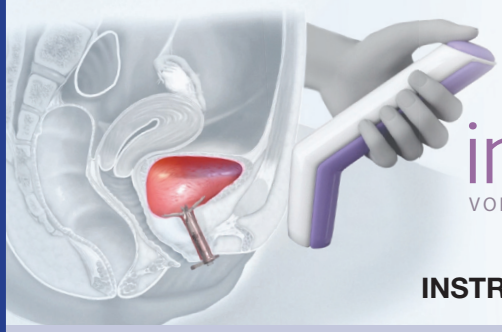


inFlow™
VOIDING PROSTHESIS™

PHYSICIAN INSTRUCTIONS FOR USE

Intraurethral Valve-Pump and Activator
Non-Surgical Urinary Prosthesis for Women

Description and Principles of Operation
The inFlow urinary prosthesis is intended to provide controlled bladder drainage for women with impaired detrusor contractility. The inFlow urinary prosthesis is a system with two components:

1. The inFlow Intraurethral Valve-Pump (the "inFlow device") – a single-use urethral insert with an internal valve-pump mechanism in a biocompatible silicone housing. The inFlow device is supplied sterile with its Introducer attached (**Figure 1**). It is intended for a maximum indwelling time of 29 days and is available in nine (9) sizes in order to accommodate individual patient anatomy.
2. The Activator – a hand-held remote control required to operate the internal valve-pump mechanism in the inFlow device (**Figure 2**). The Activator is powered by a rechargeable lithium battery and comes with a Base Station for recharging.

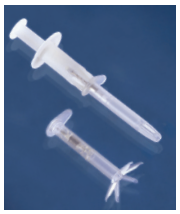


Figure 1. The inFlow device as supplied with its disposable introducer (top) and after being deployed (bottom)

Figure 2. Activator remote control

To operate the inFlow device, the Activator is held at the patient's lower pubic area near the urethral opening and its "on" button is depressed. This magnetically activates the device pump, which drains the bladder at a normal flow rate. When the button is released, the device valve is automatically engaged, stopping urine flow.

Prior to initial insertion, determine the appropriate device size by using the inFlow Sizing Device to measure the patient's urethral length. See inFlow Sizing Device Physician Instructions.

Insertion of the inFlow device is conducted in an ambulatory procedure similar to that for indwelling or intermittent catheters. The inFlow Device is inserted into the urethra until its outer silicone tab touches the edge of the meatus, preventing proximal migration. By depressing the Introducer, the Device's flexible silicone fins expand in a "flower petal" configuration within the bladder at the bladder neck, preventing migration out of the bladder.

To urinate, the patient places the Activator against her lower pubic area. The Activator's operating button is depressed and held to open the Device valve and turn on the pump, which actively draws urine out of the bladder at a flow rate similar to that of normal urination. When urination is complete, the patient releases the button but continues to hold the Activator in place for approximately 3 seconds until it beeps and its LED turns from **green** to **red**. This signals that pumping has ceased and the valve has closed, restoring continence until the next desired voided time.

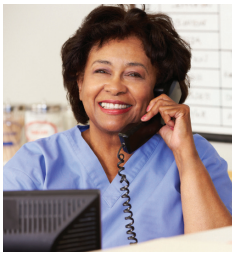
Enclosed *Patient Instructions for Use* must be given to the patient upon each device insertion

Additional information for clinicians is available in the *inFlow Supplemental Instructions*, which can be downloaded from http://vesiflo.com/how_it_works.php

One-Week Trial
The inFlow device has the potential to improve the quality of your patient's life, but it is not for everyone. The best way to find out if a patient is a device candidate is to have them try the device for a week.

QuickStart Guide
After confirming that the patient is a suitable candidate for inFlow use, follow these 5 simple steps to successfully start them on the inFlow:

1. One Week Prior to Initial Insertion: a) measure urethral length using the inFlow Sizing Device in order to determine appropriate device size and b) consider starting patient on a course of anticholinergics.
2. Patient Education: Setting realistic expectations is critical to success. Educate patient on the insertion process and potential for device awareness during the first week or so of use.
3. Insertion Procedure: Use of lubrication, local anesthetic cream/gel or oral analgesics may alleviate discomfort during initial insertion and throughout first 1-2 weeks.
4. Device Training: Immediately after insertion, take patient to the bathroom to practice using a device under guidance.
5. Follow Up: Provide active nursing support during the accommodation period. Follow-up calls by a nurse or continence consultant are recommended about 6 hours after initial insertion and again within the first week.



