AMS 800™

Urinary Control System
For Male Patients

Instructions For Use

℞ ONLY

AMS™

en English

	en Catalog Number
	en Do Not Reuse
	en Do Not Resterilize
	en Magnetic Resonance Conditional
	en Consult Instructions for Use
	en Upper Limit of Temperature
	en Sterilized Using Ethylene Oxide
	en Sterilized Using Steam
	en Lot Number
	en Date of Manufacture
	en Use by YYYY-MM-DD
	en Manufacturer
	en Authorized Representative in the European Community
	en Recyclable Packaging
	en Non-sterile
℞ ONLY	en CAUTION: Federal law (U.S.) restricts this device to sale by or on the order of a physician.

English

AMS 800™

Urinary Control System For Male Patients

Instructions For Use

NOTE: For implant procedure information, consult the AMS 800 Urinary Control System Operating Room Manual.

Brief Device Description

The AMS 800 Urinary Control System is an implantable, fluid filled, solid silicone elastomer device used to treat stress urinary incontinence. It is designed to restore the natural process of urinary control. The device simulates normal sphincter function by opening and closing the urethra at the control of the patient. The AMS 800 consists of three interconnected components: a cuff, a pump, and a pressure-regulating balloon (PRB). The three components are connected with kink-resistant tubing. The AMS 800 can be implanted at either the bulbous urethra or the bladder neck.

The AMS 800 Urinary Control System Cuff and Pump are available with InhibiZone™, an antibiotic coating of rifampin (rifampicin) and minocycline hydrochloride (minocycline HCl).* For more information please refer to the Antibiotic Information section.

Indications for Use

The AMS 800 is used to treat urinary incontinence due to reduced outlet resistance (intrinsic sphincter deficiency) following prostate surgery.

Contraindications

1. This device is contraindicated in patients whom the physician determines to be poor candidates for surgical procedures and/or anesthesia due to physical or mental conditions.
2. This device is contraindicated in patients with urinary incontinence due to or complicated by an irreversibly obstructed lower urinary tract.
3. This device is contraindicated in patients with irresolvable detrusor hyperreflexia or bladder instability.
4. The implantation of the InhibiZone version of this device is contraindicated in patients with known allergy or sensitivity to rifampin or to minocycline HCl or other tetracyclines.
5. The implantation of products with InhibiZone is contraindicated in patients with systemic lupus erythematosus because minocycline HCl has been reported to aggravate this condition.

Warnings

1. Patients with urinary tract infections, diabetes, spinal cord injuries, open sores, or skin infections in the region of the surgery have an increased risk of infection associated with a prosthesis. Appropriate measures should be taken to reduce the likelihood of infection.

* InhibiZone™ Antibiotic Surface treatment is not available in all markets.

Infection that fails to respond to antibiotic therapy may result in removal of the prosthesis. Infection followed by explantation of the device may result in scarring which may make subsequent reimplantation more difficult.

2. Erosion may be caused by infection, pressure on the tissue, improper cuff sizing, improper balloon selection, tissue damage, and component misplacement. The cuff may erode around the urethra or bladder neck. The control pump may erode through the scrotum. The pressure-regulating balloon may erode into the bladder. Acute urinary tract infection can interfere with proper functioning of the device and may lead to erosion of the urethra in the cuff area. Failure to evaluate and promptly treat the erosion may result in a substantial worsening of the condition leading to infection and/or loss of tissue.
3. Poor bladder compliance or a small fibrotic bladder may require some measure of intervention including, in some cases, augmentation cystoplasty before implanting the prosthesis.
4. Patients with urge incontinence, overflow incontinence, detrusor hyperreflexia or bladder instability should have these conditions treated and controlled (or resolved) prior to implantation of the device.
5. Do not pass a catheter or any other instrument through the urethra without first deflating the cuff and deactivating the device to prevent potential damage to the urethra or the AMS 800.
6. This device contains solid silicone elastomers. This device does not contain silicone gel. The risks and benefits of implanting this device in patients with documented sensitivity to silicone should be carefully considered.
7. Surgical, physical, psychological, or mechanical complications, if they occur, may necessitate revision or removal of the prosthesis. Removal of the device without timely reimplantation of a new device may complicate subsequent reimplantation. The timing of reimplantation should be determined by the treating physician based on the patient's medical condition and history.
8. Product wear, component disconnection or other mechanical problems may lead to surgical intervention. Mechanical complications may include malfunctioning of the components and leakage of fluid. Any mechanical malfunction that does not permit the transfer of fluid from the cuff to the balloon may result in outflow obstruction. Mechanical events should be evaluated carefully by the treating physician and the patient should consider risks and benefits of treatment options, including revision surgery.
9. Previous patient history of adverse reaction(s) to radiopaque solution precludes its use as a filling medium for the prosthesis. Instead, saline should be used to fill the device.
10. The implanter should check that there is an adequate amount of bulbospongiosus muscle to surround and support a bulbous urethral cuff implant. Thinner spongiosum typically occurs toward the distal end of the bulbous urethra, and implantation of the cuff where the spongiosum is thin increases the chance of erosion and other complications. This warning is especially important for double cuff implants, where the second cuff is placed distal to the first implanted cuff.

11. If a hypersensitivity reaction develops to a device coated with InhibiZone, the cuff and pump should be removed and the patient treated appropriately.

