string which breaks the air-tight valve seal and deflates the balloon. The Reliance® Urinary Control Insert is then removed by pulling on the meatal plate (tab) and discarded. A new device can be placed after voiding.

The single use disposable Reliance® Sizing Device (RSD) is used by the physician to select the appropriate length device for each patient. The Reliance® Urinary Control Insert ranges in size from 3.0 to 5.0 cm (0.5 cm increments). The RSD is similar in design and materials to the Reliance® Urinary Control Insert with the following modifications: a molded collar (polypropylene); a tube clamp (polypropylene); graduated markings; a fitted attachment and inflator (polypropylene). The RSD is also longer than the Reliance® Urinary Control Insert to accommodate the tube clamp and collar.

IV. CONTRAINDICATIONS, WARNINGS, AND PRECAUTIONS

The Reliance® Urinary Control Insert has the following contraindications, warnings, and precautions:

Contraindications

The use of the Reliance® Urinary Control Insert is contraindicated in women who:

1. Have anatomical anomalies that preclude the use of urinary catheters such as the Reliance® Urinary Control Insert.

2. Have interstitial cystitis, pyelonephritis, or a history of severely compromised urinary tract mucosal tissue.
3. Have an active urinary tract infection (UTI)
4. Have a prosthetic heart valve or other cardiac condition that puts the patient at increased risk of subacute bacterial endocarditis (due to the risk of infection).
5. Cannot tolerate any form of antibiotic therapy.
6. Are currently receiving anticoagulant therapy.
7. Have overflow incontinence or neurogenic bladder.

Warnings

1. Care must be taken to ensure that the correct size (length) of the Reliance® Urinary Control Insert is prescribed. During the clinical investigation, one patient was fitted with a Reliance® Urinary Control Insert that was too short, and this patient experienced device migration into the bladder.
2. Reliance® Urinary Control Insert should not be used during sexual intercourse as the effects were not studied in the clinical trial and are unknown.

Precautions

1. The Reliance® Urinary Control Insert and the Sizing Device are sterile if the package is unopened or undamaged. Do not use if the package is damaged or open.
2. This device should be prescribed by a physician trained in the management of urinary incontinence.
3. Patients who present with a history of frequent UTIs should be advised that they may be at increased risk of infection with use of the Reliance® Urinary Control Insert. Additionally, these patients should be monitored closely for symptoms of UTI during Insert use.
4. If the patient reports or develops symptoms of possible UTI, she should be instructed to temporarily discontinue use of the Reliance® Urinary Control Insert until she has been medically evaluated. If infection is diagnosed, the Insert should not be used until the infection has been treated.

5. If the patient reports visible hematuria or bleeding but no other symptoms of UTI, she should be instructed to temporarily discontinue use of the Reliance[®] Urinary Control Insert. After her symptoms resolve, she can continue using the Insert. If the symptoms persist, she should be instructed to contact her physician. If the symptoms recur after resuming the Insert use, she should be instructed to discontinue use of the device and contact her physician.
6. The safety and effectiveness of the Reliance[®] Urinary Control Insert during pregnancy have not been studied and its effects are unknown.
7. Patients often experienced urethral irritation and discomfort during the first two or three weeks of using the Reliance[®] Urinary Control Insert.
8. Use of the Insert should be discontinued in those patients who develop abrasion of the bladder wall and/or urethral meatus. Device use may be resumed once these conditions are fully resolved.
9. Long-term safety and effectiveness data on the use of the Reliance[®] Urinary Control Insert has not been developed, therefore continued close patient follow-up is recommended.
10. Urine loss was observed to increase in some patients, and decrease in others following Insert use over time. Although there was not a statistically significant increase in urine loss observed during the course of the study, the reasons for the increase in urine loss in some patients is not clear. Periodic follow-up is recommended to determine any changes in the status of urinary incontinence.
11. Patients should be counseled to wash hands and avoid touching the device prior to its insertion, as described in the patient labeling.
12. Patients should be reminded to never re-use the Reliance[®] Urinary Control Insert because of the possibility of infection
13. Patients should be counseled to always remove the device when they feel the need to urinate. Patients should be reminded that the Insert should not remain in place for more than 6 hours, or while asleep, because of the possibility of reflux if the bladder were to overflow.
14. Patients should be instructed to clean the Applicator with mild soap and water and store in a clean dry location after each use. While the Applicator can be safely used up to 50 times, patients should be counseled to use the new Applicators provided in each new carton of Inserts.

V. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Adverse events reported in association with the use of the Reliance® Urinary Control Insert include: positive urine culture, urethral discomfort/irritation, trace hematuria, urinary tract infection (UTI), urinary symptoms, hematuria, awareness of the device, gross hematuria/tinged urine, pyuria, bladder/urethral irritation on cystoscopic evaluation, bleeding/spotting, asymptomatic bacteriuria, and device migration.

ADVERSE EVENT	RATE (95% CONFIDENCE INTERVAL)
Positive Urine Culture	80% (73-88%)
Urethral Discomfort/Irritation	78% (71-84%)
Trace Hematuria	61% (51-71%)
Urinary Tract Infection (UTI)	44% (34-53%)
Urinary Symptoms ¹	42% (34-50%)
Hematuria	33% (25-41%)
Awareness of the Device	30% (21-38%)
Gross Hematuria/Tinged Urine	25% (17-32%)
Pyuria	24% (15-33%)
Bladder/Urethral Irritation (Cystoscopic Evaluation)	22% (13-32%)
Bleeding/Spotting	20% (15-25%)
Asymptomatic Bacteriuria	19% (10-27%)
Device Migration	5% (1-9%)

(1) Includes increased voiding, enuresis, nocturia, dysuria, and urgency

Other adverse events were noted to occur infrequently, and are listed later in the Clinical Studies Section.

VI. ALTERNATE PRACTICES OR PROCEDURES

Stress urinary incontinence in females is often associated with two general types of sphincter dysfunction related to abnormalities of urethral supporting tissue or

malfunction of the urethral sphincter mechanism. There are four major categories of treatments for these physiologic and anatomic disturbances:

1. Use of external devices (collecting, absorbing, or occluding) such as pads or diapers.
2. Behavioral techniques which include bladder training, habit training, prompted voiding, pelvic muscle exercises, biofeedback, vaginal cones, and electrical stimulation.
3. Pharmacological treatments which include alpha-adrenergic agonists and estrogen supplements.
4. Surgical treatments which include urinary diversion procedures, suspension or sling procedures, urethral bulking agents, and the implantation of an artificial urinary sphincter.

VII. MARKETING HISTORY

The Reliance® Urinary Control Insert became commercially available first in the Federal Republic of Germany in September of 1995, and is now also marketed in Norway, Denmark, Sweden, Finland, the United Kingdom, and the Netherlands. The device has also been judged to be in Conformity with the European Union Medical Device Directives, and, thus, can bear the CE mark of certification.

The Reliance® Urinary Control Insert has not been withdrawn from marketing for any reason relating to the safety and effectiveness of the device.

VIII. SUMMARY OF STUDIES

A. LABORATORY STUDIES (NONCLINICAL STUDIES)

PERFORMANCE TESTING

General Performance Test - One hundred devices were tested to determine if the device remains functional after prolonged exposure to a simulated *in vivo* environment. The balloon diameter was maintained for over 8 hours and the average post-test outer diameter was 0.6".

Pressure/Volume/Diameter Burst Test - Thirty devices and ten Reliance® Sizing Devices (RSDs) were tested to determine the factor of safety and point of failure by comparing burst volume to actual use volume. Proper balloon inflation was assured by comparing inflation pressure to the connector pop-off pressure. The average

volume at burst was 10.88 cc (>> 1.6 cc) and the average initiation pressure was 7.7 psi.

Valve Deseating Force Test (String Pull to Deflate Test) - Thirty devices were tested to determine the force required to pull the valve from an inflated device. The average deseating force was 0.49 lbs with a range of 0.24-0.6 lbs.

Balloon to Body Shaft Tensile Test - Thirty devices and ten RSDs were tested to determine the force necessary to peel the balloon off the device body. This tested the lamination of the balloon to the body. The average peel force was 3.28 lbs and the mode of failure was balloon breakage before the lamination was affected.

String to Ball Valve Tensile Test - Thirty devices were tested to determine the force necessary to detach the ball valve from the string and to compare this value to the deseating force to assure proper deflation. The average pull force was 16 lbs.

Connector Pop-Off Force Test - Thirty devices were tested to determine the pressure required to break the seal between the body of the device and the applicator. The average pressure was 35.5 psi.

Flex Test - Thirty devices were used to simulate the bending angles of the product found *in vivo* to evaluate the integrity of the valve seal. The average flex angle was 78°.

Pinch Test - Thirty devices were used to simulate the forces against the valve seat found *in vivo* and to assure the integrity of the valve seal during pinch. This test also demonstrated that the balloon can be pinch deflated as a secondary deflation mechanism. The average pinch force was 0.38 lbs.