For more information, please refer to the Guidance for New Patients section of this IFU.

Device Sizes
The inFlow device diameter is 24F. The inFlow is available in 9 different lengths to match the length of the patient's urethra **(Table 1)**.

Table 1: The inFlow Device - Available Lengths	
Device Lengths (cm)	3.0, 3.5, 4.0, 4.5, 5.0, 5.5, 6.0, 6.5, 7.0

One week prior to initial Device insertion, the physician determines the appropriate Device size by using the inFlow Sizing Device (**Figure 3**) to measure the patient's urethral length. Please refer to *inFlow Sizing Device Physician Instructions for Use* for a description of this procedure.

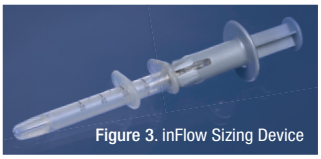


Figure 3. inFlow Sizing Device

Sterility
The inFlow device is provided STERILE (Gamma sterilization). The sterile packaging of the inFlow should be inspected for visible damage prior to use. Do not use if damage is suspected.

Indication
The inFlow Intraurethral Valve-Pump is a replaceable urinary prosthesis that is intended for use in female patients 18 years of age or older who have incomplete bladder emptying due to impaired detrusor contractility of neurologic origin, and who are capable of operating it in accordance with instructions or who have trained caregivers. The device must be replaced every 29 days (or less).

Contraindications
Use of the inFlow is contraindicated in patients with the following conditions:

1. Active urinary tract infection. The inFlow can be used once the infection has been treated.
2. Patients who are allergic to or otherwise cannot take any oral antibiotics.

Warnings
1. The inFlow device is intended for a maximum indwelling time of 29 days. Failure to replace the device at this frequency can increase the risks of infection and device malfunction.
2. Patients (and caregivers, where appropriate) must receive proper education and instruction in the insertion, removal, and use of the device. Specifically, emphasis must be placed on their responsibility to:
   - Keep the Activator available for use at all times;
   - Keep both an extra inFlow and an alternate means of bladder drainage on hand at all times, to use in the event that the current inFlow is expelled, removed, or is not working properly;
   - Urinate every three to four hours during waking hours, even if they do not have bladder sensations;
   - Contact their physician if they see blood in their urine, sense irritation or burning when urinating, suspect that the device is not functioning properly, or require MRI or radiation procedures (the device must be removed).

3. The safety and effectiveness of the inFlow device have not been evaluated and are unknown in patients with the following conditions:
   - Contracted, low-volume bladder (bladder capacity < 200 cc).
   - History of vesicoureteral reflux (Grade II or higher), impaired kidney function, recurrent pyelonephritis or hydronephrosis (moderate to severe).
   - Uninhibited bladder contractions (as documented by urodynamics study) that are not controlled by medication.
   - Neoplastic or inflammatory processes involving the lower urinary tract, uterus, cervix, or vagina.
   - History of urolithiasis within the last year.
   - Urinary tract fistula.
   - Bladder diverticula.
   - Concurrent use of external or internal medical devices with electronic or magnetic components (e.g., pacemakers).
   - Compromised immune system.
   - Significant pelvic organ prolapse (Grade III/IV) requiring surgical treatment. Physician discretion is required for patients with Grade I/II, as they may be at increased risk of device-related discomfort.
   - Pregnancy.
4. Patients with cognitive impairment (e.g., dementia) may be unable to effectively communicate discomfort or other symptoms related to inFlow device use. To ensure the benefits of device use outweigh the risks, such patients should be closely monitored for potential complications.
5. Patients with physical conditions (e.g., poor manual dexterity) that impede their ability to use the Activator as directed for routine voiding or remove the inFlow device in an emergency should have a trained caregiver who will attend to bladder emptying for the patient at least four times daily.
6. Patients with hypersensitivity of the urethra or bladder neck, as evidenced by any level of discomfort/pain observed in response to either frictional stimulus (passage of urodynamics catheter or cystoscope) or pressure stimulus (pushing on the urethra and bladder neck during pelvic exam), may not be able to tolerate the inFlow device due to increased risk of device-related discomfort.
7. Patients undergoing MRI studies or Radiation Treatments - The inFlow device contains a magnet. Therefore, the device should be removed from the urethra during imaging or treatment, and replaced by a new one after the session is complete.