Precautions

Patient Related

1. Patient selection requires thorough preoperative consultation and evaluation by the physician.
2. Patients should be counseled in order to have a realistic expectation of the physical, psychological, and functional outcome of the implantation of an AMS 800. Although the prosthesis is designed to restore urinary control, some patients continue to have a degree of incontinence after this procedure.
3. Patients may experience pain when the device is activated in the postoperative period and during the period of initial use. Cases of chronic pain associated with device have been reported. Pain with a severity or duration beyond what is expected may require medical or surgical intervention. Patients should be counseled on expected postoperative pain including severity and duration.
4. Tissue fibrosis, previous surgery, or previous radiation therapy in the area of the implant may preclude implantation of a cuff at the bulbous urethra or bladder neck.
5. Any progressively degenerative disease, e.g. multiple sclerosis, may limit the future usefulness of the implanted prosthesis as a treatment for the patient's urinary incontinence.
6. Adequate manual dexterity, strength, motivation, and mental acuity are required for proper use of the device.
7. Trauma or injury to the pelvic, perineal or abdominal areas, such as impact injuries associated with sports, can result in damage to the implanted device and/or surrounding tissues. This damage may result in the malfunction of the device and may necessitate surgical correction including replacement of the device. The physician should advise patients of these possibilities and warn them to avoid trauma to these areas.
8. Consideration should be given to the diameter of the implanted occlusive cuff relative to catheters or other trans-urethral devices. When fully deflated, the inside diameter of the smallest occlusive cuff (3.5cm) generally exceeds 28F. Additional clearance is required to accommodate the patient's urethral tissue between the trans-urethral device and the occlusive cuff. Urethral tissue thickness is patient specific and requires a physician's assessment to determine its impact on sizing.

InhibiZone™ Related

1. Use of products with InhibiZone should be carefully considered in patients with hepatic or renal disease, as use of rifampin and minocycline HCl can cause additional stress on the hepatic and renal systems.
2. Patients who receive a device with InhibiZone and are also taking methoxyflourane should be carefully monitored for signs of renal toxicity.
3. Patients who receive a device with InhibiZone and are also taking warfarin should have their prothrombin time monitored because tetracyclines have been reported to slow coagulation.
4. Use of products with InhibiZone should be carefully considered in patients using thionamides, isoniazid and

halothane, due to potential hepatic side effects that have been reported in patients using these drugs and higher doses of rifampin.

5. Devices with InhibiZone should not come into contact with ethyl alcohol, isopropyl alcohol or other alcohols, acetone or other nonpolar solvents. These solvents may remove the antibiotics from the device.
6. InhibiZone components should not be soaked in saline or other solutions prior to implantation. The components may be briefly rinsed or dipped into a sterile solution, immediately prior to implant, if desired.
7. InhibiZone does not replace your normal antibiotic protocols. Continue using any prophylactic protocols normally used for urological surgical procedures.
8. Because products with InhibiZone are impregnated with a combination of rifampin and minocycline HCl, the contraindications, warnings and precautions regarding the use of these antimicrobial agents apply and should be adhered to for the use of this device, although systemic levels of minocycline HCl and rifampin in patients receiving this device are unlikely to be detected.

Surgery Related

1. Improper cuff sizing, improper balloon selection, or other causes may result in tissue erosion, migration of components, or continued incontinence.
2. Component migration can occur if the cuff is sized improperly, if the pump or balloon is not positioned correctly, or if the tubing lengths are incorrect. Migration can result in pain, complications, device malfunction and surgical revision.
3. Unsuccessful outcomes may result from improper surgical technique, improper sterile technique, anatomical misplacement of components, improper sizing and/or filling of components.
4. Although reinforced tubing has been designed to be more resistant to tubing kinks, tubing kinks may still result from tailoring the connecting tubing to an improper length during the implant procedure.

Device Related

1. If the deactivation valve is closed when the cuff is inflated, fluid cannot transfer from the cuff to the balloon and sustained outflow obstruction may arise as a result:
    a. In the event of large pressures within the bladder, automatic pressure relief that normally occurs with the device would be prevented. Cycling the device can relieve the outflow obstruction.
    b. Cycling the device may be difficult if deactivation occurs when the pump bulb is deflated. If unable to cycle the device, squeezing the sides adjacent to the deactivation button will allow fluid to fill the pump bulb and then the pump can be cycled normally.
    c. Release of the deactivation valve may require greater pressure than that used to cycle the device.
2. System pressure changes may occur over time if you fill the balloon with radiopaque solution of incorrect concentration. Follow the instructions in the Operating Room Manual to prepare the radiopaque solution with the correct concentration.

Adverse Events

The following adverse events have been associated with the use of this product: bladder spasms, bleeding, contracture, deep vein thrombosis, delayed wound healing, difficult activation, difficult deactivation, dysuria, edema, exposure to biohazardous material, extrusion, fibrosis, fistula formation, foreign body/unretrieved device fragment, hematoma, hematuria, herniation, herniation of the device, hydrocele, impaired device function, infection, limited urethral coaptation, migration, nerve injury, overactive bladder, pain/discomfort, patient dissatisfaction, perforation, positional incontinence, recurrent incontinence, swelling, tissue erosion, tissue erosion/infection, urethral atrophy, urethral injury, urethral stricture, urge de novo, urinary retention, wound dehiscence, wound infection.

A prospective clinical study was conducted to demonstrate the safety and efficacy of the AMS 800 Urinary Control System. A total of 87 patients were enrolled in the study and 85 patients were implanted with the device. During the study, 26 patients experienced 43 device related adverse events. Table 1 lists the device related adverse events reported during the study.

This trial involved only devices without InhibiZone.