Applicator Removal Force Test - Fifteen devices were used to simulate applicator removal and to measure the force required to remove the applicator after inflation. The average removal force was 0.075 lbs.

Urethral Pull-Out Test - Thirty devices were tested to establish the failure mode of an inflated product by pulling it through an artificial urethra (made from artificial skin of the same durometer of human skin) to assure that an inflated device can be pulled through the urethra without bursting. The average pull-out force was 5.81 lbs.

Valve Pressure Deseating Test - Thirty devices were tested to measure the pressure necessary to lift the valve off the device valve seat and allow air to pass into and inflate the balloon. This pressure was then compared to the pressure generated by the applicator. The balloon pressure required to deseate the valve was measured and compared to the internal balloon pressure. The average pressure to raise the valve was 7.18 psi and the average pressure to deseate the valve was 34.27 psi.

Meatal Plate Compression Test - Thirty devices were used to simulate compression forces against the device found *in vivo* to evaluate the integrity of the valve seal. No leakage was observed after 10,000 cycles.

Bladder Simulation Test - Thirty devices were used to simulate *in vivo* pressures against the device balloon using a bladder model. No leakage was observed after constant pressure or pressure spikes applied.

General Performance Test Post-Heat Exposure - Fifteen devices were tested to evaluate the general performance of the device after exposure to various temperatures. The balloon diameter was maintained for over 8 hours after exposure to 110° F for 64 hours.

Fitting to Shaft Tensile Test (RSD) - Twenty RSDs were tested to determine the force necessary to pull the inflator fitting from the RSD shaft. The average pull force was 2.44 lbs.

The results of these laboratory tests demonstrate that the device can withstand the mechanical forces expected during clinical use.

BIOCOMPATIBILITY/TOXICOLOGY TESTING

The balloon, catheter shaft, and meatal plate contact urethral or bladder mucosa while the nylon string contacts vaginal mucosa since it remains outside the urethra during device use. The sizing device also has ink markings (graduations) on the catheter shaft.

Biocompatibility tests were performed in accordance with Good Laboratory Practices (GLPs) on raw materials and on finished devices. Short and long-term studies were performed. Short-term studies included: cytotoxicity, systemic toxicity, intracutaneous toxicity, skin sensitization maximization (in guinea pigs), vaginal mucosal irritation study in rabbits, hemolysis, pyrogenicity, mutagenicity, a 13-week subchronic toxicity study with extracts, and 7-day and 30-day muscle implantation test in rabbits. Long-term tests consisted of 180-day and 1-year muscle implantation tests on the balloon material, and 180-day implantation test on the shaft and meatal plate material. Long-term toxicity testing was required because the device is intended for repeated use over an extended period of time.

The results show that the balloon, catheter shaft, and meatal plate materials caused slight irritation in both the short and long-term studies. The nylon string was also found to cause slight irritation. The test laboratory histopathologist who reviewed these studies attributed the irritation to foreign body response and not to leachates from the device.

B. CLINICAL STUDIES

PROTOCOL

A clinical study was conducted under IDE G940135 to determine if the Reliance® Urinary Control Insert is safe and effective for the intended use of managing involuntary urine leakage due to, or associated with, stress or mixed incontinence in adult women.

The clinical study was a multi-center investigation with each patient as her own control. Effectiveness was primarily measured by using a standardized pad weight testing protocol that compared urine loss without the device to urine loss with the device inserted. Adverse events and their frequency were recorded as the primary safety criterion. These events are defined in the Results Section below.

The following Inclusion/Exclusion criteria were used in enrolling patients.

Inclusion:

1. Female patients between 30 and 75 years old.
2. Patients diagnosed with pure stress or mixed incontinence.
3. Patients with sound mental conditions and manual dexterity.
4. Patients who experience three or more incontinence episodes per week.

Exclusion:

1. Patients with overflow incontinence or neurogenic bladder conditions.
2. Patients with pyelonephritis, interstitial cystitis, or recurrent urinary tract infections.
3. Patients who are allergic to or cannot tolerate any form of antibiotics.
4. Patients who are taking anticoagulants or any medications to treat incontinence.
5. Patients with a prosthetic heart valve or other cardiac conditions that put them at increased risk of subacute bacterial endocarditis.
6. Patients who are pregnant.
7. Patients with severely compromised mucosal tissue documented during cystoscopy.
8. Patients who cannot use any urinary catheter because of anatomical anomalies.
9. Patients unable or unwilling to comply with the study protocol.

The firm also excluded, delayed entry, or terminated from the study any patients who met one of the following criteria.

1. Patients undergoing hormone replacement therapy for less than 60 days.

2. Patients with less than three incontinent episodes documented in their pre-use activity diary.
3. Patients who did not return completed diaries prior to beginning device use.
4. Patients with less than two grams of urine loss (without the device) during the first pad weight study.
5. Patients whose urine loss did not decrease significantly while using the device during the first post-enrollment pad weight study.
6. Patients who experienced four urinary tract infections while using the device. (All data from these patients were included in the safety analysis.)

The following is a summary of the clinical evaluation schedule used in the study.

At the initial visit, medical history and quality of life (QOL) forms were completed. A clinical examination (including a urine microscopy and culture, a cystoscopy, and a cystometrogram) was conducted along with a pre-device pad weighing. Sizing of the device (determining appropriate length of the Reliance[®] Urinary Control Insert) for patients accepted into the study was also done at this visit.

After 1 week, the subject returned with a completed daily activity diary that was designed to document her urine leakage without the device. The patient was then given a supply of devices and instructed to complete a daily questionnaire for the first 2 weeks of use. All patients were required to use the device on a daily basis for the duration of their enrollment in the study.

The next evaluation occurred 1 week after the first device use. At this visit, an assessment of both the device effectiveness and any adverse events was made. A urine microscopy and culture were also obtained.

Regular monthly visits were also required for the first 12 months of device use. These visits consisted of a urine microscopy and culture. The patient also completed, for the week after the visit, a daily questionnaire that was designed to document device use and urine leakage.

The 4-month and 1-year follow-up visits also included a cystoscopy, cystometrogram and pad weight study. The pad weight study was conducted first with the device and then without the device inserted. The subject also completed the QOL form. If a patient elected to remain in the study after the 1-year follow-up, regular visits were scheduled for every 2 months. These included a urine microscopy and culture. Every 6 months a cystoscopy and cystometrogram were performed.

At selected sites, subjects were required (at the 6- and 12-month evaluation) to discontinue device use for 14 days and document their incontinence symptoms in their daily activity diary. At the end of this 2-week period of discontinued device use, a pad weight study was conducted (6½- or 12½-month evaluation) first without and then

with the device inserted to determine if the patient's incontinence condition worsened as a result of the device use. After this evaluation, subjects could continue in the study.

STUDY ENROLLMENT/DEMOGRAPHICS

Three hundred seventy two patients were screened and evaluated for participation into the study. Of these, 68 did not meet the eligibility criteria and 3 were unable to enroll due to a temporary suspension of patient recruitment. Eighty-six other patients were not included in the analyses for the following reasons.

Reason for Exclusion from Analyses	# Patients
Unwillingness to use the device	15
Too much time required	12
Disinterested or the device did not fit lifestyle	10
Too much discomfort or pain involved in the screening procedures	5
Unwillingness to complete the diary or keep the required appointments	3
Too far to travel	2
Decided to try alternative treatment	2
Concerned about possibility of UTIs	1
Other or unknown	21
Inability to insert the device	2
Death in the family	1
Lost to follow-up	12

When the aforementioned patients were excluded from the analyses, 215 patients remained eligible for evaluation.

The patients were seen at 10 different study sites. The number of subjects at each site ranged from 9 (4.2%) to 41 (19.1%). The following table lists the sites, investigators, and number of enrolled patients at each site.

Study Site	Investigator	Number of Enrolled Subjects
Beth Israel Hospital	David Staskin, M.D.	28
Colorado Gynecology and Continence Center	Guillermo Davila, M.D.	9
Evanston Continence Center	Peter Sand, M.D.	13
Greater Baltimore Medical Center	Alfred Bent, M.D.	9
Methodist Hospital of Indiana	Stephen Rappaport, M.D.	26
New England Medical Center	Granum Sant, M.D.	17
The Urology Center at Charles North	Ronald Tutrone, M.D.	22
Thomas Jefferson Medical College	Joseph Montella, M.D.	20
University of Washington Medical Center	Tamara Bavendam, M.D.	30
William Beaumont Hospital	Ananias Diokno, M.D.	41

The 215 patients had the following demographics:

Patient Demographic	Value
Age at Study Entry	52.62 ± 10.26 years
Age at Onset of Incontinence	39.94 ± 13.37 years
Duration of Incontinence	12.47 ± 10.13 years
Urine Loss During Initial Pad Weight Test	41.32 ± 43.33 grams
Type of Incontinence I (slight hypermobility of the urethra and bladder) II (significant hypermobility of the urethra and bladder) III (intrinsic urethral sphincter deficiency) Unknown	49 (22.8%) 129 (60.0%) 36 (16.7%) 1 (0.5%)
Initial Leakage Without Device < 10 grams 10 - 25 grams Greater than 25 grams Unknown	43 (20.0%) 50 (23.3%) 114 (53.0%) 8 (3.7%)
Hormone Replacement Therapy Yes No Unknown	79 (36.7%) 78 (36.3%) 58 (27.0%)
Prior History of UTI Yes No Unknown	15 (7.0%) 199 (92.5%) 1 (0.5%)
Prior Corrective Surgery Yes No Unknown	54 (25.1%) 143 (66.5%) 18 (8.4%)

It is important to note that the standard deviations for Duration of Incontinence (10.13 years) and Urine Loss During Initial Pad Weight Test (43.33 grams) are so large as to minimize the value of the information provided by these parameters.