Precautions
1. A physician must insert the first inFlow device after proper sizing of the urethra, using the inFlow Sizing Device. Subsequent insertions may be performed by a nurse, healthcare provider, caregiver or patient who has received appropriate training in device insertion, removal and use.

2. The sterile packaging of the inFlow device should be inspected for visible damage prior to use. Do not use if damage is suspected.
3. The inFlow device is a single use device and reuse should not be attempted due to increased risk of infection. Do not attempt to reassemble a fully or partially deployed device onto its Introducer.
4. Device may not be an effective treatment option in subjects with concomitant urge incontinence that is not controlled by medication.
5. The inFlow Sizing Device is not intended for dilation.
6. When the Activator is not in its base station (**Figure 4**) or covered by its optional magnetic shield (**Figure 5**), it may attract metal items and may damage magnetic strips (such as those on credit cards). To minimize damage from magnetic interference, always keep the uncovered Activator at least ½ meter (1½ feet) from such items.
7. Do not immerse the Activator in water. Clean with a damp cloth only.

Figure 4. Activator in its Base Station for safe storage and charging

Figure 5. Activator with its optional magnetic shield in place

Complications

Possible complications associated with the use of the inFlow device are similar to those associated with indwelling or intermittent urinary catheters and include:

1. Leaking / urinary incontinence
2. Device awareness / discomfort
3. Frequency, urgency or bladder spasms
4. Hematuria / scant perineal bleeding
5. Device malfunction, blockage or other issues
6. Device expulsion / migration
7. Urinary tract infection
8. Accidental injury
9. Asymptomatic bacteriuria
10. Bladder inflammation
11. Autonomic dysreflexia
12. Dyspareunia
13. Dysuria
14. Gastrointestinal disorders
15. Urinary tract disorder
16. Vulvovaginal / periurethral disorders

Patient Selection

Women appropriate for the inFlow device are unable to spontaneously urinate and/or present with clinically significant post-void residuals (PVRs), typically >75cc as measured on at least three occasions, and exhibit none of the listed contraindications. Urodynamics study is recommended to confirm diagnosis, but more importantly as the most robust way to identify contraindications. As always, a medical history including voiding diary and physical exam should be performed.

Device Insertion

After determining the correct device size using the inFlow Sizing Device, follow this procedure to insert the inFlow:

1. With the patient in the lithotomy position, clean the meatus area as for Foley catheter insertion.
2. Lubricate the external body of device with an analgesic medical lubricant.
3. Insert the lubricated inFlow into the urethra until its outer tab (flange) touches the edge of the meatus **(Figure 6)**. The tab should be pointing down, towards the vagina.
4. Completely depress the Introducer's pusher **(Figure 7)** until the device is released **(Figure 8)**. Do not pull out the Introducer until the device is completely released.
5. Discard the Introducer.
6. When there is urine in the bladder, check for leakage and for proper device functioning using the Activator (see To Urinate section of this IFU).

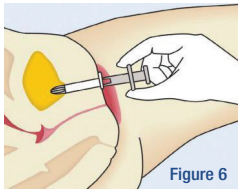


Figure 6

Tips

Generally, the outer tab should be positioned at 6 o'clock, toward the vagina; however, some women find that a 3, 9 or even 12 o'clock position, toward the Mons, is more comfortable. To change the tab position, push the device slightly inwards toward the bladder, then rotate gently. Rotating without lifting the "petals" off the bladder neck may cause discomfort.