Table 1: AMS 800 Prospective Clinical Study Device Related Adverse Events

				Interventions*		
Adverse Event Category	Total Events	Patients with AE	Events Resolved	None Reported	Medical**	Surgical
Impaired Device Function	7	6	4	2	2	4
Pain/Discomfort	6	5	4	3	3	1
Delayed Wound Healing	5	5	5	2	3	0
Bladder Spasms	2	2	0	0	2	0
Difficult Activation	2	2	2	1	1	0
Migration	3	3	1	2	0	1
Tissue Erosion	2	2	2	0	0	2
Difficult Deactivation	1	1	1	0	1	0
Infection	2	2	2	0	0	2
Recurrent Incontinence	3	3	3	1	0	2
Fistula Formation	1	1	1	0	0	1
Hematoma	1	1	1	0	1	0
Swelling	2	2	2	0	2	1
Hydrocele	1	1	1	0	1	1
Tissue Erosion/Infection	1	1	1	0	0	1
Patient Dissatisfaction	1	1	1	0	0	1
Positional Incontinence	1	1	0	1	0	0
Wound Infection	1	1	1	0	1	0
Urinary Retention	1	1	1	0	1	0

*Events may have been addressed with more than one type of intervention.

**Medical interventions included: medication, education, frequent device deactivation, dressing changes and catheterization.

How Supplied and Storage

Store device in a clean, dry, dark area at room temperature.

WARNING: Contents supplied STERILE. Do not use if sterile barrier is damaged. If damage is found, call your AMS representative.

For single patient use only. Do not reuse, reprocess or resterilize. Reuse, reprocessing or resterilization may compromise the structural integrity of the device and/or lead to device failure which, in turn, may result in patient injury, illness or death. Reuse, reprocessing or resterilization may also create a risk of contamination of the device and/or cause patient infection or cross-infection, including, but not limited to, the transmission of infectious disease(s) from one patient to another. Contamination of the device may lead to injury, illness or death of the patient. After use, dispose of the product and packaging in accordance with hospital, administrative and/or local government policy.

Clinical Studies

The data from four (4) AMS 800 studies are presented:

(a) Prospective multi-center non-randomized clinical study,
(b) Retrospective patient information form (PIF) study,
(c) Retrospective clinical study, and
(d) Prospective PIF post-market registry study.

a. Prospective Multi-center Non-randomized Clinical Study – A prospective, multi-center, non-randomized clinical study was undertaken to demonstrate that the AMS 800 can be surgically implanted without serious adverse sequelae, provides an acceptable level of continence and enhances quality of life. Each patient served as their own control. Efficacy data and safety data related to adverse events, revision surgery, diagnoses and health status evaluations were captured on case report forms. Patient self-evaluations related to health status and non-illness specific quality of life were measured on two validated outcome instruments. Patient and physician assessments of continence were measured on a recognized, standardized non-validated instrument.

Eighty-seven (87) male patients were enrolled in the study of which 85 patients were implanted with the device during the study. Patients available at the follow-up intervals were 6-months (n=67), 12-months (n=60), 18-months (n=55), and 24-months (n=41). Patients diagnosed with intrinsic sphincter deficiency (ISD) resulting from prostate surgery were eligible for enrollment. Patients with a history of allergy/sensitivity to silicone, pre-existing autoimmune or connective tissue disease or active urogenital infection were excluded from the study.

This trial involved only devices without InhibiZone.

Endpoints

The primary effectiveness endpoint evaluated the effect of the prosthesis on patient quality of life using the *Incontinence Impact Questionnaire*, an incontinence-specific quality of life questionnaire. The primary safety endpoint evaluated the five-year revision-free rate using a Bayesian hierarchical model. The safety endpoint was a five-year revision-free rate equivalent to 75% using a 10% delta with a two-sided 95% lower bound greater than 65%.

Incontinence Impact Scores

The primary effectiveness endpoint was a reduction in Incontinence Impact Score from pre-to post-implant status. Incontinence impact was measured pre- and post-implant at 6, 12, 18, and 24 months. Thirty-nine (39) patients answered the *Incontinence Impact Questionnaire* (IIQ) at 24-month follow-up. The IIQ is a 30-item, self-administered questionnaire designed to assess the impact of urinary incontinence on several subscales including physical, emotional, and social. The IIQ used in the study was developed from a validated instrument.[1] The mean pre-implant score was significantly higher ($p<0.0001$) than mean scores at all follow-up visits. Therefore, the impact of incontinence was reduced for patients following AMS 800 implantation and the primary objective was met.

Physician and Patient Assessment of Continence

Physician assessed continence was 63.6% dry and 34.1% required some additional protection at one-year follow-up (n=43). At two-year follow-up (n=30), 73.3% were dry and 23.3% required some additional protection. Patient assessed continence was 61.7% dry and 36.7% required some additional

protection at one year follow-up (n=60). At two-year follow-up (n=41), 65.9% were dry and 31.7% required some additional protection. No significant difference existed between physicians' assessment and the patients' assessment of their incontinence.

Patient Evaluation of Health Status, and Self-esteem

General Quality of Life as measured by the *Health Status Questionnaire* and the *Rosenberg Self-esteem Questionnaire* was evaluated at pre- and post-implant at 6, 12, 18, and 24 months. Thirty-eight (38) patients answered the *Health Status* and *Rosenberg Self-esteem Questionnaires* at 24-month follow-up. The self-administered *Health Status Questionnaire*[2] was used to assess non-illness specific parameters such as physical functioning, social functioning, energy/fatigue, pain, health perception, and emotional problems. A high score indicates that overall health was perceived to be high. The mean score was 596 at pre-implant and 612 at two-year follow-up. No significant difference in health status scores was observed during the study. The self-administered *Rosenberg Self-esteem Questionnaire*[3] was used to assess changes in patient self-esteem. The range of possible scores is 0-6, with a score of 6 indicating high self-esteem. The mean score at implant was 3.5 and at two-year follow-up was 4.1. The increase in mean score indicates a more positive self-esteem following AMS 800 implant. The device did not have an adverse effect on sexual function. Some patients with improved continence following implant also reported increased sexual activity. The positive impact of the device on patient's lives measured in the clinical study is consistent with results obtained by other authors.[4,5,6]

