OPTILUME®

URETHRAL DRUG COATED BALLOON CATHETER

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1 DEVICE DESCRIPTION

1.1 Balloon Catheter

The Optilume® Urethral Drug Coated Balloon (Optilume DCB) Catheter is a 0.038" (0.97 mm) over-the-wire (OTW) guidewire compatible catheter with a dual lumen design and a tapered, atraumatic tip. The Optilume DCB is used to exert radial force to dilate narrow urethral segments (strictures). The distal end of the catheter has a semi-compliant inflatable balloon that is coated with a proprietary coating containing the active pharmaceutical paclitaxel. The drug coating covers the working length of the balloon body. The device has two radiopaque marker bands that indicate the working length of the balloon where the drug coating is applied. The drug coated balloon is covered with a protective sheath that is discarded prior to use.

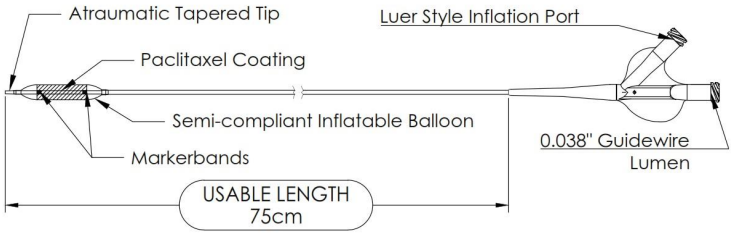

Figure 1-1. Optilume DCB Design

The device is sterilized using ethylene oxide in a Tyvek pouch. Post sterilization the sterile, pouched catheter is sealed in a foil pouch with desiccant and placed within a single unit carton.

1.2 Available Sizes and Nominal Paclitaxel Dose

The Optilume DCB device sizes and catalogue numbers are provided in Table 1-1. The 18F-30F (6-10mm) balloon diameters are flexible cystoscope compatible. The drug coating consists of the active pharmaceutical ingredient paclitaxel and excipients. The drug coating covers the working length of the balloon component of the catheter. The drug coating is evenly distributed across the balloon surface at a concentration of 3.5 µg/mm^2. The drug coating is released from the balloon and transferred to the urothelium during balloon inflation.

Table 1-1: Optilume® DCB Available Sizes and Paclitaxel Dose

Catalog Number	Diameter	Length	Rated Burst Pressure (RBP)	Paclitaxel Dose (µg)
1110-06030D	18F / 6mm	30 mm	12 atm	1,979
1110-06050D	18F / 6mm	50 mm	12 atm	3,299
1110-08030D	24F / 8mm	30 mm	12 atm	2,639
1110-08050D	24F / 8mm	50 mm	12 atm	4,398
1110-10030D	30F / 10mm	30 mm	10 atm	3,299
1110-10050D	30F / 10mm	50 mm	10 atm	5,498

2 INTENDED USE

The Optilume Urethral Drug Coated Balloon (DCB) Catheter is intended for the treatment of strictures in the anterior urethra in adult males.

3 INDICATIONS FOR USE

The Optilume Urethral Drug Coated Balloon is used to treat patients with obstructive urinary symptoms associated with anterior urethral stricture. It is designed to be used in adult males for urethral strictures of ≤3 cm in length.

4 CONTRAINDICATIONS

The Optilume Urethral Drug Coated Balloon is contraindicated for use:

- in patients with known hypersensitivity to paclitaxel or structurally related compounds, and
- in patients with urologic implants such as penile implants or artificial urinary sphincters.

5 WARNINGS

- The Optilume DCB is supplied STERILE for single use only. Do not reprocess or re-sterilize. Reprocessing and re-sterilizing could increase the risk of patient infection and risk of compromised device performance.
- The foil pouch and the outer surface of the inner Tyvek pouch are NON-STERILE. The CONTENTS of the inner Tyvek pouch are STERILE.
- Do not use this device if there is an active infection in the urinary tract (UTI). Infection must be resolved before treating the stricture with the Optilume DCB.
- Do not use after the "Use By" date.
- Men should abstain from sex or use barrier contraception (wear a condom) for 30 days post treatment to avoid exposure of sexual partner to paclitaxel. Paclitaxel may still be present at very low levels after 30 days.
- The Optilume DCB contains paclitaxel, a known genotoxic aneugen. Because paclitaxel may be present in semen after treatment with the Optilume DCB, men with partners of child-bearing potential should use highly effective contraceptive and avoid fathering children until at least 6 months after treatment with the Optilume DCB. Paclitaxel was detectable in semen in 60% (9/15), 39% (5/13) and 8.3% (1/12) of subjects at 1 month, 3 months, and 6 months post-treatment, respectively.