EFFECTIVENESS

Of the 215 evaluable patients, 123 (57.2%) used the device for 4 months and 50 (23%) used the device for at least 12 months. The following table provides the reasons given for the patients who discontinued from the study.

Primary Reason	1 Month or Less	1-4 Months	Greater than 4 Months	Total
Discomfort	12	17	11	40
Unwilling/Unable to Use Device	6	14	16	36
Other	3	4	13	20
Noncompliance with Protocol	1	3	8	12
Urgency	2	5	4	11
Site Termination	0	1	9	10
UTI	0	7	3	10
Lost to Follow-Up	3	1	5	9
Leakage with Use	2	1	4	7
Medical Complication	1	5	1	7
Unknown	3	0	0	3
Total	33	58	74	165

Three methods were used to determine the device effectiveness: (1) pad weight tests, (2) entries in patient diaries, and (3) interviews at follow-up visits. In addition, quality of life (QOL) was also assessed from patients' responses to a generic questionnaire (i.e., the Medical Outcomes Survey - Short Form, hereafter referred to as the SF-36). Of these various methods, the pad weight test was considered to be the primary criterion for effectiveness because it is the most objective test.

The effectiveness analysis of the device is, therefore, primarily based on the pad weight data which measures the change in urine loss (i.e., urine loss without the device minus urine loss with the device). This test involved a set of specific exercises (e.g., coughing, running in place, jumping, washing hands under water, stair climbing and deep knee bends) in the physician's office.

Of the 215 evaluable patients, 194 were considered to be acceptable for this analysis. Of the 21 excluded, 12 were protocol deviations, 5 utilized an earlier prototype device, and 4 did not have complete pad weight data at baseline. Ninety seven patients had complete data at 4 months, and 36 patients had complete data at 12 months. The following table illustrates these data.

Time of Follow-up	Sample Size	Mean Urine Loss Without Device (gm)	Mean Urine Loss With Device (gm)
Baseline	194	44.40 ± 44.28	2.64 ± 7.41
Four Month			
Baseline	97	43.72 ± 46.61	1.81 ± 5.45
Four Month	97	43.60 ± 53.83	2.43 ± 6.93
Twelve Month			
Baseline	36	40.77 ± 43.01	2.13 ± 5.59
Four Month	36	33.41 ± 41.19	1.50 ± 6.40
Twelve Month	36	34.84 ± 39.29	2.19 ± 6.80

Even though the standard deviations are very large, the pad weight study does show that the device is highly effective in reducing the amount of urine loss ($p = 0.0001$).

Of the 194 patients that had pad weight data at baseline, 21 patients had mixed incontinence. This group remained small throughout the study: 12 of the 97 patients at 4 months and 4 of the 36 patients at 12 months belonged to this group. The stratified data for pure stress incontinence patients are similar to the data shown in the table above, demonstrating the effectiveness of the Reliance® Urinary Control Insert in reducing urine leakage in subjects with pure stress incontinence. However, there was an insufficient number of patients with mixed incontinence to evaluate the safety and effectiveness for this patient population.

Prior to October 1993, four slightly different devices, referred to as initial device design (IDD), were developed. The term Reliance® Urinary Control Insert refers to the post-October 1993 device. The two devices which were primarily used for most of the clinical studies are the January 1993 IDD version and the current Reliance® Urinary Control Insert. These two versions differ only slightly in design, materials, and physical properties. The Reliance® Urinary Control Insert was introduced into the study at one site and limited to four patients in October 1993 and full clinical conversion was initiated in February 1994. The applicant has adequately justified the acceptability of the IDD data for the purpose of demonstrating safety and effectiveness for the Reliance® Urinary Control Insert. Using a stratified repeated measures analysis, the applicant was able to show that there was no significant difference

($p = 0.1243$) in the mean change of urine loss among patients using the earlier version, the current Reliance[®] Urinary Control Insert, or a combination of the two designs.

The applicant also presented analyses that tested for statistical significance in the primary effectiveness endpoint (mean change in urine loss) over a variety of parameters. No significance was found (at baseline, 4, or 12 months) for patients with varying degrees of incontinence (amounts of leakage) or with different types of stress incontinence (I, II, or III) or for those on hormone replacement therapy. Patients who had prior surgery did have a statistically significant greater mean reduction in urine loss at baseline. Since only a small number of these patients had long-term follow-up, this significance cannot be seen at 12 months.

Patients who had greater urine loss without the device at baseline had a significantly greater reduction in urine loss with the device at baseline, 4, and 12 months. An analysis of patients who withdrew from the study was performed to determine if the study results for change in the amount of urine loss were biased. The analysis showed that time of withdrawal from the study did not influence the change in urine loss results.

The patient diary assessment utilized a 5-point scoring system for determining effectiveness. In this system, a score of 1 represented no leakage, a score of 3 represented moderate leakage (enough to wet pad and/or undergarments), and a score of 5 represented a large amount of leakage (enough to wet pad and/or undergarment and run down legs). This information was collected for various activity categories (sitting/lying, standing, walking, lifting/bending). These data showed that a statistically significant ($p < 0.005$ for all categories) difference existed between pre-device urine loss and device urine loss at baseline, 4, and 12 months.

A similar scoring system was used for patient recollections of urine leakage in the interview method. These results parallel the diary score results.

Quality of Life assessments based on SF-36 surveys filled out by the subjects showed that at 12 months, patients reported a significant improvement ($p < 0.05$) in the physical function and general health when compared to baseline. However, due to the small number of patients who remained in the study at 12 months, and the fact that this evaluation was not specific to urological health, these data are of limited value.

The effectiveness results of this clinical study demonstrate that the Reliance[®] Urinary Control Insert did reduce urine leakage in women with stress urinary incontinence who elected to use this device. It should be noted, however, that patients whose urine loss did not significantly decrease during the first pad weight test were denied further participation in the study.

SAFETY

The safety analysis of the device is based on the adverse event rates determined by the Kaplan-Meier Lifetable Analysis (95% confidence interval). This analysis only is based on an updated patient population of 255 patients enrolled into the study. All other analyses are based on 215 patients. These rates are essentially similar to the adverse event rates observed on the 215 patients except for hematuria (33% vs 28%) and awareness of the device (30% vs 24%).

The following table contains the rates based on the Kaplan-Meier Lifetable Analysis on the updated patient population:

ADVERSE EVENT	RATE (95% CONFIDENCE INTERVAL)
Positive Urine Culture	80% (73-88%)
Urethral Discomfort/Irritation	78% (71-84%)
Trace Hematuria	61% (51-71%)
Urinary Tract Infection (UTI)	44% (34-53%)
Urinary Symptoms ¹	42% (34-50%)
Hematuria	33% (25-41%)
Awareness of the Device	30% (21-38%)
Gross Hematuria/Tinged Urine	25% (17-32%)
Pyuria	24% (15-33%)
Bladder/Urethral Irritation (Cystoscopic Evaluation)	22% (13-32%)
Bleeding/Spotting	20% (15-25%)
Asymptomatic Bacteriuria	19% (10-27%)
Device Migration	5% (1-9%)

(1) Includes increased voiding, enuresis, nocturia, dysuria, and urgency

Other reported symptoms which occurred at a rate of <3% in the 215 patients include: discomfort/difficulty during device insertion/removal, bladder pressure, vaginal irritation, urethral/voiding sensation, bladder pain/spasms/sensation, increased leakage, nocturnal enuresis, general discomfort, irritation associated with bowel movement, pain in the left kidney area, rubbing sensation, and device/tab rotation.

Other complications which occurred in the 215 patients at a rate of < 2% include: detrusor contraction, vaginal insertion, acute urinary retention, bladder irritation, detrusor instability, external urethral meatus abrasion, inclusion cyst-meatus, large uterine impression, low back pain, worsened cystometric parameters, and yeast infection.