Surgical Revisions

A revision is a surgical intervention related to the function, placement, or site reaction to the implanted device. For the 85 patients implanted with the device followed under the prospective clinical study, 14 patients (16.5%) experienced a total of 15 revisions up to 24 months following implant. One patient had two revisions. Three (3) revisions were due to mechanical malfunction. Two (2) revisions were due to recurrent incontinence. Two (2) revisions were due to erosion. Two (2) revisions were due to infection. One (1) revision each (total = 6) was due to migration, pain, erosion/infection, persistent incontinence/patient dissatisfaction, recurring incontinence/malfunction, and infection/pain/urethrocutaneous fistula. Multiple reasons were provided for some revisions. Four of the 14 patients who experienced revisions elected to have the device removed and 10 elected to have the device replaced. The probability of remaining revision-free 24 months following implant was 79.5% (95% CI with 95% lower confidence bound 69.8%) based on the prospective clinical study.

Additional data on the number of surgical revisions and their reasons were collected under two retrospective studies. Each of these studies are briefly described below and comparisons of revision data of these two retrospective studies and the prospective study are presented in Tables 2 and 3.

b. Retrospective Patient Information Form (PIF) Study – The PIF study was a retrospective analysis of patients implanted (n=12,713) in the U.S during the five-year period 1995-1999. The study examined PIF data voluntarily sent to the manufacturer by the implanting physician for original implants and revisions. PIF data is required to be on file with the manufacturer in order to be eligible for product replacement. Revision data presented in Table 2 and Table 3 below are based on a total of 2,116 revisions reported for 2,014 patients that

required one or more revisions during the five-year period of the study.

c. Retrospective Clinical Study – The retrospective clinical study was an analysis of patients implanted (n=390) in the U.S. between 1987-1990. The study examined pre- and post-implant medical records and follow-up data collected by questionnaires and physician examinations. Post-implant data was available for 356 patients. The study followed patients for up to ten years (mean: 4.1 years; range: 0.03-10.3 years). The revision data presented in Table 2 and Table 3 below are based on a total of 317 revisions reported on 164 patients that required one or more revisions during the ten-year period of the study.

The data in Table 2 presents the percentage of patients revised during the specified follow-up period, the average number of revisions conducted on patients requiring a revision and the number of revisions expected per 100 patients for these studies in comparison with the data of the prospective clinical study.

Table 2: Comparison of Revision Data from Three Different Clinical Studies

	Prospective Study (85 pts. over 24 months)	PIF Study (12,713 pts. over 5 years)	Retrospective Study (356 pts. over 9 years)
% pts. revised	16.5% (14/85)	15.8% (2014/12713)	46.1% (164/356)
avg.. # of revisions per pts. revised	1.07 (15/14)	1.05 (2116/2014)	1.93 (317/164)
# of revisions per 100 pts.	18 (15/85)	17 (2116/12713)	89 (317/356)

Table 3 shows revision data stratified by each reported reason for revision from three different studies of male patients implanted with the AMS 800. Under the PIF Study and Retrospective Study multiple reasons were sometimes provided for a single revision. Therefore, in order to stratify this revision data by reason, all occurrences were included and presented as "% reason." The total number of reasons therefore exceeds the total number of revisions reported for these studies.

Table 3: Reasons for Revision in Three Different Studies

Revision Reason[a]	Prospective Study (n=85)		PIF Study (n=12713)		Retrospective Study (n=356)	
	revisions		reason[sb]		reasons	
	%	#	%	#	%	#
Infection	2.4%	(2)	2.3%	(297)	8.1%	(29)
Infection/erosion	1.2%	(1)	----	----	----	----
Erosion	2.4%	(2)	3.6%	(451)	22.5%	(80)
Recurring Incontinence	2.4%	(2)	5.7%	(724)	42.4%	(151)
Fluid Loss	----	----	2.3%	(298)	9.3%	(33)
Fluid Transfer Impaired	----	----	0.3%	(38)	----	----
Pressure too low	----	----	1.1%	(140)	----	----
Mechanical Malfunction	3.5%	(3)	0.7%	(89)	13.8%	(49)
Migration/ Malposition	3.5%	(3)	0.4%	(46)	4.8%	(17)
Iatrogenic Complications	----	----	0.4%	(51)	0.6%	(2)
Reimplantation/ Replacement	----	----	----	----	3.1%	(11)
Pain	1.2%	(1)	0.2%	(22)	1.4%	(5)
Patient Dissatisfaction	1.2%	(1)	0.2%	(27)	1.7%	(6)
Other[c]	----	----	2.4%	(305)	----	----
Not indicated	----	----	1.9%	(242)	----	----

a Note that some adverse events in the table such as fluid loss, pressure too low, fluid

transfer impaired and malposition could fall into the category of mechanical malfunction or iatrogenic error. Since information is not available to place them in either category, they are listed separately.

b Numbers of reasons can vary for the same percentage due to rounding.

c Other includes: double cuff, pressure too high, unable to activate, unable to deactivate, atrophy, difficult to operate, urinary retention, air in the system, hematoma.

Device Survival

Although it is not possible to predict exactly how long an implanted prosthesis will function in a particular patient, American Medical Systems, Inc. gathered data from two sources on device removals and revisions to help gain insight into product performance over time. Figure 1 presents device survival results from the prospective clinical study and a Bayesian analysis that uses data from the prospective clinical study and the PIF Study to estimate device survival at five years.