  Maximum paclitaxel concentrations in semen were 17.6, 3.5, and 0.9 ng/mL at 1 month, 3 month and 6 months, respectively, while group mean (SD) paclitaxel concentrations in semen at those same timepoints were 3.0 (4.9), 0.5 (1.0), and 0.1 (0.2) ng/mL. Mean paclitaxel semen concentrations approached the lower limit of quantitation (0.1 ng/mL) at 6 months post-treatment. The risks associated with these paclitaxel concentrations in semen are unknown. The effect of treatment with the Optilume DCB on sperm and spermatogenesis is also unknown.
- Do not manipulate the Optilume DCB in an inflated state. Aspirate (deflate) the balloon completely before gently removing the device from the urethra.
- If resistance is encountered at any time during the insertion or withdrawal of the device do not force passage. Resistance may cause damage to device or urethra.
- The impact of multiple treatments with the Optilume DCB for the same stricture has not been extensively studied. Multiple treatments of the same stricture will increase exposure to paclitaxel, the risks associated with this are currently unknown.

6 PRECAUTIONS

- Carefully inspect the Optilume DCB and package prior to use. Do not use the catheter if it is damaged or if the size, shape, or condition is unsuitable for the intended procedure. Use immediately once the foil pouch has been opened.
- Use dry sterile gloves or dry gauze pads to handle the Optilume DCB prior to use. Care should be taken to minimize contact with the coated balloon portion of the device.
- Never inflate the Optilume DCB outside the body or prior to reaching the target stricture as it may disrupt the coating integrity. Preparation of the device should be done with the balloon still within the balloon protector to avoid inflating the balloon.

- Do not immerse or wipe the balloon section of the Optilume DCB with any fluid as the integrity of the drug coating may be damaged or compromised. Replace any Optilume DCB where the balloon has come into contact with fluids prior to use.
- Prior to use of the Optilume DCB, physicians should read and understand the instructions for use. Failure to follow the indications, contraindications, restrictions, warnings, and precautions may result in complications.
- The Optilume DCB should be manipulated under direct visualization via cystoscopy or high-quality fluoroscopic observation during use.
- Monitor for signs of anaphylaxis or hypersensitivity to paclitaxel
- Never use air or any gaseous medium to inflate the Optilume DCB.
- The Optilume DCB should be used only by physicians who are experienced and knowledgeable in the clinical and technical aspects of urethral balloon dilatation.
- The Optilume DCB should not be inflated in excess of the rated burst pressure (RBP). See Table 1-1 or individual device labeling for the listed RBP for each balloon size. To ensure proper regulation of balloon pressure, use of a balloon inflation device with pressure gauge is recommended.
- Do not attempt to pass the Optilume DCB through a smaller French size cystoscope than indicated on the label.
- The working length of the balloon must cover the entire target stricture length. See Section 12.2 for device sizing instructions.
- For proper drug transfer to the urothelium, allow the coating to hydrate in the urethra for a minimum of 60 seconds prior to inflation and maintain inflation of the Optilume DCB for a minimum of 5 minutes.
- If the product has a failure prior to or during inflation, replace the Optilume DCB and repeat the procedure. If failure is after achieving inflation to RBP, do not replace the device as sufficient dilation and drug transfer has been accomplished.
- After use, this product may be a potential biohazard. Handle and dispose of in accordance with accepted medical practice and applicable local regulations.
- No long-term studies have been performed to evaluate the carcinogenic potential of the Optilume DCB.

7 DRUG INFORMATION

7.1 Mechanism of Action

The Optilume DCB coating contains paclitaxel, an anti-mitotic pharmaceutical agent that specifically binds to and stabilizes microtubules. Paclitaxel has been reported to inhibit smooth muscle cell and fibroblast proliferation and migration as well as secretion of extracellular matrix. The combination of these effects may result in the inhibition of urothelium hyperplasia/scar tissue formation and therefore stricture recurrence.

