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Policy Effective Date	**06/15/2024**
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Drug-Coated Urethral Balloon for Obstructive Urinary Symptoms

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Related Policies (if applicable)
None

Disclaimer

Carefully check state regulations and/or the member contract.
Each benefit plan, summary plan description or contract defines which services are covered, which services are excluded, and which services are subject to dollar caps or other limitations, conditions or exclusions. Members and their providers have the responsibility for consulting the member's benefit plan, summary plan description or contract to determine if there are any exclusions or other benefit limitations applicable to this service or supply. **If there is a discrepancy between a Medical Policy and a member's benefit plan, summary plan description or contract, the benefit plan, summary plan description or contract will govern.**

Coverage

The use of a drug-coated urethral balloon (e.g., Optilume® Urethral Drug Coated Balloon, Optilume® BPH Catheter System) **is considered experimental, investigational and/or unproven** for all indications including but not limited to the treatment of obstructive urinary symptoms associated with benign prostatic hyperplasia and/or urethral stricture.

Policy Guidelines

None.

Description

Drug-coated Urethral Balloon Devices

Recently there has been interest regarding the use of a drug-coated urethral balloon to treat obstructive urinary symptoms associated with urethral stricture or benign prostatic hyperplasia. These catheter-based devices act as a device/drug combination product. First, the device via a catheter dilates the urethra, then when the drug coated balloon is inflated it deposits a drug coating that consists of the active pharmaceutical ingredient paclitaxel. Several studies in animal models have also shown that paclitaxel applied locally inhibits smooth muscle cell and fibroblast proliferation and migration. Based on these animal models, it is thought that the urethral balloon application of paclitaxel may help maintain patency following the procedure. (1, 2)

Benign Prostatic Hyperplasia (BPH)

Benign prostatic hyperplasia (enlarged prostate) affects 70% of men 60-69 years of age and 80% of those 70 years of age or older. An enlarged prostate gland can block the flow of urine. As the gland enlarges it presses against the urethra making the diameter of the urethra smaller and possibly decreasing the ability to completely empty the bladder, this in turn can cause other urinary tract issues. Some of the following symptoms are associated with BPH and include: urinary frequency, trouble starting a urine stream, urinary retention, urinary incontinence, urinary tract infections, and possible bladder and kidney damage. The prevalence of BPH and lower urinary tract issues rises markedly with increased age.

Urethral Strictures

Urethral strictures (a narrowing of the urethral tube) are often caused by infections, trauma, and other medical procedures that injure the lining of the urethra. Urethral strictures typically develop slowly and result in a progressive narrowing of the urethral lumen. Symptoms are similar to those usually associated with bladder outlet obstruction from benign prostatic hyperplasia. Close to 95-98% of urethral strictures in the United States are treated with endoscopic means, meaning with a dilation or urethrotomy. An open surgical procedure called urethroplasty, another treatment option for urethral stricture, is noted to have a better success rate however, it may require a longer recovery and possible side effects.

Regulatory Status

<u>Optilume® Urethral Drug Coated Balloon for Anterior Urethral Stricture</u>

The Optilume® Drug Coated Balloon is inserted with the aid of a cystoscope. The device is a small, cylindrical balloon coated with paclitaxel, it is positioned across the stricture, inflated to both open/dilate the urethra and allow drug penetration to the area with the stricture. The balloon is then deflated and removed. Paclitaxel has been reported to inhibit smooth muscle cell and fibroblast proliferation and may result in the inhibition of scar tissue formation and therefore stricture recurrence. (2)

In December 2021, the U.S. Food and Drug Administration (FDA) approved Optilume® Urethral Drug Coated Balloon (DCB) through the premarket approval application (PMA) process to be 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. Product Code: QRH. (2)

Optilume™ BPH Catheter System

The Optilume BPH Catheter System is a drug-coated balloon that is inserted into the urethra via a telescopic camera to the prostate. Once the catheter is in place, the balloon is expanded and releases the drug (paclitaxel) into the pre-dilated prostatic urethra and prostate. After the drug coating on the balloon is fully released, the balloon is deflated and removed. (1)

In June 2023, the FDA approved the Optilume™ BPH Catheter System through the PMA process with the following indications: "This device is indicated for the treatment of obstructive urinary symptoms associated with Benign Prostatic Hyperplasia (BPH) in men ≥ 50 years of age." Product Code QXB. (3)

Rationale

This medical policy was created in December 2017 and has been updated periodically with searches of the PubMed database. The most recent update was with a review of the literature through April 15, 2024.