Prospective Clinical Study – A device survival curve was calculated from data collected during a prospective clinical study (n=85) with two-year follow-up. Using Kaplan-Meier analysis, the two-year revision-free rate for the AMS 800 was 79.5% (95% CI with 95% lower confidence bound 69.8%).

Bayesian Analysis – A Bayesian hierarchical model was used to evaluate device safety in the prospective clinical study. The Bayesian model estimated device survival using historical data

(PIF Study n=12,713) on the AMS 800 and prospective clinical study data (n=85) on the AMS 800. A log-normal distribution fit the AMS 800 historical data. Based on the log-normal hierarchical model, it was estimated that the five-year revision-free rate for the AMS 800 is approximately 73.8% with 95% CI ranging from 67.3% to 79.6%. The results met the primary safety endpoint for the clinical study of a five-year revision free rate at 75% using a 10% delta with two-sided 95% lower bound greater than 65%.

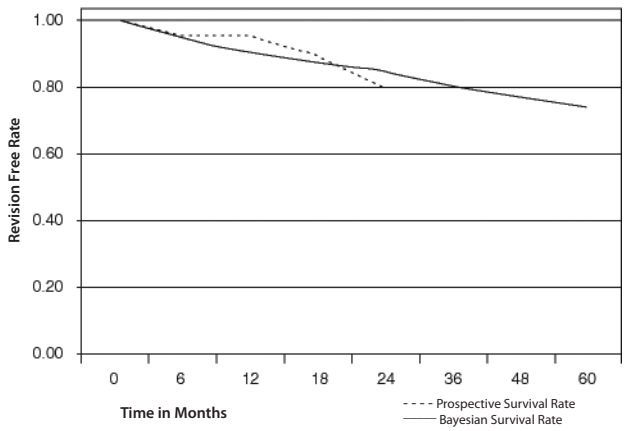

Figure 1: Estimated Device Survival Rates for the AMS 800

Device Use

The study included male AMS 800 patients (n=390) implanted between 1987-1990. Data from this study was used to estimate the device use for patients (n=356) with available data through 1997 (range: 0.03-10.3 years). For the retrospective study, "device use" means the span of time from implant to removal, including revisions. Life table analysis indicated that the probability for a 9-year span of device use was 83.9%. Thirty-three (33) of the 356 patients had their device removed. The remaining 323 patients had a functioning device at last contact.

d. Prospective PIF Post-market Registry Study – The AMS 800™ Urinary Control System, with InhibiZone™ Treatment, received FDA approval in 2006 with the approval condition that AMS

conduct a five (5) year registry study. The actual average follow-up period study was 5.8 years.

The Inhibizone™ (IZ) antibiotic treatment, a combination of minocycline HCl and rifampin, is impregnated into the surfaces of AMS 800 cuff and control pump components in order to reduce colonization of bacteria on the device at implant. The pressure regulating balloon (PRB) component is not IZ treated. The IZ antibiotics are intended to specifically target the organisms most commonly seen in urological implant infection and cultures. The data are specific to the AMS 800 with InhibiZone treatment and should not be generalized to any other IZ related devices.

As commercially approved and per the post-market registry protocol, the individual device components implanted may or may not be IZ treated, the choice resides with the healthcare provider.

Summary of the Prospective PIF Post-market Registry Study Methods

Study Objective

To evaluate the long-term performance of the AMS 800 device with InhibiZone as compared to non-IZ impregnated AMS 800 device as it relates to the antimicrobial effectiveness and safe use over a five (5) year period, i.e., the rate of infection, mechanical component, or system failures and surgical revision rates. The AMS 800 System's urinary control efficacy data were not analyzed.

Study Design

The study was based on the voluntary submission of AMS implant registration data using the AMS Patient Information Form (PIF). The PIF data is required to be on file with the manufacturer in order to be eligible for product replacement under warranty. The study focuses on two patient groups identified as: Original Surgery Group and the Revision Surgery Group.

For the Original Surgery Group, device event time is defined as the time between the implantation of the original device in the study period and the first replacement, revision or removal of any component of the device due to infection, mechanical malfunction, patient problem, or other reason. If there was no event, the patient was censored at end of the study period.

For the Revision Surgery Group, device event time is defined for the time between the implantation of a revision and a second revision due to infection, mechanical malfunction, patient problem or other reason. If there was no event, the patient was censored at end of the study period. The protocol's statistical analysis evaluated the AMS 800 overall system (IZ and Non-IZ) for the two (2) patient subgroups.

For the Original Surgery Group, the endpoint at an overall system level is the first revision (Revision, Replacement or Removal) due to infection, mechanical malfunction, patient problem, or other reason. For the Revision Surgery Group, the endpoint at an overall system level is the second revision after the implantation of the first revision due to infection, mechanical malfunction, patient problem, or other reason.

Study Population

The patient population included all US-based patients implanted with the AMS 800 as well as all patients implanted after October 13, 2006 with the AMS 800 or the AMS 800 with IZ up to July 31, 2012. Additionally, the study included data from all sites and all physicians using either system (or their

components) within the US and its territories only if PIF reports were provided to AMS.

Data Source

AMS' Patient Information Form (PIF) is entered into the AMS PIF database. The AMS PIF database is updated regularly as new and/or updated patient information is received by AMS. The PIF information fields used in this analysis included:

- Concomitant conditions and etiologies including both neurogenic and non-neurogenic origins.
- Device information, such as model, part number and serial number,
- Revision surgeries and the reason for revision, and
- Demographic and surgical variables, such as age and surgical approach used.

