Clinical Policy: Mitomycin Instillation Solution (Jelmyto, Zusduri)

Reference Number: CP.PHAR.495
Effective Date: 09.01.20
Last Review Date: 08.25
Line of Business: Commercial, HIM, Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Mitomycin (for pyelocalyceal solution [Jelmyto®] and for intravesical solution [Zusduri™]) is an alkylating drug.

FDA Approved Indication(s)

Jelmyto is indicated for the treatment of adult patients with low-grade upper tract urothelial cancer (LG-UTUC).

Zusduri is indicated for the treatment of adult patients with recurrent low-grade intermediate-risk non-muscle invasive bladder cancer (LG-IR-NMIBC).

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Jelmyto and Zusduri are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Low-Grade Upper Tract Urothelial Cancer (must meet all)**:**

1. Request is for Jelmyto;
2. Newly diagnosed or recurrent LG-UTUC that is non-metastatic;
3. Prescribed by or in consultation with an oncologist or urologist;
4. Age ≥ 18 years;
5. Lesion(s) measure ≤ 15 mm;
6. Member is not a candidate for or is not seeking nephroureterectomy as definitive treatment;
7. One of the following (a or b):
   a. Member has had complete or near complete endoscopic resection or ablation;
   b. Member is not a candidate for endoscopic/surgical intervention;
8. Prescribed as monotherapy;
9. Request meets one of the following (a or b):*
   a. Dose does not exceed 60 mg once weekly for 6 instillations per kidney;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 3 months (6 instillations per kidney)

B. Non-Muscle Invasive Bladder Cancer (must meet all)**:**
1. Request is for Zusduri;
2. Diagnosis of NMIBC characterized as both of the following (a and b):
   a. Ta low-grade;
   b. Intermediate-risk (*see Appendix D*);
3. Prescribed by or in consultation with an oncologist or urologist;
4. Age ≥ 18 years;
5. Member has previously undergone transurethral resection of bladder tumor (TURBT);
6. Request meets one of the following (a or b):*
   a. Dose does not exceed 75 mg once weekly for 6 instillations into the bladder;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

   **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 3 months (up to 6 total intravesical instillations)

C. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**
1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving mitomycin instillation solution for a covered indication and has received this medication for at least 30 days;
2. For Jelmyto, both of the following (a and b):
   a. If member has received 6 instillations, complete response (CR) has been achieved at 3 months after initiation of therapy as evidenced by complete absence of tumor lesions on urine cytology and ureteroscopy;
   b. Member has not received more than 17 instillations;
3. For Zusduri, member has not received ≥ 6 instillations;
4. If request is for a dose increase, request meets one of the following (a, b, or c):*
   a. For Jelmyto requests, one of the following (i or ii):

i. If member has completed < 6 weekly instillations: New dose does not exceed 60 mg once weekly for up to 6 instillations per kidney;
ii. If member has completed ≥ 6 weekly instillations: New dose does not exceed 60 mg once monthly for up to 11 instillations per kidney;

b. For Zusduri requests: New dose does not exceed 75 mg once weekly for 6 instillations into the bladder;
c. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Jelmyto – 12 months (up to 17 total instillations per kidney)
Zusduri – 3 months (up to 6 total intravesical instillations per lifetime)

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration
LG-UTUC: low-grade upper tract urothelial cancer
NCCN: National Comprehensive Cancer Network
NMIBC: non-muscle invasive bladder cancer
TURBT: transurethral resection of bladder tumor

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Jelmyto: perforation of the bladder or upper urinary tract
  - Zusduri: perforation of the bladder, prior hypersensitivity reaction to mitomycin or any component of the product
- Boxed warning(s): none reported

Appendix D: General Information

- NCCN Compendium currently recommend Jelmyto with a Category 2A recommendation for primary treatment for a non-metastatic, residual, low-grade, low volume (5-15 mm), solitary tumor in the upper urinary tract for a patient who is not a candidate for or not seeking nephroureterectomy as a definitive treatment. Complete or near complete endoscopic resection or ablation is recommended prior to mitomycin ureteral gel application.
- Intermediate-risk NMIBC is defined as having one or two of the following: the presence of multiple tumors, a solitary tumor > 3 cm, and/or early or frequent recurrence (≥ 1 occurrence of low-grade NMIBC within 1 year of current diagnosis).