Lower Urinary Tract Symptoms (LUTS) Related to Urethral Strictures

In 2020, Virasoro et al. reported on interim results from the ROBUST I study. (4) Men with bulbar urethral strictures ≤2 cm with 1-4 prior endoscopic treatments were enrolled at four study sites after Ethics Committee approvals. All subjects were treated with mechanical balloon dilation or direct visualization internal urethrotomy prior to drug-coated balloon treatment. Patients were evaluated at 2-5 days, 14 days, 3-, 6-, and 12-months posttreatment. The primary safety endpoint was serious complications through 90 days post procedure. The preliminary efficacy endpoint was anatomic success, defined as urethral lumen ≥14 Fr at 12 months. A total of 53 subjects were enrolled and treated; 46 completed the 12-month follow up. Forty-three percent of men had undergone >1 previous dilation; the mean for the overall study population was 1.7 prior dilations. There were no serious adverse events related to the treatment within 90 days. Anatomic success was achieved in 32/46 (70%; 95% confidence interval [CI] 54-82%) at 12 months. The 14 failures included seven cystoscopic recurrences, five retreatments, and two patients who exited the study early due to symptom recurrence. The authors concluded that the 1-year data indicates the Optilume® paclitaxel-coated balloon is safe for the treatment of recurrent bulbar urethral strictures. Early efficacy results are encouraging and support further follow-ups of these men through 5 years, as well as further investigation with a randomized trial.

Mann et al. (2021) presented two-year safety and efficacy outcomes, with efficacy defined as functional success (i.e., symptom score) from the ROBUST I study. (5) The primary safety endpoint was serious urinary adverse events. The primary efficacy endpoint was ≥50% improvement in International Prostate Symptom Score (IPSS) at 24 months. Secondary outcomes included quality of life, erectile function, flow rate, and post-void residual urine volume. Forty-six subjects completed the 24-month follow-up. Forty-three percent of men had undergone >1 previous dilations, with a mean of 1.7 prior dilations. There were no serious

adverse events related to treatment at two years. Success was achieved in 32/46 (70%), and baseline IPSS improved from a mean of 25.2 to 6.9 at 24 months ($p<0.0001$). Quality of life, flow rate, and post-void residual urine volumes improved significantly from baseline. There was no impact on erectile function. The authors' concluded that the two-year data indicates the Optilum® paclitaxel-coated balloon is safe for the treatment of recurrent bulbar urethral strictures. Early efficacy results are encouraging and support further follow-ups of these men through five years, as well as further investigation with a randomized trial.

In 2022, Virasoro et al. reported on 3-year results from the ROBUST I study. (6) Adult men with recurrent bulbar urethral strictures ≤2 cm in length and 1–4 prior endoscopic interventions were treated with the Optilume drug-coated balloon (DCB). Functional success was defined as ≥50% reduction in IPSS without need for retreatment. Other outcomes included quality of life, maximum flow rate, post-void residual urine volume, erectile function, and freedom from repeat intervention. Results noted, that of the 53 enrolled and treated men, 33 completed the 3-year visit, with 10 patients experiencing clinical failures at previous visits, giving a total of 43 subjects evaluable for the functional success endpoint. Functional success was achieved in 67% (29/43) and freedom from retreatment in 77% (33/43). Functional success in this study was based on improvement in IPSS and had similar rates at 2 and 3 years (68% and 67%, respectively). The reduction in IPSS by an average of 72% (19.7 points) was considered clinically meaningful through 3 years post-treatment for a population with moderate-to-severe symptoms at baseline. Significant improvements were also observed in voiding function, with average peak urinary flow rate (Qmax) remaining >15 mL/sec at all follow-up visits through 3 years. Although Qmax has decreased over time, all patient-reported measures (IPSS, International Prostate Symptom Score Quality of Life (IPSS QOL), Urethral Stricture Surgery Patient-Reported Outcome Measure (USS-PROM), International Index of Erectile Function (IIEF) remained consistently and significantly improved from baseline. Erectile function was not affected by treatment. Device-related adverse events were mild or moderate in nature and resolved quickly after onset. There were no serious treatment-related adverse events. Study limitations include the lack of a control arm, although higher rates of stricture recurrence would be expected in this population based on published data of patients with multiple repeat endoscopic treatments. Although cystoscopy was not performed after one year, both retreatment rate and patient reported questionnaires symptoms were used to determine long-term success. Subject follow-up will continue through 5 years to further evaluate durability of the treatment.