Based upon the nature of the device, the target population, and the adverse events profile as summarized in the preceding adverse event table, the issue of device related urinary tract infections, secondary to ascending bacteria, was examined in further detail. Unfortunately no data exist on the rates of positive culture and UTI in the study cohort prior to entry; therefore, we cannot calculate relative risk with and without the device for this patient population. Despite the large number of patients noted to have experienced clinical UTI and/or positive urine cultures, no cases of upper urinary tract infection or sepsis were reported. All patients requiring treatment were able to resume use of the device following a short course oral antibiotics.

PATIENT WITHDRAWALS

As pointed out earlier, a large number of patients withdrew from the study. Even those that continued in the study did not all participate in the 12-month pad weight test. Since only 36 of the 215 enrolled patients completed the 12-month follow-up, a question was raised as to whether this patient group differed from the large group of patients that withdrew or were unavailable for the test. Analysis of the 12-month group (36 patients) and the larger < 12-month group (179 patients) with respect to several baseline characteristics such as age, type of incontinence, pre-device urine loss, hormone replacement therapy, prior UTI history, prior incontinence surgery, mean urine loss before device use, duration of incontinence, and age at onset showed no significant differences clinically or demographically between the two groups. The only difference noted was that there were significantly less Type I incontinence patients and more Type III incontinence patients in the 12-month group. The main reasons for the high rate of patient withdrawals were the clinical protocol requirements, extension of the study from 4 to 12 months and urethral discomfort/irritation associated with the device use

DEVICE FAILURES

As of March 18, 1996, an estimated 144,450 devices had been used in the study. Six hundred eighty-two devices (0.5%) were returned. Only 36 (5.3%) of the returned devices were determined to be defective. These data demonstrate a very low device malfunction rate.

IX. CONCLUSIONS DRAWN FROM THE STUDIES

The laboratory, animal and clinical data provide reasonable assurance of the safety and effectiveness of the Reliance® Urinary Control Insert for the management of stress urinary incontinence in adult women, when used as indicated.

X. PANEL RECOMMENDATION

The Gastroenterology and Urology Advisory Panel met on July 25, 1996, to discuss the application. The Panel recommended that the application be approved subject to submission to, and approval by the Center for Devices and Radiological Health (CDRH) of modifications to the device's labeling and the inclusion of a plan for postapproval study. The Panel recommended that the labeling be modified to state that the Reliance® Urinary Control Insert be prescribed only for the management of stress urinary incontinence in female patients and that prescribing physicians have adequate training in the management of such patients.

The Panel also recommended a postapproval study on 150 women for 5 years to evaluate the long-term effects of the Reliance® Urinary Control Insert use on UTIs and urethral integrity, and a shorter term study to evaluate use of the device during sexual intercourse.

XI. CDRH DECISION

CDRH granted expedited review status for the Reliance® Urinary Control Insert. The decision to expedite the review of this device was based on the belief that the Reliance® Urinary Control Insert represented a specific public health benefit for the treatment of female stress urinary incontinence, when compared to existing treatment options.

CDRH agreed with the Panel's recommendations that the PMA be approved subject to conditions which include labeling changes and a 5-year postapproval study of the use of the Reliance® Urinary Control Insert. CDRH also required information explaining the inconsistencies reported in the clinical data.

FDA issued a status letter, dated July 29, 1996, to UroMed Corporation advising them that CDRH agreed with the panel that the PMA was approvable subject to the above conditions and resolution of outstanding issues in the PMA. In the amendment received by FDA on August 14, 1996, UroMed submitted the required information.

The applicant addressed the labeling, including appropriate changes to the physician and patient labeling, and postapproval study as stated in the status letter and subsequent discussions with FDA staff. To fulfill the conditions of approval, the applicant will conduct a 5-year study on 150 women diagnosed to have stress urinary incontinence regarding potential safety issues associated with long-term use of the

Reliance® Urinary Control Insert. The applicant asked CDRH to reconsider the Panel's recommendation for a study on the effects of Reliance® Urinary Control Insert use during sexual intercourse. FDA disagrees with the Panel's recommendation because the device labeling already contains a warning not to use the device under these circumstances. FDA will not require this study unless the applicant wishes to delete this warning from the label.

CDRH determined that, based on the modified labeling, the postapproval study plan and the additional information submitted to explain the clinical data inconsistencies, the sponsor's response was adequate.

Following an FDA inspection which was completed on July 26, 1996, the manufacturing facilities were determined to be in compliance with the Good Manufacturing Practices (GMP) regulation.

CDRH issued an approval order for the application on August 16, 1996.

RELIANCE[®] URINARY CONTROL INSERT AND SIZING DEVICE
PHYSICIAN LEAFLET

CAUTION: Federal (USA) law restricts this device to sale by or on the order of a physician trained in the management of urinary incontinence..



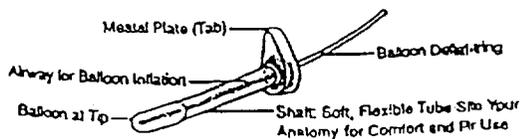
PLEASE RETAIN THESE INSTRUCTIONS FOR USE

THE RELIANCE[®] URINARY CONTROL INSERT
AND SIZING DEVICE

DEVICE DESCRIPTION

The Reliance[®] Urinary Control Insert is a sterile, balloon-tipped device. It is inserted into the urethra by the user after appropriate training by a physician. The Reliance device consists of the following components: a catheter shaft and a meatal plate (tab) molded from a thermoplastic elastomer; a balloon also molded from a thermoplastic elastomer; a braided nylon deflation string coated with a nylon resin; and a ball valve with an internal lubricant. The balloon-tip is inflated using a removable, reusable Applicator. The Insert is easily deflated and removed when the woman wants to void. Afterwards, a new, sterile Reliance[®] Urinary Control Insert can be inserted.

The Reliance Device

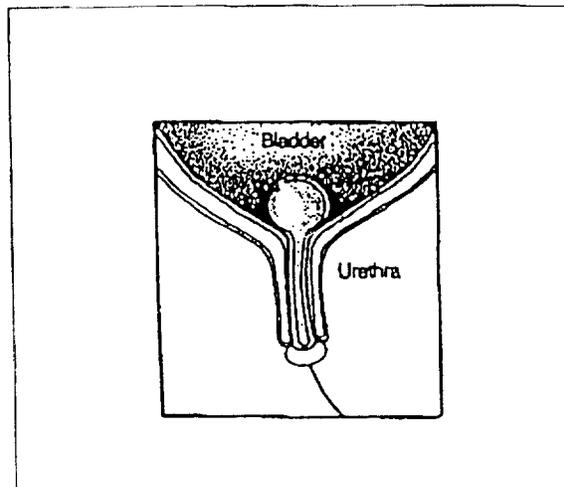


The Reliance Applicator



The Reliance[®] Urinary Control Insert and Removable Applicator.

The Reliance[®] Urinary Control Insert in place.



Before prescribing the Reliance[®] Insert the Physician uses the Sizing Device to determine the length of the urethra. The Sizing Device is a sterile balloon tipped catheter-like device designed for measuring the size of the patient's urethra. It consists of a balloon tip molded from a thermoplastic elastomer, a beaded shaft, also molded from a thermoplastic elastomer, and a syringe applicator. The appropriate size Insert for each patient is then determined from the size of the urethra. The Inserts are available in 5 sizes 3.0, 3.5, 4.0, 4.5, and 5.0 centimeters.

INDICATIONS FOR USE

The Reliance[®] Urinary Control Insert is intended for use in the management of stress urinary incontinence in adult women.

CONTRAINDICATIONS

The use of the Reliance[®] Urinary Control Insert is contraindicated in women who:

1. Have anatomical anomalies that preclude the use of urinary catheters such as the Reliance[®] Urinary Control Insert.
2. Have interstitial cystitis, pyelonephritis, or a history of severely compromised urinary tract mucosal tissue.
3. Have an active urinary tract infection (UTI).

4. Have a prosthetic heart valve or other cardiac condition that puts the patient at increased risk of subacute bacterial endocarditis (due to the risk of infection).
5. Cannot tolerate any form of antibiotic therapy.
6. Are currently receiving anticoagulant therapy.
7. Have overflow incontinence or neurogenic bladder.

WARNINGS

1. Care must be taken to ensure that the correct size (length) of the Reliance[®] Urinary Control Insert is prescribed. During the clinical investigation, one patient was fitted with a Reliance[®] Urinary Control Insert that was too short and this patient experienced a device migration into the bladder.
2. Reliance should not be used during Sexual Intercourse as the effects were not studied in the clinical trial and are unknown.