Key Registry Endpoints

This study compared the rates of device replacement surgery subsequent to infection or mechanical failure between IZ and Non-IZ AMS 800 devices.

At the study's conclusion survival from infection and mechanical failure of the IZ and Non-IZ device groups were compared by standard survival analysis. The comparison was performed by using a survival analysis separately on infection and mechanical failure events.

Total Number of Enrolled Registry Sites and Subjects, Follow-up Rate

- 24,257 AMS 800 patient implants total
- 17,063 Original Surgery Group patients
- 7,194 Revision Surgery Group patients
- 3,548 physicians total
- 2,240 sites total, with all 50 States and several U.S. territories represented

The study was based on the voluntary submission of AMS implant registration data using the AMS PIF. While there was a relatively high PIF return rate, there was not 100% compliance.

Study Visits and Length of Follow-up

As the study utilizes a voluntary implant registration data form to report events (i.e., PIF for Original Surgery Group and the Revision Surgery Group), there were no specified "study visit" intervals. Overall endpoints were analyzed to 2117 days, i.e., 5.8 years post-procedure.

Summary of the Prospective Post-market Registry Study Results

The study evaluated the antimicrobial effectiveness and safe use over a five (5) year period, including the rate of infection, mechanical component, or system failures and surgical revision rates.

Final Safety Findings

The final safety findings are described in Table 4 and the associated text below.

Table 4: Original Surgery Group and the Revision Surgery Group Analyzed for Overall Revision, Infection (only) Revision, and Mechanical Malfunction (only) Revision

	Original Surgery Group	Revision Surgery Group
OVERALL REVISION		
Total Implant Surgeries	17,063	7,194
• IZ devices	13,060 (76.5%)	4,352 (60.5%)
• Non-IZ devices	3,742 (21.9%)	1,891 (26.3%)
• Mixed (IZ & Non-IZ*)	261 (1.5%)	951 (13.2%)

Table 4: Original Surgery Group and the Revision Surgery Group Analyzed for Overall Revision, Infection (only) Revision, and Mechanical Malfunction (only) Revision

	Original Surgery Group	Revision Surgery Group
Revision Free Patients	14,410 (85.8%)	4,969 (79.6%)
Revision Events	2,392 (14.2%)	1,274 (20.4%)
• IZ devices [% revision free]	1,621 (12.4%) [87. 6%]	776 (17.8%) [82.2%]
• Non-IZ devices [% revision free]	771 (20.6%) [79.4%]	498 (26.3%) [73.7%]
Relative Risk Reduction** [absolute reduction]	39.8% [8.2%]	32.3% [8.5%]
INFECTION (only) REVISION		
Infection Free Patients	16,570 (98.6%)	6,083 (97.4%)
Infection Reported Revisions	232 (1.4%)	160 (2.6%)
• IZ devices [% revision free]	173 (1.3%) [98.7%]	100 (2.3%) [97.7%]
• Non-IZ devices [% revision free]	59 (1.6%) [98.4%]	60 (3.2%) [96.8%]
Relative Risk Reduction** [absolute reduction]	16.0% [0.3%]	27.6% [0.9%]
MECHANICAL MALFUNCTION (only) REVISION		
Malfunction Free Patients	16,226 (96.6%)	5,945 (95.2%)
Malfunction Reported Revisions	576 (3.4%)	298 (4.8%)
• IZ devices [% revision free]	426 (3.3%) [96.7%]	183 (4.2%) [95.8%]
• Non-IZ devices [% revision free]	150 (4.0%) [96.0%]	115 (6.1%) [93.9%]
Relative Risk Reduction** [absolute reduction]	18.6% [0.7%]	30.9% [1.9%]

*Were removed from additional statistical analysis.

**Relative Risk Reduction (%) = [1 – (IZ event rate / Non-IZ event rate)] x 100

Original Surgery Group

Revisions Analyses OVERALL

The AMS 800 PIF reports included in the survival analyses were from a total of 17,063 original implant surgeries, including 13,060 (76.5%) IZ devices and 3,742 (21.9%) Non-IZ devices. The remaining 261 (1.5%) implants, a mix of IZ and Non-IZ components, were removed from additional statistical analysis.

Revision free patients totaled 14, 410 (85.8%).

Only 2,392 revisions (14.2%) were recorded, of which 1,621 (12.4%) revisions were in the IZ group (i.e., 87. 6% revision free rate), while 771 (20.6%) revisions were in the Non-IZ treated group (i.e., 79.4% revision free rate). The IZ group demonstrated an 39.8% relative risk reduction of overall revision compared to the Non-IZ group.

Revision Due to INFECTION

Infection free patients totaled 16,570 (98.6%).

Only 232 infection related events (1.4%) were recorded, i.e., 173 (1.3%) infection related events with IZ devices (infection free rate 98.7%) and 59 (1.6%) infection related events in the Non-IZ group (infection free rate 98.4%). The IZ group demonstrated a 16.0% relative risk reduction of infection compared to the Non-IZ group.

Revisions Due to MECHANICAL MALFUNCTION

Malfunction free patients totaled 16,226 (96.6%).

Only 576 reported mechanical malfunction events (3.4%) occurred. A total of 426 (3.3%) devices experienced mechanical malfunction in the IZ group (malfunction free rate 96.7%) while there were 150 (4.0%) in the Non-IZ group (malfunction free rate 96.0%). The IZ group demonstrated a 18.6% relative risk reduction of mechanical malfunction compared to the Non-IZ group.