7.2 Drug Interactions

Formal drug interaction studies have not been conducted for the Optilume DCB. The respective instructions for use for all drugs used in conjunction with the Optilume DCB should be consulted for interactions with paclitaxel. Consideration should be given to the potential for systemic and local drug interactions in the urethra in a patient who is taking a drug with known interactions with paclitaxel or when deciding to initiate drug therapy in a patient who has been treated with the Optilume DCB. The metabolism of paclitaxel is catalyzed by cytochrome P450 isoenzymes CYP2C8 and CYP3A4 and it is a substrate of P-glycoprotein. Potential drug interactions may occur with any drug that affects these isoenzymes. In the absence of formal drug interaction studies, caution should be exercised when administering paclitaxel.

7.3 Carcinogenicity, Genotoxicity and Reproductive Toxicology

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effective contraceptive and avoid fathering children until at least 6 months after treatment with the Optilume DCB. Paclitaxel was detectable in semen in 60% (9/15), 39% (5/13) and 8.3% (1/12) of subjects at 1 month, 3 months, and 6 months post-treatment, respectively.

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7.4 Vascular Paclitaxel Coated Device Meta-Analysis

A meta-analysis of randomized, controlled trials for the use of paclitaxel coated devices in treating patients with peripheral arterial disease (PAD) was published by Katsanos et. al in 2018.[1] This analysis suggested the possibility of an increased risk of mortality resulting from the use of paclitaxel-coated vascular devices. This higher risk of death was observed at time points at least two years after treatment with the paclitaxel-containing devices. The presence and magnitude of the late mortality risk should be interpreted with caution because of multiple limitations in the available data, including wide confidence intervals due to a small sample size, pooling of studies of different paclitaxel-coated devices that were not intended to be combined, substantial amounts of missing study data, no clear evidence of a paclitaxel dose effect on mortality, and no identified pathophysiologic mechanism for the late deaths.

In January 2021, Nordanstig and colleagues published interim results of a large, randomized national registry trial evaluating paclitaxel coated devices against uncoated control devices that showed no significant increase in mortality for paclitaxel coated devices through a median of 2.5 years follow-up.[2] These results compliment published outcomes from large national health insurance databases in the US and Germany showing no increase in mortality risk with the use of paclitaxel coated devices. Longer term follow-up through 5 years is ongoing for these studies.

Patients receiving the Optilume DCB will be treated with a paclitaxel-coated balloon for a different condition (stricture) in a different part of the body (the urethra). Unlike the cardiovascular application, the drug is deposited on the urethra and not in the blood, although a small amount of drug can diffuse through the urethra into the blood. The mortality rate in the ROBUST series of trials evaluating the Optilume DCB was 0.6 deaths per 100 patient follow-up years, which is no different than the expected rate of mortality for men in this age group.

8 POTENTIAL ADVERSE EFFECTS

The potential adverse effects of the Optilume DCB related to mechanical dilation are similar to urethral balloon dilation catheter and include but not limited to the following:

- Dissection of the urethra
- Perforation of the urethra
- Hematuria
- Inflammation
- Infection
- Recurrence of the stricture
- Detachment of a component of the catheter
- Bothersome urinary symptoms or painful urination
- Genital or pelvic pain

Although systemic effects from the paclitaxel coating are not anticipated, adverse effects observed during IV administration of paclitaxel for chemotherapy include, but are not limited to, the following:

[1] Katsanos K, Spiliopoulos S, Kitrou P, Krokidis M, Karnabatidis D. Risk of death following application of paclitaxel-coated balloons and stents in the femoropopliteal artery of the leg: a systematic review and meta-analysis of randomized controlled trials. J Am Heart Assoc. 2018;7(24):e011245

[2] Nordanstig J, James S, Andersson M, Andersson M, Danielsson P, Gillgren P, et al. Mortality with paclitaxel-coated devices in peripheral artery disease. N Engl J Med. 2020;383(26):2538-46

- Allergic reaction
- Alopecia
- Anemia
- Gastrointestinal symptoms
- Hematological dyscrasia (including leucopenia, neutropenia, thrombocytopenia)
- Hepatic enzyme changes
- Myalgia/athralgia
- Myelosuppression
- Peripheral neuropathy

9 HOW SUPPLIED

The Optilume DCB catheter is supplied STERILE for single use only (ethylene oxide sterilization). The Optilume DCB is in a double pouch packaging system (foil and Tyvek pouches) contained within a single unit box.