PRECAUTIONS

1. The Reliance Urinary Control Insert and the Sizing Device are sterile if the package is unopened or undamaged. Do not use if the package are damaged or open.
2. This device should be prescribed by a Physician trained in the management of Urinary Incontinence.
3. Patients who present with a history of frequent UTIs should be advised that they may be at increased risk of infection with use of the Reliance Urinary Control Insert. Additionally, these patients should be monitored closely for symptoms of UTI during Insert use.
4. If the patient reports or develops symptoms of possible UTI, she should be instructed to temporarily discontinue use of the Reliance[®] Urinary Control Insert until she has been medically evaluated. If infection is diagnosed, the Insert should not be used until the infection has been treated.
5. If the patient reports visible hematuria or bleeding but no other symptoms of UTI, she should be instructed to temporarily discontinue use of the Reliance[®] Urinary Control Insert. After her symptoms resolve, she can continue using the Insert. If the symptoms persist, she should

be instructed to contact her physician. If the symptoms recur after resuming Insert use, she should be instructed to discontinue use of the device and contact her physician.

6. The Safety and Effectiveness of the Reliance[®] Urinary Control Insert during pregnancy have not been studied and its effects are unknown.
7. Patients often experienced urethral irritation and discomfort during the first two or three weeks of using the Reliance[®] Urinary Control Insert.
8. Use of the Insert should be discontinued in those patients who develop abrasion of the bladder wall and/or urethral meatus. Device use may be resumed once these conditions are fully resolved.
9. Long term safety and effectiveness data on the use of the Reliance[®] Urinary Control Insert has not been developed, therefore continued close patient follow up is recommended.
10. Urine loss was observed to increase in some patients, and decrease in others following Insert use over time. Although there was not a statistically significant increase in urine loss observed during the course of the study, the reasons for the increase in urine loss in some patients is not clear. Periodic follow up is recommended to determine any changes in the status of urinary incontinence.
11. Patients should be counseled to wash hands and avoid touching the device prior to its insertion, as described in the patient labeling.
12. Patients should be reminded to never re-use the Reliance[®] Urinary Control Insert because of the possibility of infection.
13. Patients should be counseled to always remove the device when they feel the need to urinate. Patients should be reminded that the Insert should not remain in place for more than 6 hours, or while asleep, because of the possibility of reflux if the bladder were to overfill.
14. Patients should be instructed to clean the Applicator with mild soap and water and store in a clean dry location after each use. While the Applicator can be safely used up to 50 times, patients should be counseled to use the new Applicators provided in each new carton of Inserts.

POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Adverse events reported in association with the use of the Reliance Urinary Control Insert include: positive urine culture, urethral discomfort/irritation, trace hematuria, urinary tract infection (UTI), urinary symptoms, hematuria, awareness of the device, gross hematuria/tinged urine, pyuria, bladder/urethral irritation on cystoscopic evaluation, bleeding/spotting, asymptomatic bacteriuria, and device migration.

ADVERSE EVENT	RATE (95% CONFIDENCE INTERVAL)
Positive Urine Culture	80% (73 - 88%)
Urethral Discomfort/Irritation	78% (71 - 84%)
Trace Hematuria	61% (51 - 71%)
Urinary Tract Infection	44% (34 - 53%)
Urinary Symptoms ¹	42% (34 - 50%)
Hematuria	33% (25 - 41%)
Awareness of the Device	30% (21 - 38%)
Gross Hematuria/Tinged Urine	25% (17 - 32%)
Pyuria	24% (15 - 33%)
Bladder/Urethral Irritation on Cystoscopic Evaluation	22% (13 - 32%)
Bleeding/Spotting	20% (15 - 25%)
Asymptomatic Bacteriuria	19% (10 - 27%)
Device Migration	5% (1 - 9%)

¹ Includes increased voiding, enuresis, nocturia, dysuria, and urgency.

Other adverse events occurred infrequently, and are described later in the clinical trial section.

CLINICAL TRIAL

A multi-center (Urologists and Urogynecologists participated) clinical trial was conducted to assess the safety and effectiveness of the Reliance Urinary Control Insert, using women as their own control. A total of 215 women, between the ages of 30 and 75 years of age, were enrolled in the clinical trial.

Patient Withdrawal

Of the 215 women enrolled in the study, approximately 57% (123) continued in the study for four months or more, 46% (99) continued for six months or more and 23% (50) remained in the study for 12 months. The reported effectiveness rates listed are based on 36 patients at one year, as these were the patients who had completed pad weight tests at 12 months. Statistical analysis shows no significant differences in the safety or effectiveness of the device between the smaller one year group (36 patients) and the larger group of patients who withdrew from the study and did not have 12-month follow up.

The reasons for patient withdrawal in the clinical study include: reports of urethral discomfort/irritation while using the device(19%), inability or unwillingness to use the device(17%), various personal reasons(9%), unwillingness to abide by the demands of the clinical protocol(6%), urgency(6%), termination of investigational site(5%), urinary tract infection(5%), lost to follow up(4%), leakage with use(3%), medical complications(3%), and for unknown reasons(1%).

Effectiveness Evaluation

The device's effectiveness was assessed by pad weight using a standardized protocol, and study subjects' assessments of urine leakage during daily activities using a five-point rating scale recorded on diaries and through interviews. For determination of effectiveness a total of 194 patients were included in the analysis at baseline, 97 patients who completed four months of device use, and 36 patients who completed an optional follow-up period of at least one year.

For the pad weight studies, patients performed a series of exercises that are likely to induce urine leakage in women with stress incontinence with the device inserted, and then repeated the exercises without the device inserted. The device significantly decreased study subjects' involuntary urine leakage during the pad weight studies (see table below). Study subjects also reported a significant decrease in urine loss with use of the device during their daily activities, as reported by both patient diaries and interviews. These improvements were demonstrated throughout the 12 month study.

Mean Urine Loss Detected in Pad Weight Studies

Pad Weight Analysis	Sample Size	Mean Urine Loss Without Device (grams)	Mean Urine Loss With Device (grams)	Mean Change in Urine Loss (grams)
Baseline	194	44.40 SD(44.28)	2.64 SD(7.41)	41.76 SD(42.26)
Four-Month	97	43.60 SD(53.83)	2.43 SD(6.93)	41.17 SD(51.96)
Twelve-Month	36	34.84 SD(39.29)	2.19 SD(6.80)	32.65 SD(36.64)

34

Safety Evaluation

The adverse event rates as previously described in the adverse events section (pages 5 and 6) reported in the Reliance[®] clinical investigation through 12 months of follow-up are provided below. This is based on an updated base of 255 patients. These rates reflect the risk of patients experiencing the specified adverse event at some point during the 12 month study. No attempt was made to distinguish between device-related and non device-related events.

Adverse Event	Rate	(95% Confidence Interval)
Positive Urine Culture	80%	73 - 88%
Urethral Discomfort/Irritation	78%	71 - 84%
Trace Hematuria	61%	51 - 71%
Urinary Tract Infection	44%	34 - 53%
Urinary Symptoms ¹	42%	34 - 50%
Hematuria	33%	25 - 41%
Awareness of the Device	30%	21 - 38%
Gross Hematuria/Tinged Urine	25%	17 - 32%
Pyuria	24%	15 - 33%
Bladder/Urethral Irritation on Cystoscopic Evaluation	22%	13 - 32%
Bleeding/Spotting	20%	15 - 25%
Asymptomatic Bacteriuria	19%	10 - 27%
Device Migration	5%	1 - 9%

¹ Includes increased voiding, enuresis, nocturia, dysuria, and urgency.

Many of these adverse events required no intervention. For example, urethral or urinary symptoms, pyuria and bacteriuria in the absence of other clinical indicators of infection, hematuria, and trace hematuria were not routinely treated. For the majority of other adverse events, other than when antibiotics were prescribed for infection, temporary cessation of device use was the only intervention required.

Based upon the nature of the device, the target population, and the adverse events profile as summarized in the adverse event table above, the issue of urinary tract infection, secondary to ascending bacteria, related to the use of this device, was examined in further detail. Unfortunately no data exists on the rates of positive culture and UTI in the study cohort prior to entry; therefore, we cannot calculate relative risk with and without the device for this patient population. Despite the number of patients noted to have experienced clinical UTI and/or positive urine cultures, no cases of upper urinary tract infection or sepsis were reported. All patients requiring treatment were able to resume use of the device following a short course of oral antibiotics.

Other Events

Other symptoms which were reported in the clinical study in less than 3% of patients included the following listed in order of decreasing frequency: Discomfort/Difficulty During Device Insertion/Removal, Bladder Pressure, Vaginal Irritation, Urethral/Voiding Sensation, Bladder Pain/Spasms/Sensation, Cramping, Increased Leakage, and Nocturnal Enuresis.

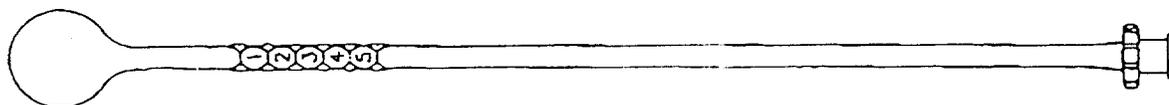
* Other complications which occurred in the clinical study in less than 2% of patients include: detrusor contraction, vaginal insertion, acute urinary retention, bladder irritation, detrusor instability, external urethral meatus abrasion, inclusion cyst-meatus, large uterine impression, low back pain, worsened cystometric parameters, and yeast infection.