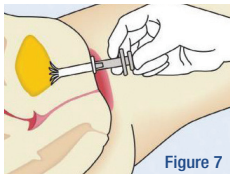


Figure 7

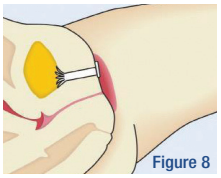


Figure 8

During the accommodation period, should a patient become unable or unwilling to tolerate the device, it can be safely and easily removed at any time and by anyone – by simply grasping the tab and pulling the device straight out. (The patient should then be instructed to resume her former method of bladder drainage).

For sexually active patients, recommend use of adequate vaginal lubrication and positions that reduce direct friction with the urethral area. Rotating the tab away from the clitoris as discussed above may also be a good practice.

Encourage patients to drink between 1 and 2 liters (up to 2.5 quarts) of liquid per 24 hours.

Remind patients to always carry the Activator with them!

Provide patients with a contact number of a nurse or continence advisor that she can call during and outside normal business hours should she experience problems.

To Urinate

1. The patient sits on the toilet as for normal urination.
2. The Activator is removed from its Base Station or magnetic shield. NOTE: The Activator will not operate unless the protective shield is removed.
3. The Activator is held against the lower pubic area, just above the urethral opening (**Figure 9**).
4. The Activator's button is pressed continuously to initiate urination. (The LED will turn **green**).
5. When urine flow has completely stopped, the button is released, but the Activator is held in place for an additional 3 seconds until it beeps and the LED turns from **green** to **red**. This signals that the valve has closed, completing the urination process.
6. To prevent dislodging of the device, the vaginal area should be patted dry, not wiped.
7. If necessary, the Activator should be wiped dry.
8. Place the Activator back in its Base Station or in its magnetic shield.

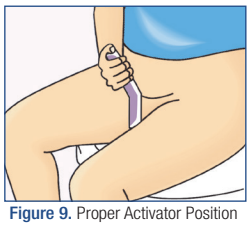


Figure 9. Proper Activator Position for Urination

If the patient moves the Activator before the inFlow valve closes, they will leak. If that happens, instruct the patient as follows:

- **a.** Sit on the toilet again.
- **b.** Position the Activator so that its bottom section pushes into your body, as described in Step 3 above.
- **c.** Press the button for 10 seconds and then let go.
- **d.** Keep the Activator in position until you hear a loud beep and see the LED light change from **green** to **red**.

Device Removal

With the patient in the lithotomy position, gently pull the device straight out of the urethra. **(Figure 10)**.

Due to the flexibility of the silicone fixation system, no damage to the bladder neck or urethra should result **(Figure 11)**.

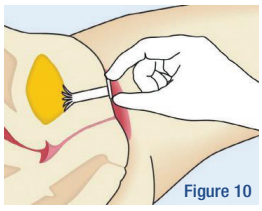


Figure 10

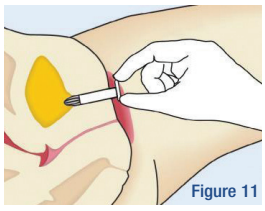
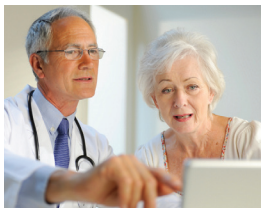


Figure 11



Guidance for New Patients

The following sections expand on the QuickStart Guide and provide recommendations intended to successfully start a new patient on the inFlow device.

Three office visits are recommended in the first three weeks: the first to measure urethral length, start a course of anticholinergics and orient the patient; the second to insert the device and fully in-service the patient and/or her caregiver; and the third to follow up.

1. One Week Prior to Initial Insertion

Measure urethral length using the inFlow Sizing Device in order to determine appropriate device size. Please refer to inFlow Sizing Device Physician Instructions for Use for instructions on device sizing.

To relieve possible sensation of urgency, consider prescribing anticholinergics prior to initial device insertion and continue for the first 2 weeks of use. Since the drugs take up to 5 days to work up to full effect, this therapy should commence 5-7 days prior, or the patient should be informed of this fact if commencing such medication after insertion of the inFlow device. The patient may need to be warned that these drugs have some common side effects, such as blurred vision, dry mouth and constipation.