Revision Surgery Group

Revisions Analyses OVERALL

The AMS 800 PIF data included a total of 7,194 revision implant surgeries with 4,352 (60.5%) IZ devices and 1,891 (26.3%) Non-IZ devices. The remaining 951 (13.2%) implants, a mix of IZ treated and Non-IZ components, were removed from additional statistical analysis.

Revision free patients totaled 4,969 (79.6%).

A total of 1,274 events (20.4%) were recorded. The IZ group reported 82.2% revision free while 73.7% Non-IZ were revision free. The IZ group demonstrated a 32.3% relative risk reduction of overall revision compared to the Non-IZ group.

Revisions Due to INFECTION

Infection free patients totaled 6,083 (97.4%).

A total of 160 events (2.6%) were recorded as events due to infection. For IZ devices, 100 (2.3%) reported events occurred (i.e., 97.7% infection free rate), while 60 (3.2%) events occurred in the Non-IZ (i.e., 96.8% infection free rate). The IZ group demonstrated a 27.6% relative risk reduction of infection compared to the Non-IZ group.

Revisions Due to MECHANICAL MALFUNCTION

Malfunction free patients totaled 5,945 (95.2%).

A total of 298 events (4.8%) were recorded as events due to mechanical malfunction, with the IZ group reporting 183 (4.2%) events (i.e., 95.8% malfunction free rate) and 115 (6.1%) events in the Non-IZ group (i.e., 93.9% malfunction free rate). The IZ group demonstrated a 30.9% relative risk reduction of mechanical malfunction compared to the Non-IZ group.

Final Effectiveness Findings (key endpoints)

The study demonstrated the IZ antimicrobial impregnation devices in both original and revision surgery groups consistently had slightly higher revision free rates, overall, for infection and mechanical malfunction (Table 5).

Table 5: Summary of Original and Revision Groups' "Revision Free" Rates

	Original Surgery Group	Revision Surgery Group
OVERALL REVISION		
Overall Revision Free Patients	85.8%	79.6%
• IZ devices Revision Free	87. 6%	82.2%
• Non-IZ devices Revision Free	79.4%	73.7%
Relative Risk Reduction [absolute reduction]	39.8% [8.2%]	32.3% [8.5%]
INFECTION (only) REVISION		
Infection Free Patients	98.6%	97.4%

Table 5: Summary of Original and Revision Groups' "Revision Free" Rates

	Original Surgery Group	Revision Surgery Group
• IZ devices Revision Free	98.7%	97.7%
• Non-IZ devices Revision Free	98.4%	96.8%
Relative Risk Reduction [absolute reduction]	16.0% [0.3%]	27.6% [0.9%]
MECHANICAL MALFUNCTION (only) REVISION		
Malfunction Free Patients	96.6%	95.2%
• IZ devices Revision Free	96.7%	95.8%
• Non-IZ devices Revision Free	96.0%	93.9%
Relative Risk Reduction [absolute reduction]	18.6% [0.7%]	30.9% [1.9%]

Study Strength and Weaknesses

As a voluntary registration, there was a relatively high PIF return rate (strength), but there was not 100% compliance (weakness). Additionally, the PIF return did not guarantee that all requested data fields were completed (weakness). The PIF system collects data when a surgical revision occurs (strength). However, two (2) limiting factors (weaknesses) include:

1. The PIF database does not record events (e.g., infection) that are successfully treated without a surgical explant procedure, i.e., if no implanted system component changes occur, or no surgical device adjustment occurs, then no PIF is completed and the event (infection) is not recorded in the database.
2. There are currently no mechanisms for removing patients from the database who have died (or lost to follow-up) and therefore lack any reported follow-up data. AMS expects the "lost to follow-up" occurrence to be similar and consistent between groups; regardless of over (or under) reporting the reported rates would remain comparable.

Final Safety Findings (key endpoints)

The study demonstrated the IZ antimicrobial impregnation did not affect the mechanical performance of the device. The study demonstrated the IZ antimicrobial impregnation devices in both original and revision surgery groups consistently had slightly higher revision free rates, overall, for infection and mechanical malfunction. In addition, the corresponding relative risk reduction for the original surgery IZ group demonstrated a 16.0% relative risk reduction for infection and a 18.6% relative risk reduction for mechanical malfunction. The data demonstrate that the AMS 800 (IZ and Non-IZ) device is and remains safe and effective.

Patient Counseling Information

Patients should be counseled in order to have a realistic expectation of the physical, psychological and functional outcome of the implantation. The risks, benefits and potential adverse events of all available treatment options should be discussed with the patient and considered by the physician and patient when choosing a treatment option.

An appropriate patient history, including history of personality disorders, and diagnostic work-up should be a part of the patient decision making process.

Some patients may become dissatisfied by the presence of the prosthetic device in their body. This issue should be discussed with the patient prior to the surgery. Patient dissatisfaction may lead to device removal. Patients should also be aware that the

AMS 800 is not considered to be a lifetime implant.

It is also important that the physician discusses with the patient the possibility of an allergic reaction to the materials in the device (See Silicone Information).

Antibiotic Information

The antibiotics present in InhibiZone, minocycline HCl and rifampin, are well characterized and have been in use for years. The dosage present on the artificial urinary sphincter is intended to act on organisms that attempt to colonize on the device.

The AMS 800 components are treated with very low levels of antibiotics. AMS provides numerous completed configurations of the AMS 800 to individualize treatment, however, while the AMS 800 PRB component is not InhibiZone treated, a complete device (PRB, pump, and one or two cuffs), regardless of configuration, contains ≤ 6.5 mg rifampin and ≤ 8 mg minocycline HCl. This represents less than 2% of an oral dose exposure for a complete course of rifampin or minocycline HCl with the maximum dose calculated from the means and 95% tolerance interval.