28

INSTRUCTIONS FOR DETERMINING THE URETHRA LENGTH OF THE PATIENT

The Reliance[®] Urinary Control Insert is indicated for adult woman with stress urinary incontinence. Nevertheless, physicians should be aware of the Clinical Practice Guidelines for the treatment of incontinence published by the Agency for Health Care Policy and Research, U.S. Department of Health and Human Services. These guidelines recommend a gradual approach to the treatment of incontinence. The insert offers an alternative for women who prefer not to have surgery or where surgery is not an option. Thus, before prescribing, physicians should inform their patients of the various therapies available, and discuss the inherent risks and benefits associated with each. A complete Urinary Incontinence workup as suggested by the Clinical Practice Guidelines for the treatment of incontinence should be performed prior to prescribing.

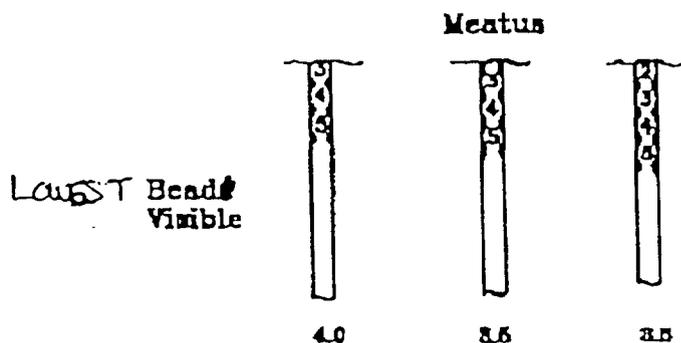
Please note that the Sizing Device is sterile if the package is unopened or undamaged. Do not use if the package is damaged.



Please refer to the above diagram when following these instructions.

1. Place the patient in the dorsal recumbent position, as if for vaginal examination and bimanual palpation.
2. Using normal sterile precautions, pull plunger of the Inflator provided with The Sizing Device as far back as possible.
3. Attach Inflator to The Sizing Device by firmly twisting their connecting parts together.
4. Use sterile, water soluble lubricant on the tip of The Sizing Device for ease of insertion and patient comfort. NOTE: Do not coat the entire Sizing Device with lubricant because it will be difficult to determine the correct size.
5. Insert The Sizing Device into urethra and gently push in until no beads are visible. This will ensure that the balloon on the tip of The Sizing Device is inside the bladder.
6. Inflate balloon on tip of The Sizing Device by completely depressing Inflator plunger. Keep the Inflator connected to The Sizing Device.

7. Gently withdraw The Sizing Device from urethra until slight resistance is felt as the balloon reaches the bladder neck. Then, allow The Sizing Device to return to its natural position while keeping the shaft of the device horizontal.
8. Determine which beads or portions of beads are visible. **Do not pull on The Sizing Device while reading the size.** Sizing determination is as follows (see diagram):



Lowest Bead Number Visible	Reliance® Size
5	5.0 cm
4	4.5 cm
3	4.0 cm
2	3.5 cm
1	3.0 cm

Note: If any portion of a bead is visible, count it as a full bead.

Note: If you are unable to see the beads clearly, rotate the shaft of The Sizing Device 90° in either direction.

9. Stabilize The Sizing Device by holding it steady with your non-dominant hand, and deflate the balloon by removing the Inflator.
10. Remove The Sizing Device from patient and discard along with the Inflator. **Do not reuse or re-sterilize The Sizing Device.**

Handwritten mark

11. Place the appropriate size Reliance[®] into the patient as determined by The Sizing Device. Ask the patient to engage in activities such as squatting, bending, running in place, sitting with crossed legs, etc. She should wear the Insert for 10 to 15 minutes in the office. If the patient experiences "pinching", the Insert is most likely too short. If she experiences discomfort, especially during activities such as sitting, and the tab of the Insert is extending below the meatus, the device may be too long. The patient should be re-sized one size larger or smaller as appropriate.

PATIENT COMMUNICATION AND TRAINING

Patients should be informed of the various Urinary Incontinence management options to make an informed decision to use the Reliance[®] Insert. Factors such as familiarity with one's anatomy, inability to use the product according to the instructions, ability to tolerate urethral discomfort/irritation and lifestyle patterns may alter a patient's choice to use the Reliance Insert. Patients should be instructed that the Insert may not be suited for every woman.

Patients should be thoroughly instructed on how to insert, inflate, deflate and remove the Reliance Urinary Control Insert. In addition, patients should be counseled about the potential adverse effects and when to seek medical care.

When the patient first begins using the device, she should receive the Reliance[®] Urinary Control Insert Starter Set. The Starter Set includes five sterile Inserts, an Applicator, a mirror, a carrying case and a copy of the Patient Instructions For Use. The Insert is also provided in Maintenance Packages containing 20, 50 or 100 Inserts with two Applicators and a Patient Instructions For Use.

The Patient Instructions For Use contains detailed information on proper use of the Reliance[®] Urinary Control Insert, and highlights when the patient should contact her physician. It is important that each patient be thoroughly instructed on the proper use of the Insert, and is able to comprehend the instructions in the patient booklet.

The list below, as well as the Patient Instructions For Use, highlights the key points that should be discussed with each patient. In addition, it may be helpful for the patient to practice using and inserting the device during her initial office visit when the Insert is first prescribed.

Irritation and Discomfort - Patients should be informed that they may experience some urethral irritation/discomfort with the Reliance[®] Urinary Control Insert for several weeks until they become accustomed to the device. If the irritation/discomfort is severe and/or persists, the use of the Insert should be discontinued and the patient should be reevaluated to determine the cause of the problem.

11

Urinary Tract Infection - Patients should be instructed to immediately report any signs of a urinary tract infection including persistent bleeding, and to temporarily discontinue device use until the patient has been medically evaluated.

Hematuria and Bleeding - Patients should be instructed to temporarily discontinue use of the Reliance[®] Urinary Control Insert if they notice any hematuria or bleeding from the urethra but have no other signs of a urinary tract infection. Patients can be instructed to resume use of the Insert after the bleeding resolves. If the bleeding does not resolve, or recurs after resuming device use, the patient should be instructed to discontinue use of the device and contact her physician.

Device Migration - Patients should be instructed to gently insert the Reliance[®] Urinary Control Insert into the urethra only until it comfortably stops at the tab, or device migration may occur. Patients should be instructed to immediately contact their physician if the Insert migrates into the proximal urethra or bladder and cannot be retrieved. In all but one case (where the Insert was cystoscopically removed), patients were able to retrieve the device themselves without any physician intervention. The patients were soon able to resume device usage without any clinical sequelae.

Device Expulsion/Removal with Inflated Balloon - Some patients unintentionally removed the Insert prior to balloon deflation, or reported the device being expelled during coughing, sneezing, or voiding. These events, observed in less than 1% of all device uses, were sometimes associated with awareness of the device, urethral discomfort or irritation, frequency, urgency, dysuria, bleeding, urethral meatus abrasion, urethritis or other symptoms. Patients may be instructed to continue use of the Reliance[®] Urinary Control Insert unless they have visible hematuria or bleeding, or symptoms of urinary tract infection or urethral meatus abrasion. In the event of significant discomfort, visible hematuria, or bleeding but no other signs of urethral abrasion or urinary tract infection, patients should be advised to temporarily discontinue use of the Reliance[®] Urinary Control Insert until the symptoms resolve; if the symptoms persist, or recur after resuming Insert use, patients should temporarily discontinue device use and contact their physician. In the event of signs of urethral abrasion or urinary tract infection, patients should be instructed to temporarily discontinue device use and contact their physician immediately.

Patient Evaluation - Patients should be instructed on the nature of their incontinence problem, and the amount of leakage prior to using the Insert. Patients should be periodically evaluated to determine the status of their incontinence without using the Reliance[®] Urinary Control Insert and the occurrence of adverse events/complications.

Device Insertion - Patients should be counseled to wash hands and avoid touching the device prior to device insertion, as described in the patient labeling.

Reuse - Patients should be reminded to NEVER reuse the Reliance[®] Urinary Control Insert because of the possibility of infection.

Six Hour Maximum - Patients should always remove the device when they feel the need to void. Patients should be reminded that the Insert should not remain in place for more than six hours, or while asleep, because of the possibility of reflux if the bladder were to overflow.

Applicator Use - Patients should be instructed to clean the Applicator with mild soap and water after each use, and to store it in a clean, dry location. While the Applicator can be safely used up to 50 times, patients should be counseled to use the new Applicators provided in each new carton of Inserts.

If you have any questions on how to use The Reliance[®] Urinary Control Insert and Sizing Device, please call one of our Customer Service Representatives toll free at 1-888-987-6633.