10 STORAGE

The Optilume DCB should be stored at room temperature in a dry location in its original packaging. The device should be used prior to the "Use by" date on the packaging.

11 RECOMMENDED ITEMS

Prepare the following items using sterile technique:

- 0.038" or smaller guidewire (flexible tip)
- Flexible or rigid cystoscope
- Sterile saline or sterile water for irrigation
- Inflation device with manometer and ≥20cc capacity
- Three-way stopcock to connect the inflation device to the catheter. Alternatively, the inflation device can be directly connected to the catheter.
- Contrast media NOTE: Optional for use with fluoroscopic guided procedures

12 DIRECTIONS FOR USE

12.1 Peri Procedural Medication

It is recommended that physicians follow local guidelines for pre-procedure medications and preparation for an endoscopic procedure, including the administration of a pre-procedure antibiotic as appropriate. Oral NSAIDs are also recommended to be given prior to the procedure.

If a urinary tract infection (UTI) is present, it is recommended that the patient be treated with antibiotics until the infection is resolved before the treatment procedure.

12.2 Device Size Selection

Pre-operative or intra-operative retrograde urethrogram (RUG) or voiding cystourethrography (VCUG) is recommended to identify stricture location, stricture length, and degree of lumen narrowing to inform device size selection. Recommended device diameter selection may depend on anatomic location of the urethral stricture, however for strictures in both the penile and bulbar urethra select an Optilume DCB balloon length that is slightly longer than the stricture length to be treated. The balloon length must extend approximately 0.5-1 cm beyond the stricture on both sides to ensure full coverage of the treated area with the drug coating.

12.2.1 Bulbar Urethral Stricture Device Sizing

For strictures in the bulbar urethra, it is recommended to select a balloon diameter that is slightly larger than the distal healthy urethra diameter. Do not to oversize the Optilume DCB by more than 30% relative to the distal healthy urethra. The majority of bulbar strictures evaluated in the ROBUST III clinical program utilized a 30F Optilume DCB.

Table 12-1: Bulbar Urethra Balloon Sizing Guide

Distal Healthy Urethra Diameter	Optilume® DCB Size	
	Stricture Length ≤ 1.5 cm	Stricture Length 1.5 cm – 3 cm
<19F	18F (6mm) x 30 mm	18F (6mm) x 50 mm
19F – 23F	24F (8mm) x 30 mm	24F (8mm) x 50 mm
>23F	30F (10mm) x 30 mm	30F (10mm) x 50 mm

12.2.2 Penile Urethral Strictures

For urethral strictures in the penile or pendulous urethra, it is recommended to select the balloon diameter that most closely matches the distal healthy urethra diameter. Size selection for penile strictures evaluated in the ROBUST III clinical study were roughly split between 24F and 30F Optilume DCB.

Table 12-2: Penile Urethra Balloon Sizing Guide

Health Distal Urethral Diameter	Optilume® DCB Size	
	Stricture Length ≤ 1.5cm	Stricture Length 1.5 - 3cm
<22F	18F (6mm) x 30 mm	18F (6mm) x 50 mm
22F – 27F	24F (8mm) x 30 mm	24F (8mm) x 50 mm
>27F	30F (10mm) x 30 mm	30F (10mm) x 50 mm

12.3 Balloon Preparation

1. Open the sterile inflation device package and remove the inflation device and 3-way stopcock. If use of a 3-way stopcock is desired, connect the stopcock to the inflation device.

   NOTE: Use of a 3-way stopcock is optional, if the inflation device has a male luer connection it can be directly connected to the female luer hub on the catheter.

2. Fill the inflation device half-way with sterile saline and attach to the Optilume DCB. It is recommended that the balloon remain covered with the balloon protector sheath during preparation.

3. With the inflation device pointing downwards, draw back plunger to aspirate air from the balloon. Hold until no air bubbles can be seen coming out of the saline in the inflation device. Disconnect the inflation device and purge air from the inflation device, reattach and repeat as needed to until no air is left in the balloon.

4. With catheter preparation complete, disconnect the inflation device.

5. If using fluoroscopy fill the inflation device with a 1:1 normal saline-contrast mixture, otherwise fill will sterile saline.

6. Attach inflation device to the stopcock or the female luer hub on the balloon catheter and pull vacuum on the inflation device.