Explain to the patient that the first week of device use will be a trial period and schedule a follow-up appointment for one week following device insertion. Prior to initial insertion, the patient may wish to view the Patient Instructions for Use, to see the actual device and/or to speak with other users.

2. Pre-Insertion Patient Education

Patient education is important for successful inFlow use. When properly introduced, the inFlow device has the potential to improve the quality of your patient's life, but it is not for everyone. Some women cannot or will not tolerate the inFlow device. The urethra is a sensitive part of the body and at least initially many patients will experience a sense of device awareness/discomfort. For many patients who experience it, this sensation will subside in 1-2 weeks as they accommodate to the device and can be helped with pain relievers and hot baths.

Clinicians report that for patients who experience discomfort, the key determinant of device success is their motivation to persevere through the accommodation period. Such motivation is best achieved with patient education and active nursing support. To set appropriate expectations and increase motivation, use these clinically-tested talking points for all patients:

A. Explain that the inFlow will be inserted into the urethra, which is a very sensitive part of the body. As a result, it can require a period of accommodation similar to that required for hard contact lenses.

B. Let her know that some discomfort is normal and is unlikely to have any serious or lasting effects. Instruct the patient to contact you or your nurse immediately if she is concerned about the level of her discomfort and remind her that she can easily and safely remove the device at any time.

Note: Should discomfort be acute, slightly manipulating the device position may help as well. (Please refer to the Tips section of this IFU.)

C. Emphasize that persistence with the inFlow can potentially improve her daily life in very tangible ways by: a) eliminating the need to self-catheterize multiple times daily; or b) eliminating tubes and bags, improving body image (as well as hygiene); and c) likely allowing her to void without assistance, increasing self-reliance, and d) allowing use of a toilet again - a psychologically significant benefit, since it is the "normal" way to void.

Provide active nursing support for all patients in the first two weeks and invite them to call with questions or concerns.

3. **Insertion Procedure**: For initial device insertion, many physicians use a topical anesthetic and administer a course of prophylactic antibiotics for the first 5 days of device use. Please refer to the Device Insertion section of this IFU for instructions on inserting the device.
4. **Device Training**: After device insertion, patients need to practice voiding and using the Activator before they leave the office. A supportive nurse is usually the best person to train the patient and/or caregiver.
5. **Follow Up**: Follow-up calls by nurses are crucial to appropriately identify any problems and reassure patients. Suggested points of contact are about 6 hours after the initial insertion, with further phone follow-up again within the first week.

Recharging the Activator

The Activator contains a rechargeable lithium battery. If the battery is low, the Activator LED will flash red and you will hear a beep when its button is pushed. To recharge, follow this simple procedure:

1. Insert the Vesiflo-supplied charger (**Figure 12**) into the jack in the back of the Base Station (**Figure 13**).
2. Plug the Charger into an AC outlet.
3. Place the Activator in its Base Station.

Figure 12. Vesiflo-suppplied charger

The LED light on the Activator will turn **red** and blink while it is being charged. When the Activator is fully charged, the LED light will change to a solid **green**.


Figure 13. Charger input

Instruct patients as follows:

- Tell them to leave the Activator in its Base Station each night so that it will always be fully charged to start the day.
- Emphasize that they should ***always*** keep the Activator close at hand during the day.
- Remind them that the Activator magnet can attract metal objects and damage credit cards when the Activator is not in its Base Station or its magnetic shield is not in place.

Enclosed Patient Instructions for Use must be given to the patient upon each device insertion

Additional information for clinicians is available in the inFlow Supplemental Instructions, which can be downloaded from http://vesiflo.com/how_it_works.php

Clinical Trials

An 18-site, single-arm crossover study (n=273) was performed to compare safety, effectiveness, and patient satisfaction of the inFlow device versus clean intermittent catheterization ("CIC"), the current standard of care. The study was limited to females with atonic bladder who were successfully using CIC. Clinically minor adverse events, primarily foreign body awareness/discomfort, caused approximately 50% of subjects to discontinue device use (see below); however, 97% of subjects who completed the study chose to continue device use. Clinical endpoints and results for this study were as follows:

Primary Endpoint: Post-void residual (PVR). All subjects with PVR data available for both Baseline and Treatment were considered to be evaluable. This resulted in a total of 115 evaluable subjects (including some dropouts). 98% (113/115) of evaluable subjects had a median inFlow Treatment PVR that was no greater than the median CIC Baseline PVR or both medians were <50 cc, with median PVR at each visit during inFlow Treatment ranging from 10-20cc. (1-sided exact 95% confidence lower limit: 95%; 2-sided exact 95% confidence interval 94-99.8%). 92-98% of all subjects had comparable PVRs at every treatment visit.