Reliance[®] Urinary Control Insert

Manufactured by UroMed Corporation
Needham, Massachusetts 02194, USA

Reliance[®] is a Registered Trademark of UroMed Corporation
Patent 5,090,424

Part Number Rev # MM/YY

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RELIANCE® URINARY CONTROL INSERT

PATIENT INSTRUCTIONS FOR USE

This pamphlet provides instructions to help you correctly use the RELIANCE® Urinary Control Insert. The RELIANCE® Urinary Control Insert is not a cure for incontinence but it may help you manage your bladder control problem.

Read these instructions completely before you use the RELIANCE® Urinary Control Insert. If you have any questions at all, contact your physician or call one of our Customer Service Representatives at 1-888-987-6633.

RELIANCE® URINARY CONTROL INSERT
UROMED CORPORATION
64 A STREET
NEEDHAM, MA 02194
1-888-987-6633
1-888-9UROMED

CAUTION:

Federal (USA) law restricts this device to sale by or on the order of a physician trained in the management of urinary incontinence.

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updated 8/16

TABLE OF CONTENTS

ABOUT STRESS INCONTINENCE	PAGE 3
INTRODUCING THE RELIANCE® URINARY CONTROL INSERT FOR STRESS INCONTINENCE	PAGE 3
WHEN NOT TO USE RELIANCE® URINARY CONTROL INSERT	PAGE 4
WARNINGS	PAGE 6
HOW TO USE THE RELIANCE® URINARY CONTROL INSERT	PAGE 7
MOST COMMONLY ASKED QUESTIONS	PAGE 15
GLOSSARY OF TERMS	PAGE 21

updated 8/16

ABOUT STRESS INCONTINENCE

Urinary incontinence or loss of bladder control can happen to anyone at any age. There are many different types of incontinence. Each type has a different set of symptoms and causes. A very common type is "stress incontinence." In stress incontinence, urine may spill or leak without warning when there is a sudden rise in pressure on the bladder, such as when you cough, sneeze, walk, exercise, or lift. Many factors can cause stress incontinence. The most common causes are hormonal changes that occur during menopause and weak pelvic floor muscles, usually a result of pregnancy and childbirth.

INTRODUCING THE RELIANCE® URINARY CONTROL INSERT FOR STRESS INCONTINENCE

There are different treatment alternatives for urinary incontinence. You should be familiar with all options available for urinary stress incontinence to be sure the Reliance® Insert is right for you. The Reliance® Urinary Control Insert is a prescription option for women with urinary stress incontinence. The insert helps women manage stress incontinence similar to the way many women manage their menstrual period by using tampons, instead of pads. Unlike a tampon, the insert does not absorb urine. Instead, it acts as a barrier when placed inside a small opening above the vagina, called the urethra. You may choose to use the insert daily, on specific occasions, or you may find the insert is not for you. It helps block urine from leaking. An applicator places the insert into the urethra.

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After gently inserting the RELIANCE® Urinary Control Insert into the urethra as shown to you by your physician, you inflate a small balloon at the tip of the insert. This balloon keeps the insert in your bladder and blocks the bladder opening to help prevent urine from leaking. The insert remains in place as the bladder fills with urine. The bladder and the urethra are normally sterile areas. To prevent infection, you must keep those areas as clean as possible. Always wash your hands with mild soap and water to help prevent infection.

When you want to go to the bathroom, a tug on the insert's string will deflate the balloon. Then, you can remove the insert and throw it away. You may feel a bit nervous the first few times you use the Reliance Insert -- this is normal.

WHEN NOT TO USE RELIANCE® URINARY CONTROL INSERT

Most women with stress incontinence can use the RELIANCE® Urinary Control Insert. There are a few medical conditions when you should not use the insert and when you may need to temporarily stop using the Insert. Ask your physician if you have any questions about whether you should use the RELIANCE® Urinary Control Insert.

Do NOT Use the RELIANCE® Urinary Control Insert If ...

- you currently have a urinary tract infection.
- you have an artificial heart valve.
- you are allergic to or cannot take any form of antibiotics.
- you are taking a blood-thinning drug.
- you have ongoing conditions related to the urinary tract (i.e., kidney stones, bleeding or blockage)

48

updated 8/16

Temporarily Stop Using the Insert and Contact Your Physician If ...

- you have signs of a urinary tract infection or bladder infection (see below).
- you notice any bleeding from the vaginal area that is not menstrual *or* notice blood in your urine.
- or, after you remove the insert, the balloon is still fully inflated and you are bleeding.
- you are pregnant or think you are.

Signs of a urinary tract infection include burning, frequent urination, abdominal pain, cloudy urine or blood in your urine. Using the insert while you have an infection could make the infection worse.

Your physician will let you know when it is safe to start using the Reliance® Insert again.

CAUTION

If you are pregnant or think you are, call your physician as soon as possible to talk about whether you can to use the RELIANCE® Urinary Control Insert. Use of the Insert has not been studied during pregnancy, and its effects are unknown.

If you have any other questions about whether you should use the RELIANCE® Urinary Control Insert, ask your physician.

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WARNINGS

Using the Reliance® Insert incorrectly can cause infection, irritation or injury. Also, if you frequently had urinary tract infections in the past, you might have an increased risk of infection with use of the Reliance® Insert. Here are some important points to remember to help you use the insert correctly.

To prevent infection:

- NEVER use an opened or damaged package.
- NEVER touch the insert directly. Always handle through the package.
- NEVER re-use the RELIANCE® Insert.
- NEVER use the insert without first washing your hands with soap and water.
- NEVER wear one insert for more than 6 hours at a time or while sleeping at night.

To prevent irritation or injury:

- NEVER use the RELIANCE® Insert during sex.
- NEVER use any personal or feminine hygiene product around the urethra or vagina; this includes all powders, sprays, antiseptics and fragrances.
- NEVER force the insert beyond where the tab comfortably stops.
- NEVER try to remove the RELIANCE® Insert without deflating the balloon.

- NEVER Use an oil-based lubricant such as Vaseline Petroleum Jelly or face/hand/body moisturizers to help insert the product. Oil-based lubricants will damage the insert. (Always use a water-based lubricant, such as K-Y® lubricating jelly).

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HOW TO USE THE RELIANCE® URINARY CONTROL INSERT

There are four steps to using the Reliance® Urinary Control Insert. They are listed below. Before you try inserting the insert into yourself, you should practice Step 1: How to connect the applicator to the Reliance Urinary Control Insert *and* Step 3: How to inflate and disconnect the applicator to get used to handling the insert.

updated 8/16

After you have practiced Step 1 and Step 3 a few times, find a comfortable position to insert a new Reliance® Urinary Control Insert. Below are some suggestions:

9/2

updated 8/16

***STEP 1: How to Connect the Applicator to the Reliance® Urinary Control
Insert***

1. Wash your hands with soap and water.
2. Remove the applicator from its package.
3. Pull the plunger as far back as it will go without disconnecting it from the barrel.
4. To keep the insert sterile, only open the insert package at the end where the tab and string are; do not remove the insert completely from the wrapper. Hold the body of the insert through the package.

89

6. Gently slide the insert into the urethra until it comfortably stops at the tab. Do NOT force the tab into your urethra.

CAUTION

If you accidentally place the insert in the vagina or anus, throw out the insert. Do NOT try to reinsert into the urethra.

Step 3: How to inflate the insert and disconnect the applicator

1. Push the applicator plunger with the index finger to inflate the balloon as shown below. Keep the applicator and Insert in a straight line during inflation, or the balloon may deflate. Continue to hold the plunger firmly in place until the next step



updated 8/16

2. While keeping your finger on the plunger, hold the Insert tab with your free hand. Tilt the end of the applicator upward towards your stomach to disconnect it. Do NOT twist the applicator or move it from side-to-side while disconnecting it. Removing the applicator incorrectly could deflate the balloon.

3. After disconnecting the applicator, gently but firmly pull on the tab. The balloon is inflated if you feel resistance.

Step 4: How to Remove the Reliance® Urinary Control Insert

1. Wash your hands with soap and water
2. When you want to urinate, hold the insert tab with one hand and find the string with the other hand.
3. Pull the string out gently and evenly. The balloon will deflate as you remove the string.
4. Remove the RELIANCE® Insert using its tab, and put into the trash. Never flush the insert down the toilet because it may cause blockage.

WARNING

NEVER reuse a RELIANCE® Urinary Control Insert. The Insert is sterile for your protection to help prevent infection.

updated 8/16

5. If pulling the string does not deflate the balloon, place your finger to one side of the tab. Gently push the tab to one side and squeeze the valve area. You may hear air escaping from the Insert as the balloon deflates. Then, gently remove the Insert.

How to Clean and Store the Mirror and Applicator

1. To remove the mirror, slide it off the barrel of the applicator. As you become more familiar with the RELIANCE® Insert, you may find that you no longer need to use the mirror.
2. Always wash your hands and the applicator with mild soap and water after use.
3. Always dry the applicator with a clean towel.
4. Store the applicator with new, sterile RELIANCE® Insert packages. You can safely use your applicator up to 50 times. We recommend you use a new applicator provided in each new Maintenance set of Reliance® Urinary Control Inserts. If you need more applicators, call 1-888-987-6633.