Elliott et al. (2022) provided 1- year results for the ROBUST III RCT evaluating Optilume® DCB for anterior urethral strictures. (7) The ROBUST III is a randomized, single blind trial evaluating the safety and efficacy of the Optilume DCB against endoscopic management of recurrent anterior urethral strictures. Eligibility criteria were: adult men with anterior strictures ≤12F in diameter and ≤3cm in length, at least 2 prior endoscopic treatments, IPSS ≥11, and maximum flow rate <15 mL/sec. 127 subjects were enrolled at 22 sites. The primary study endpoint was anatomic success (≥14F by cystoscopy or calibration) at 6 months. Key secondary endpoints included freedom from repeat treatment, IPSS, and Qmax. The primary safety endpoint included freedom from serious device or procedure related complications. Baseline characteristics were

similar between groups, with subjects having an average of 3.6 prior treatments and average length of 1.7 cm. Anatomic success for Optilume DCB was significantly higher than Control at 6 months (75% vs 27%, p <0.001). Freedom from repeat intervention was significantly higher in the Optilume DCB arm. Immediate symptom and urinary flow rate improvement was significant in both groups, with the benefit being more durable in the Optilume DCB group. The most frequently adverse events included urinary tract infection, post-procedural hematuria, and dysuria. The authors' concluded the results of this randomized controlled trial support that Optilume is safe and superior to standard direct visual internal urethrotomy (DVIU)/dilation for the treatment of recurrent anterior urethral strictures <3 cm in length. The Optilume DCB may serve as an important alternative for men that have had an unsuccessful direct vision internal urethrotomy/dilation but want to avoid or delay urethroplasty.

ECRI

ECRI noted in their Clinical Evidence Assessment on Optilume Drug-coated Balloon for Treating Urethral Stricture Disease (2022) that the evidence was inconclusive. (8) The following evidence gaps were noted: Additional double-blind RCTs comparing Optilume with other urethral stricture treatments and reporting on patient-oriented outcomes at longer follow-up times (i.e., >2 years) are needed to assess Optilume's comparative safety and effectiveness. Three ongoing clinical studies may provide additional data and may partially address evidence gaps.

Lower Urinary Tract Symptoms (LUTS) Related to Benign Prostatic Hyperplasia (BPH)

Kaplan et al. (2021) provide the 1-year outcomes of the EVEREST-I study evaluating the safety and efficacy of the Optilume® BPH Catheter System, a prostatic paclitaxel-coated balloon catheter system, for the treatment of lower urinary tract symptoms (LUTS) related to benign prostatic hyperplasia (BPH). (9) Subjects were men >50 years old with moderate-to-severe LUTS secondary to BPH, peak urinary flow rate of 5-15 ml/s, prostatic urethra length 30-55 mm, and prostate volume 20-80 g. All were treated with the Optilume BPH Catheter System and followed at Foley removal, 2 weeks, 30 days, 3, 6, and 12 months after treatment. The primary endpoint was the proportion of subjects with ≥40% improvement in IPSS. The rate of post-procedural complications was evaluated. Eighty subjects were treated at six sites in Latin America and 75 completed the 1-year follow-up. The percent of subjects with an improvement ≥40% in IPSS from baseline was 81% at 3 months and 1 year. IPSS improved from 22.3 at baseline to 7.9 at 1 year, Qmax improved from 10.9 to 18.4 ml/s, and IPSS QOL improved from 4.6 to 1.3. Post-procedural complications included common urologic events and the rate of complications was significantly impacted by device diameter. Study limitations included the lack of a control group. A randomized clinical trial is currently ongoing to confirm the findings. This initial experience helped inform development of the technology to improve outcomes. In this case, removal of the large diameter balloon led to an improved safety profile with no impact to efficacy as compared to the overall cohort. When considering the smaller diameter balloon catheter subgroup, 86.2% (50/58) achieved a 40% reduction in IPSS at 3 months and none of these subjects experienced a major treatment-related complication. The average IPSS was reduced from 22.2 at baseline to 7.8 at 1 year in this subgroup. Longer term follow-up is needed to collect robust durability data for the device. Conclusions reached by the authors included treatment with the minimally invasive Optilume BPH Catheter System is safe and

showed subjective and objective improvements in LUTS. Benefits were rapid and persisted through 1 year. The initial results warrant further evaluation of this therapy as a treatment option for patients with LUTS related to BPH.