The following in vitro data are available, but their clinical significance is unknown. No clinical studies have been performed to evaluate the effect of the antibiotic surface treatment on reducing the incidence of artificial urinary sphincter implant infections.

Table 6: In vitro Zone of Inhibition for Device Samples* with InhibiZone Treatment

Organism	Mean (mm)	S.D. (mm)	Number of Isolates
Staphylococcus epidermidis	22.6	2.9	21
Staphylococcus aureus	17.5	5.0	25
Escherichia coli**	6.5	2.6	24
Enterococcus faecalis**	4.8	6.7	21
Candida albicans**	0.1	0.4	21
Proteus mirabilis**	0.6	1.0	17

*obtained using standardized kink-resistant tubing test samples containing approximately 12µg minocycline HCl and 26 µg rifampin

**the isolates tested were not susceptible to rifampin and/or minocycline HCl control disks

An animal infection study was conducted using 11 rabbits. Five rabbits were implanted subcutaneously with 6 test samples each and five rabbits were implanted subcutaneously with 6 control samples each. One rabbit received three test samples and three control samples. The test samples were portions of an InhibiZone treated AMS 700 pump and the control samples were portions of a standard AMS 700 pump without InhibiZone. The AMS 700 Pumps used in the 700 Series of Inflatable Penile Prostheses is similar to AMS 800 Pumps used in the 800 Series of Artifical Urinary Sphincters in regards to material composition, adhesive, and InhibiZone application process. All samples were soaked in a 10^3-10^4 CFU solution of staphylococcus aureus, Sheretz strain for 8 hours. Samples were then allowed to dry for 30 minutes prior to surgical placement in the rabbit. After 2 days, all samples were removed and observed for growth on the samples. The number of coated samples that were infected was statistically significantly lower than the number of control samples that were infected.

Silicone Information

This device is composed of a number of materials, including solid silicone elastomers and a fluorosilicone lubricant. Silicone gel is not a component in the materials of this device.

Solid silicone elastomers have been commonly used in a variety of biomedical devices for over 40 years. Silicone fluids have an extensive history of use in medical devices.

Scientific literature has included reports of adverse events and other observations in patients with implantable silicone devices. As reported, these events/observations indicate "allergic-like" symptoms and in other cases a symptom complex associated with immunological disorders. No causal relationship has been established between these events and silicone elastomer or fluoro-silicone lubricant.

There are reports of malignant tumor formation in laboratory animals only associated with implants of relatively large size. Many different materials are associated with this effect in animals, silicone elastomers among them. No such effect has been described in humans.

Extensive testing has been conducted on all materials that comprise the AMS 800. This testing has indicated no toxicological response attributable to the materials. However, some of the materials caused minor irritation when implanted in animals.

Silicone elastomer particulate shedding and particulate migrations to regional lymph nodes have been reported in the literature on penile implants. There are no known clinical sequelae to this phenomenon.

Magnetic Resonance Imaging (MRI) Important Safety Information

MR Conditional

Non-clinical testing has demonstrated the AMS 800 product line is MR Conditional. The device can be scanned safely under the following conditions:

Static Magnetic Field	1.5 Tesla[a]	3.0 Tesla[b]
Spatial Gradient Field	450 Gauss/cm or less	720 Gauss/cm or less
Maximum whole body averaged Specific Absorption Rate (SAR)	1.5 W/kg for 15 minutes of scanning as assessed by calorimetry	2.9 W/kg for 15 minutes of scanning as assessed by calorimetry

MRI-Related Heating

Non-clinical testing has demonstrated the AMS 800 product line produced the temperature rises during MRI performed for 15 minutes of scanning in the respective MR systems which would not pose a hazard to the human subject.

Static Magnetic Field	1.5 Tesla[a]	3.0 Tesla[b]
Highest Temperature Change	≤ + 0.4° C	≤ + 2.0 ° C
(a) 1.5T - 64 MHz MR System (General Electric Healthcare, Milwaukee, WI)		
(b) 3.0T MR Excite, General Electric Healthcare, software version 14X.M5		

Artifact Information
Non-clinical testing has demonstrated that the AMS 800 product line may compromise the MR image quality if the area of interest is relatively close to the position of the implant. The maximum image artifact produced by a MR gradient echo pulse sequence was a "moderate" localized signal void in size and shape of the implant. Optimization of MR imaging parameters to compensate for the presence of the device may be necessary.

Pulse Sequence	T1-SE	T1-SE	GRE	GRE
Signal Void Size	5,800 mm^2	1,956 mm^2	6,096 mm^2	2,650 mm^2
Plane Orientation	Parallel	Perpen-dicular	Parallel	Perpen-dicular

Inventory Returns and Product Replacement Information

A Patient Information Form (PIF) must be filled out and filed with AMS at the time of implant to activate the product warranty. Before returning any components, whether explanted or unused (sterile or nonsterile), customers must fill out the Return Goods Form located on the last page of the Patient Information Form.

Follow **all** of the instructions on the form carefully, and be sure that the components have been thoroughly cleaned before returning them to AMS. Request an AMS Product Return Kit from the AMS Customer Service Department to return any explanted components to AMS.

In all cases, obtaining credit or percentage of credit for a returned component is subject to approval under the terms of the AMS Return Goods Policy and the AMS Limited Warranty Policy . For complete information regarding these policies, contact the AMS Customer Service Department.

Outside the United States

Customers outside of the United States should contact their local AMS Representative prior to returning any product.

This document is written for professional medical audiences. Contact American Medical Systems for lay publications.

American Medical Systems periodically updates product literature. If you have questions about the currency of this information, contact American Medical Systems.

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