12.4 Optilume DCB Insertion and Dilation

1. With aid of a cystoscope and utilizing saline irrigation, position a 0.038” guidewire across the stricture with the flexible tip coiled in the bladder.
2. Remove the protective sheath from the tip of the Optilume DCB.

   ***Caution**: Care should be exercised when passing a balloon coated with paclitaxel through any cystoscope system. Minimize excessive handling and do not touch the balloon. Do not wipe the balloon with dry, wet or lubricated gauze, or any solvent which could damage the integrity of the drug coated balloon.*
3. Place the Optilume DCB catheter over the guidewire and advance through the working channel of a flexible or rigid cystoscope. Alternately, balloons may be placed by positioning the guidewire and Optilume DCB side by side with the cystoscope.

   ***Caution**: Do not advance the guidewire or the Optilume DCB if resistance is met without first determining the cause of resistance and taking appropriate action to correct.*
4. Position the Optilume DCB across the stricture with the cystoscope placed distal to the balloon (away from the bladder) to visualize the proper placement of the balloon across the stricture. Leave the balloon in position uninflated for a minimum of 1 minute prior to inflation to adequately hydrate the drug coating prior to inflation. Alternatively, the position the Optilume DCB with fluoroscopy by using the radiopaque markers demarking the working length of the balloon.
5. Inflate the balloon to the rated burst pressure (RBP) using the inflation device. Maintain pressure for a minimum of 5 minutes, or until desired dilation is achieved.

   ***Caution:** DO NOT exceed RBP of the balloon. RBP for each balloon size is provided on the Tyvek pouch label and in Table 1-1 of this document. Inflation in excess of RBP may cause the balloon to rupture.*

   ***Caution**: Inflation devices are capable of attaining very high pressures with minimal effort. The use of an inflation device with a pressure gauge is highly recommended to optimize dilatation force to yield the urethral stricture and allow drug penetration into the urothelium.*

12.5 Deflation and Removal

1. Deflate balloon by applying vacuum to the balloon with the inflation device. When the balloon is completely deflated, withdraw guidewire and Optilume DCB slowly. If slight resistance is felt when the balloon is being removed, gently rotate the catheter to help the balloon fold around the catheter shaft and facilitate withdrawal.

   ***Caution:** If resistance is encountered when removing the guidewire and/or Optilume DCB through a cystoscope, STOP and remove them together as a single unit to prevent damage to the guidewire, catheter or patient anatomy.*
2. If the product has a failure prior to inflation or during inflation at a pressure less than RBP, replace Optilume DCB and inflate per above instructions. If the failure is after inflation to RBP, do not repeat the Optilume DCB procedure as sufficient dilation and drug transfer has been accomplished.
3. Insert a 12-14 Fr lubricious Foley catheter and leave in place for a minimum of 2 days or per standard of care, whichever is greater.

13 WARRANTY

Urotronic warrants that reasonable care has been used in the design and manufacture of this product. This warranty is in lieu of and excludes all other warranties not expressly set forth herein, whether express or implied by operation of law or otherwise, including, but not limited to, any implied warranties for a particular purpose. Handling, storage, cleaning and sterilization of this device as well as other factors relating to the patient, diagnosis, treatment, surgical procedures and other matters beyond Urotronic’s control directly affect the device and the results obtained from its use. Urotronic’s obligation under this warranty is limited to the repair or

replacement of this device and Urotronic shall not be liable for any incidental or consequential loss, damage or expense directly or indirectly arising from the use of this device. Urotronic assumes no liability with respect to devices reused, reprocessed or resterilized and makes no warranties, express or implied, including but not limited for a particular purpose, with respect to such devices.

14 SYMBOLS USED IN THE DEVICE LABELS

	Quantity of 1 per box
	Prescription use only
	Indicates the date when the medical device was manufactured.
	Do not resterilize
	Do not re-use
	Do not use if package is damaged
	Fragile
	Use-by date
	Keep away from sunlight
	Keep Dry
	Manufacturer
	Does not contain latex
	Temperature limit 15°C - 30°C
	Caution: Consult instructions for use
	Sterilized using ethylene oxide
	Single sterile barrier system
	Single sterile barrier system with protective packaging outside
	Catalog number
	Lot number
	Medical Device
	Unique Device Identifier
	Contains a medicinal substance

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