In 2023, Pichardo et al. reported on the 2-year outcomes from the EVEREST-I study. (10) The single-arm, open-label study enrolled eighty subjects with LUTS secondary to benign prostatic hyperplasia who were treated with the Optilume BPH Catheter System. This was a multicenter study conducted at six sites in Latin America. Symptoms were recorded utilizing the International Prostate Symptom Score (IPSS) and Benign Prostatic Hyperplasia Impact Index (BPH-II). Functional improvement was measured utilizing peak urinary flow rate (Qmax) and post-void residual urine volume (PVR). Subjects treated with the Optilume BPH Catheter System experienced a significant improvement in LUTS from baseline through 2 years of follow-up, as measured by IPSS (22.3 vs 8.2, $p<0.001$) and BPH-II (6.9 vs 2.3, $p < 0.001$). Functional improvement was also significant, with Qmax improving from an average of 10.9 mL/s at baseline to 17.2 mL/s at the 2-year follow-up and PVR improving from 63.1 to 45.0 mL. Treatment-related adverse events were typically minor, with none occurring between 1- and 2-year post-treatment. The authors concluded in this feasibility study that the Optilume BPH Catheter System is a unique minimally invasive surgical therapy that combines mechanical and pharmaceutical aspects for the treatment of BPH. The functional and symptomatic improvements seen after treatment are significant and have been sustained through 2 years in this early feasibility study. The limitations identified include lack of a control arm and short duration of follow-up.

In 2023, Kaplan et al. reported on a prospective, randomized, double-blind, sham-controlled clinical trial (The PINNACLE Study) evaluating the safety and efficacy of Optilume BPH, for the treatment of lower urinary tract symptom due to BPH. (11) Eligible patients were men 50 years or older with symptomatic benign prostatic hyperplasia and a prostate size between 20 and 80 g. Subjects were randomized 2:1 to receive treatment with Optilume BPH or a sham surgical procedure. Blinding was maintained for subjects in both arms and evaluating personnel through 1 year post procedure. Follow-up assessments included the International Prostate Symptom Score, uroflowmetry, and other quality-of-life and sexual function assessments. One hundred forty-eight men were randomized to either active treatment (100) or sham treatment (48) at 18 centers in North America. Subjects receiving Optilume BPH saw a reduction in International Prostate Symptom Score of 11.5 ± 7.8 points at 1 year posttreatment, as compared to a reduction of 8.0 ± 8.3 points at 3 months in the sham arm. Flow rate was dramatically improved after treatment with Optilume BPH, with an improvement of +10.3 mL/s from baseline to 1 year (+125%). The authors concluded that treatment with Optilume BPH provides immediate and sustained improvements in obstructive symptoms and flow rate while preserving erectile and ejaculatory function. Treatment is well tolerated and can be done in an office or ambulatory setting. Limitations of this study include the fact that eligibility criteria limited enrollment to those men with prostates below 80 g and with moderate or severe symptoms and restricted flow at baseline; results may not be generalizable to all men with LUTS secondary to BPH. The mechanism of action described above is inferred from established action of paclitaxel in the prevention of smooth muscle cell growth and cystoscopic observations and functional

maintenance of flow rate improvement during long-term follow-up from earlier studies; however, direct mechanistic evidence is lacking.

ECRI

ECRI noted in their Clinical Evidence Assessment on Optilume BPH Catheter System for Treating Benign Prostatic Hyperplasia (2024) that the evidence was "favorable". (12) ECRI identified one randomized controlled trial (RCT) and one case series that examined how well the Optilume BPH Catheter System works. The RCT compared active with sham Optilume. ECRI noted that a limitation in the evidence base is the lack of studies comparing the device with other BPH treatments. ECRI's findings pertain only to comparisons with no treatment.

Summary of Evidence

For individuals with obstructive urinary symptoms associated with anterior urethral stricture; the use of a device with a drug-coated urethral balloon catheter was designed to be used in adult males for anterior urethral strictures of ≤3 cm in length. Several studies were noted. While early efficacy results are encouraging, with the ROBUST I study providing follow up for three years, the evaluation is on a small number of individuals. Other studies noted are for shorter follow up time spans. Limitations in the studies included lack of a control group, short duration of follow-up and studies that include small numbers of individuals being evaluated. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with obstructive urinary symptoms associated with benign prostatic hyperplasia, the use of a device with a drug-coated urethral balloon catheter was designed for the treatment of obstructive urinary symptoms associated with benign prostatic hyperplasia (BPH) in men ≥ 50 years of age. Two studies were noted. The EVEREST-I study- a feasibility study that evaluated the safety and efficacy of the drug-coated urethral balloon device, with one- and two-year outcomes on 80 subjects. The other study, the PINNACLE Study, reported on a prospective, randomized, double-blind, sham-controlled clinical trial that included 148 subjects. In both studies the authors noted favorable outcomes. However, several limitations were noted including: small to medium size studies, no studies to comparative treatments, and short duration of follow-up. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Ongoing and Unpublished Clinical Trials