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Mitomycin for pyelocalyceal solution (Jelmyto)	LG-UTUC	Jelmyto is for pyelocalyceal use only and not for intravenous use, topical use, or oral administration. The dose of Jelmyto to be instilled is 4 mg/mL via ureteral catheter or nephrostomy tube, with total instillation volume based on volumetric measurements using pyelography, not to exceed 15 mL (60 mg of mitomycin). Instill Jelmyto once weekly for six weeks. For patients with a complete response 3 months after Jelmyto initiation, Jelmyto instillations may be administered once a month for a maximum of 11 additional instillations.	60 mg/instillation; 17 instillations
Mitomycin for intravesical solution (Zusduri)	NMIBC	75 mg (56 mL) instilled once weekly for six weeks into the bladder via a urinary catheter	75 mg/instillation; 6 instillations

VI. Product Availability

Drug Name	Availability
Mitomycin for pyelocalyceal solution (Jelmyto)	Carton containing the following: • Two 40 mg (each) single-dose vials of mitomycin for pyelocalyceal solution • One vial of 20 mL sterile hydrogel for reconstitution
Mitomycin for intravesical solution (Zusduri)	Kit containing the following: • Two 40 mg (each) single-dose vials of mitomycin for intravesical solution • One vial of 60 mL sterile hydrogel for reconstitution

VII. References

1. Jelmyto Prescribing Information. Princeton, NJ: UroGen Pharma, Inc.; October 2024. Available at https://www.jelmyto.com/. Accessed April 9, 2025.
2. Zusduri Prescribing Information. Princeton, NJ: UroGen Pharma; June 2025. Available at: https://www.urogen.com/download/pdf/zusduri_prescribing.pdf. Accessed June 25, 2025.
3. Kleinmann N, Matin S, Pierorazio P, et al. Primary chemoablation of low-grade upper tract urothelial carcinoma using UGN-101, a mitomycin-containing reverse thermal gel (OLYMPUS): an open-label, single-arm, phase 3 trial. Lancet Oncol 2020. Published online April 29, 2020. Available at https://doi.org/10.1016/S1470-2045(20)30147-9.
4. Prasad SM, Shishkov D, Mihaylov NV, et al. Primary chemoablation of recurrent low-grade intermediate-risk nonmuscle-invasive bladder cancer with UGN-102: A single-arm, open-label, phase 3 trial (ENVISION). J Urol. 2025;213(2):205-216.
5. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed May 16, 2025.
6. National Comprehensive Cancer Network. Bladder Cancer Version 1.2025. Available at https://www.nccn.org/professionals/physician_gls/pdf/bladder.pdf. Accessed June 25, 2025.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J9281	Mitomycin pyelocalyceal instillation, 1 mg
J9999	Not otherwise classified, antineoplastic drugs (*Zusduri*)
C9399	Unclassified drugs or biologicals (*Zusduri*)

Reviews, Revisions, and Approvals	Date	P&T Approval Date
3Q 2021 annual review: no significant changes; references to HIM.PHAR.21 revised to HIM.PA.154; added HCPCS codes; references reviewed and updated.	03.17.21	08.21

Reviews, Revisions, and Approvals	Date	P&T Approval Date
3Q 2022 annual review: updated initial approval criteria to include "member is not candidate for or seeking nephroureterectomy as definitive treatment" to mirror NCCN bladder cancer guidelines, added Appendix D for additional information from NCCN Compendium to support this addition; references reviewed and updated.	04.25.22	08.22
Template changes applied to other diagnoses/indications.	10.03.22	
3Q 2023 annual review: added criteria that LG-UTUC be non-metastatic; added requirement for endoscopic resection or ablation if member is a candidate per NCCN and New Century Health; references reviewed and updated.	04.13.23	08.23
3Q 2024 annual review: no significant changes; references reviewed and updated.	05.06.24	08.24
3Q 2025 annual review: removed requirement for cancer location above the ureteropelvic junction per NCCN; removed exclusion for "recent history of carcinoma in situ in the urinary tract, invasive urothelial carcinoma, or high-grade papillary urothelial carcinoma" as this is not excluded per NCCN or the FDA indication; added requirement for use as monotherapy per NCCN; references reviewed and updated. RT4: added criteria for newly approved Zusduri; policy renamed to "Mitomycin Instillation Solution."	06.30.25	08.25

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.