52

MOST COMMONLY ASKED QUESTIONS

- **What was the experience of other women who used the RELIANCE® Urinary Control Insert?**

215 women from 32 to 76 years of age participated in a clinical study run by urologists and urogynecologists to determine if the RELIANCE® Urinary Control Insert was safe and effective. Effectiveness was measured by the decrease in the amount of urine leakage women experienced. Reliance® Inserts were found to be effective in reducing urine leakage.

Reliance® Inserts were also found to be safe for women who took part in the study. Some women did experience problems when using the RELIANCE® Urinary Control Insert. The adverse events are listed below:

Risk of Adverse Events Over One Year

• Positive Urine Culture	80%
• Urethral Discomfort / Irritation	78%
• Trace Hematuria	61%
• Urinary Tract Infection	44%
• Urinary Symptoms	42%
• Hematuria	33%
• Awareness of Device	30%
• Gross Hematuria / Tinged Urine	25%
• Pyuria	24%
• Bladder / Urethral Irritation on Cystoscopic Evaluation	22%
• Bleeding / Spotting	20%
• Asymptomatic Bacteriuria	19%
• Device Migration	5%

Many of these adverse events required no medical intervention. For the majority of other adverse events, other than when antibiotics were prescribed for infection, temporary stoppage of device use was the only intervention required. In cases where the device migrated up into the bladder, patients had to visit their physician.

updated 8/16

Other Events

Other symptoms reported in less than 3% of patients included: Discomfort/Difficulty During Device Insertion/Removal, Bladder Pressure, Vaginal Irritation, Urethral/Voiding Sensation, Bladder Pain/Spasms/Sensation, Cramping, Increased Leakage, and Bed Wetting.

Other complications which occurred in the clinical study in less than 2% of patients included: contraction of the muscles which line the bladder, accidental insertion of the device into the vagina, a short-term inability to urinate and empty your bladder completely, overactivity of the bladder muscles, scrapes around the outside opening of the urethra (meatus), cysts containing skin cells around the outside opening of the urethra (meatus), pressing of the uterus against the bladder, lower back pain, worsening over time in how well the bladder fills, stores and releases urine and in the pressures involved, and vaginal yeast infection.

60

Patient Withdrawal

Of 215 women enrolled in the study, about half continued in the study for at least six months, and despite the rigorous, invasive testing required by the protocol, about one out of every five women, chose to continue in the study for at least 12 months. For the 36 women who continued to use the insert for 12 months during the optional follow-up period, the benefits of use were clear: 97% said they would recommend the insert to another woman with stress incontinence, and 89% said the insert had improved their quality of life moderately to very significantly.

For a variety of reasons, not all of the women in the clinical study decided to continue to use the Insert. The reasons for withdrawal are shown in the chart below:

- Discomfort with Device Use 19%
- Unable / Unwilling to Use Device 17%
- Personal Reasons / Unwilling to Abide Protocol 15%
- Urgency 6%
- Termination of Study Site 5%
- Urinary Tract Infection 5%
- Lost to Follow-up / Unknown 5%
- Leakage with Use 3%
- Medical Complications 3%

• **Are there any medications I should avoid when using the RELIANCE® Urinary Control Insert?**

You should not use the RELIANCE® Urinary Control Insert if you are taking a blood thinning drug because of the chance of bleeding. Ask your physician if any other medications or medical conditions may prevent you from using the insert.

61

- **How long can one RELIANCE® Urinary Control Insert be used?**

You can use each RELIANCE® Urinary Control Insert for a maximum of six hours. If you leave the insert in longer than six hours, your bladder may become too full which could increase your risk of an infection. You should not use the insert while sleeping at night.

- **Can the RELIANCE® Urinary Control Insert fall out?**

In rare cases, a RELIANCE® Urinary Control Insert might fall out. Some women, in rare cases, find that an insert sometimes comes out after sneezing, coughing, or similar situations. If this happens to you, throw the insert in the trash and review the instructions for proper insertion and inflation. If you have more problems or further questions, call your physician.

- **What is the RELIANCE® Urinary Control Insert made of?**

The RELIANCE® Urinary Control Insert is made of a commonly used medical plastic material that has been tested for safety. The device is sterilized for the users protection.

- **Is there any discomfort I should report to my physician?**

When you first start using the RELIANCE® Urinary Control Insert, you may feel some discomfort for several weeks. Like tampons, there is a period where it will take getting used to the insert. If the discomfort does not go away, gets worse or happens again, please contact your physician. A different size insert may be more comfortable for you.

- **Are there any symptoms I should report to my physician immediately?**

Call your physician immediately if you have any signs of a urinary tract infection or bladder infection. These signs include burning, frequent urination, abdominal or unusual back pain, cloudy urine, or blood in your urine. Discontinue use of the RELIANCE® Urinary Control Insert until your physician tells you it is O.K. to resume use of the insert.

updated 8/16

- **What if I cannot find the RELIANCE® Urinary Control Insert to remove it? Can it get lost inside me?**

The tab will keep the RELIANCE® Urinary Control Insert from being pushed inside your bladder, except in rare cases. If you cannot locate the tab, the insert may have been pushed inside your bladder. Call your physician immediately. Your physician will be able to remove the insert.

- **Can I reuse the RELIANCE® Urinary Control Insert?**

No. For your safety, throw away the RELIANCE® Urinary Control Insert after use. NEVER reuse an insert because it could increase your chance of infection.

- **Can I use the RELIANCE® Urinary Control Insert during my menstrual period?**

Most women find it very easy and convenient to use the RELIANCE® Urinary Control Insert along with the pads or tampons they use for their menstrual period.

- **I have a friend who also has incontinence problems. Can I let her try one of my inserts?**

No. The RELIANCE® Urinary Control Inserts were specifically sized to your body and will only fit you. Also, it is important that a physician evaluate incontinence to determine its cause before someone uses the insert. The insert is only recommended for women with certain types of incontinence. You may want to encourage your friend to contact her physician about her incontinence and for more information about whether it would be appropriate for her to use the RELIANCE® Urinary Control Insert.

- **How many RELIANCE® Urinary Control Inserts can I get in my prescription and how long will it last?**

Your physician will determine how many RELIANCE® Urinary Control Inserts you get and how long your prescription will last. As with any continence management program, it is important to see your physician from time to time to monitor your condition. Your physician will let you know how often you should come in for follow-up visits.

63

updated 8/16

- **How do I reorder RELIANCE® Urinary Control Inserts?**

You may call one of our Customer Service Representatives at 1-888-987-6633 to have the prescription filled. Have your prescription available

If you have any questions, contact your physician.

64

updated 8/16

GLOSSARY OF TERMS

- **Asymptomatic Bacteriuria**

Back-to-back **Positive Urine Cultures** which show the same type of bacteria. You would not feel any pain or have any other symptoms and you would not need to take any antibiotics.

- **Bladder or Urethral Irritation**

Urethral or bladder irritation would look like scrapes or bruises (sometimes with bleeding) on the inside of your bladder or urethra. Your physician could tell whether your bladder or urethra were irritated by using the Reliance® Urinary Control Insert. Your physician will use a cystoscope, a long flexible tube, inserted into your bladder to see if you have bladder or urethral irritation.

- **Device Migration**

An event in which the tab of Reliance® enters your body, either just inside your urethra, or all the way into your bladder. Your doctor may need to remove Reliance® using a cystoscope (see **Bladder Irritation**).

- **Hematuria**

The presence of red blood cells in your urine when a urine sample is examined under a microscope. You would not feel any pain or need to take antibiotics unless you also had a urinary tract infection (see **Urinary Tract Infection**). There are three levels of hematuria:

- 1) trace hematuria--very few red blood cells which can only be seen under a microscope.
- 2) hematuria--more red blood cells than in trace hematuria, but they still can only be seen under a microscope.
- 3) gross hematuria/tinged urine--you would be able to see blood in your urine and your urine color could range from dark yellow to bright red.

- **Positive Urine Culture**

The presence of bacteria in a urine sample which is greater than the number usually considered "normal" by a laboratory.

- **Pyuria**

The presence of white blood cells or pus in your urine when a urine sample is examined under a microscope. You would not feel any pain or need to take antibiotics unless you also had a urinary tract infection (see **Urinary Tract Infection**).

69

updated 8/16

- **Urinary Tract Infection**

A positive urine culture (see **Positive Urine Culture**) AND symptoms such as burning or pain when you urinate, needing to urinate more often, abdominal pain, blood in your urine, or foul-smelling urine. Your doctor would prescribe antibiotics to cure it.

- **Urgency**

A strong need to go to the bathroom to urinate.

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RELIANCE® Urinary Control Insert

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67