Some current ongoing and unpublished trials that might influence this policy are listed in Table 1.

Table 1. Summary of Key Trials

NCT Number	Trial Name	Planned Enrollment	Completion Date
Ongoing			

NCT03270384[a]	Re-establishing Flow Via Drug Coated Balloon for The Treatment Of Urethral Stricture Disease (ROBUST-II).	16	Jun 2024
NCT03423979[a]	Optilume™ BPH Prostatic Drug Coated Balloon Dilation Catheter (EVEREST-I).	80	Mar 2024
NCT03499964[a]	ROBUST III- Re-Establishing Flow Via Drug Coated Balloon for The Treatment Of Urethral Stricture Disease (ROBUST-III).	127	Dec 2025
NCT04131907[a]	A Clinical Study to Evaluate the Safety and Efficacy of the Optilume™ BPH Catheter System in Men with Symptomatic BPH (PINNACLE).	500	May 2027
NCT05567666[a]	Optilume BPH Catheter System in Benign Prostatic Hyperplasia (BPH) (SUMMIT)	30	Dec 2024 (Not yet recruiting)
NCT05383274[a]	Optilume PoST AppRoval Clinical Evaluation of Andrology ParaMeters (STREAM)	34	Aug 2024
NCT05479422	Optilume Registry for Treatment of Stricture of the Anterior Urethra	150	Aug 2029
NCT06312722[a]	Safety and Effectiveness of the Optilume® BPH Catheter System in a Post-Market Study (PEAK)	92	Feb 2031

NCT: National Clinical Trial.

[a] Denotes industry-sponsored or cosponsored trial.

Coding

Procedure codes on Medical Policy documents are included **only** as a general reference tool for each policy. **They may not be all-inclusive.**

The presence or absence of procedure, service, supply, or device codes in a Medical Policy document has no relevance for determination of benefit coverage for members or reimbursement for providers. **Only the written coverage position in a Medical Policy should be used for such determinations.**

Benefit coverage determinations based on written Medical Policy coverage positions must include review of the member's benefit contract or Summary Plan Description (SPD) for defined coverage vs. non-coverage, benefit exclusions, and benefit limitations such as dollar or duration caps.

CPT Codes	52284, 0619T, [Deleted 1/2024: 0499T]
HCPCS Codes	None

*Current Procedural Terminology (CPT®) ©2023 American Medical Association: Chicago, IL.

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Centers for Medicare and Medicaid Services (CMS)

The information contained in this section is for informational purposes only. HCSC makes no representation as to the accuracy of this information. It is not to be used for claims adjudication for HCSC Plans.

The Centers for Medicare and Medicaid Services (CMS) does not have a national Medicare coverage position. Coverage may be subject to local carrier discretion.

A national coverage position for Medicare may have been developed since this medical policy document was written. See Medicare's National Coverage at <http://www.cms.hhs.gov>.

Policy History/Revision	
Date	**Description of Change**
06/15/2024	Document updated with literature review. The following change was made to the Coverage: Editorial changes were made and examples of other indications were added to the experimental, investigational and/or unproven statement; intent unchanged. References 3, 10-12 added, one reference removed. Title changed from: Optilume (Drug Coated Balloon) for the Treatment of Urethral Stricture Conditions.
05/01/2023	Document updated with literature review. Coverage unchanged. Added references 2, 5, 8-9; one reference updated.
12/01/2022	Reviewed. No changes.
01/01/2022	Document updated with literature review. Coverage unchanged. Added references 3-5.
01/15/2021	Reviewed. No changes.
03/15/2020	Document updated with literature review. Coverage unchanged. Added reference 2.
10/15/2018	Reviewed. No changes.
01/01/2018	New medical document. The use of Optilume™ (a drug coated balloon [DCB]), is considered experimental, investigational and/or unproven for all indications including but not limited to the treatment of urethral stricture conditions.