Secondary Endpoint: Quality of life (QOL). Among those subjects with both Baseline and Treatment QOL data (n=85), on a 100-point scale, patient scores for the Wagner I-QOL increased by a mean of 25 points while using the inFlow. The median percent improvement was 54%. The results were clinically significant.

Safety: Rate of Urinary Tract Infection (UTI). Per subject-month rates for subjects completing the study declined with continued inFlow use (CIC Baseline=0.12, first half of inFlow Treatment period=0.11 and second half of Treatment period=0.08). This analysis was performed with completers (n=77) only in order to compare event rates during different study periods with the same set of subjects; however, the UTI experience presented in this study is based on 417 patient-months cumulative exposure in 157 patients. Thus, the observed UTI rate is a representative and robust estimate of what might be expected with device use and the finding of equivalence is notable in that no indwelling bladder drainage device has ever been shown to have the same UTI rate as intermittent catheters.

Safety: Other Adverse Events. No serious or long-lasting adverse events associated with inFlow use were reported. The most common adverse events and their incidence rates are listed here:

There were no significant differences in event rates between the CIC Baseline and inFlow Treatment periods except for hematuria, genitourinary pain, bladder inflammation, and urinary incontinence. All hematuria events were of mild or moderate severity and none required treatment or device removal. All bladder inflammation events were mild in severity. All genitourinary pain and incontinence events were mild to moderate in severity. Device awareness/discomfort increased during inFlow Treatment and although all cases were mild in severity, this was the primary reason given for device discontinuance. Approximately 50% of subjects discontinued use for device-related reasons, a rate similar to that reported for contact lenses.* As a result of this discontinuation rate, caution should be exercised when interpreting the above stated adverse event rates. Per post-analysis, the safety profiles for subjects who withdrew from the study did not differ significantly from those who completed the study.

Table 2: Most Common Adverse Events in Pivotal Trial

Adverse Event	Baseline (N=190)		Treatment (N=157)	
Asymptomatic bacteriuria	69	36%	47	30%
Bladder inflammation	0	0%	9	5.7%
Frequency, urgency, bladder spasms	26	14%	32	20%
Gastrointestinal disorder	10	5.3%	17	11%
Genitourinary pain	43	23%	48	31%
Hematuria / scant perineal bleeding	3	1.6%	17	11%
Urinary incontinence1 / leakage	40	21%	83	53%
Urinary tract infection	40	21%	44	28%
Vulvovaginal / periurethral disorders	17	8.9%	24	15%

[1] 42% of all subjects reported pre-existing UI

Six additional studies (total n=190 unique patients) have been published in peer-reviewed journals; two were long-term studies (n=41) of between one and almost four years. All six studies concerned similar populations to the pivotal study and for the most part reported similar findings. The device performed as expected in all instances and no serious or lasting adverse events were reported. These studies reported a similar device discontinuance rate to the pivotal study, with the exception of Lynch et al (2003), who reported only one subject dropped out due for device-related reasons in their one-year study (n=20), which they attributed to pre-insertion patient education and post-insertion nursing support, particularly during the first two weeks following initial insertion.

*The TFOS International Workshop on Contact Lens Discomfort: Report of the Subcommittee on Neurobiology (2013)

REF

inFlow Device, Cat. No. 203511
inFlow Activator, Cat. No. 403507
Magnetic Shield, Cat. No. 403350

Manufactured in the USA by:

Vesiflo
ADVANCING PELVIC HEALTH®

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LATEX

MR unsafe

Single use only – do not reuse

Caution: Federal (U.S.) law restricts sale or use of this device to the order of a physician or other licensed practitioner.

P/N 203135 Rev K - July 2021