Clinical Policy: Valrubicin (Valstar)

Reference Number: LA.PHAR.439
Effective Date: 05.23.24
Last Review Date: 11.24
Line of Business: Medicaid

Coding Implications
Revision Log

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

Please note: This policy is for medical benefit

Description
Valrubicin (Valstar®) is an anthracycline topoisomerase inhibitor.

FDA Approved Indication(s)
Valstar is indicated for the intravesical therapy of bacillus Calmette-Guerin (BCG)-refractory carcinoma *in situ* (CIS) of the urinary bladder in patients for whom immediate cystectomy would be associated with unacceptable morbidity or mortality.

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 Louisiana Healthcare Connections® that Valstar and valrubicin are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Bladder Cancer (must meet all)**:**

1. Diagnosis of recurrent or persistent CIS of the urinary bladder;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Member meets one of the following (a or b)*:
   a. Failure of intravesical BCG treatment, unless contraindicated or clinically significant adverse effects are experienced;
   b. Adjuvant intravesical chemotherapy for non-muscle invasive bladder cancer (NMIBC) in the event of a BCG shortage (*see Appendix D for information on BCG shortage*);

   **Prior authorization may be required for BCG immunotherapy*
5. For brand Valstar requests, member must use generic valrubicin, unless contraindicated or clinically significant adverse effects are experienced
6. Request meets one of the following (a or b):*
   a. Dose does not exceed 800 mg per week for a total of 6 doses;
   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: 6 weeks (6 doses)

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 LA.PMN.255
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: LA.PMN.53 for Medicaid.

II. Continued Therapy

A. Bladder Cancer (must meet all)**:**
1. Currently receiving medication via Louisiana Healthcare Connections benefit, or documentation supports that member is currently receiving Valstar or valrubicin for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. Member has not yet received a total of 6 doses;
4. For brand Valstar requests, member must use generic valrubicin, unless contraindicated or clinically significant adverse effects are experienced;
5. If request is for a dose increase, request meets one of the following (a or b):*
   a. New dose does not exceed 800 mg per week;
   b. 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: Up to a total of 6 weeks (up to a total of 6 doses)

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 LA.PMN.255
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: LA.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 – LA.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
BCG: bacillus Calmette-Guerin
CIS: carcinoma *in situ*

FDA: Food and Drug Administration
NMIBC: non-muscle-invasive bladder cancer

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
BCG	81 mg intravesically once a week for 6 weeks	Undetermined

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings
- Contraindication(s):
  - Perforated bladder or compromised bladder mucosa
  - Known hypersensitivity to anthracyclines or polyoxyl castor oil
  - Concurrent urinary tract infections
  - Small bladder capacity, i.e., unable to tolerate a 75 mL instillation
- Boxed warning(s): none reported

Appendix D: General Information
- Carcinoma *in situ* (Tis in TNM staging system) refers to early cancer that has not spread to neighboring tissue.
- The American Urological Association (AUA) recommends several management approaches to maintain high quality care for patients with non-muscle-invasive bladder cancer (NMIBC). As always, these recommendations are subject to physician judgment in individual cases:
  - BCG should not be used for patients with low-risk disease.
  - Intravesical chemotherapy should be used as the first-line option for patients with intermediate-risk NMIBC. Patients with recurrent/multifocal low-grade Ta lesions who require intravesical therapy should receive intravesical chemotherapy such as mitomycin, gemcitabine, epirubicin, or docetaxel instead of BCG.
  - If BCG would be administered as second-line therapy for patients with intermediate-risk NMIBC, an alternative intravesical chemotherapy should be used rather than BCG in the setting of this BCG shortage.
  - For patients with high-risk NMIBC, high-grade T1 and CIS patients receiving induction therapy, they should be prioritized for use of full-strength BCG. If not available, these patients and other high-risk patients may be given a reduced 1/2 to 1/3 dose, if feasible.
  - If supply exists for maintenance therapy for patients with NMIBC, limit BCG dose to one year.

- In the event of BCG supply shortage, maintenance therapy should not be given and BCG naïve patients with high-risk disease should be prioritized for induction BCG.
- If BCG is not available, alternatives to BCG such as gemcitabine, epirubicin, docetaxel, valrubicin, mitomycin, or sequential gemcitabine/docetaxel or gemcitabine/mitomycin may also be considered with an induction and possible maintenance regimen.
- Patients with high-risk features (i.e., high-grade T1 with additional risk factors such as concomitant CIS, lymphovascular invasion, prostatic urethral involvement or variant histology) who are not willing to take any potential oncologic risks with alternative intravesical agents, should be offered initial radical cystectomy, if they are surgical candidates.

- The NCCN guidance in the event of a BCG shortage is generally in accordance with AUA stance. They advise BCG should be prioritized for induction of high-risk patients NMIBC (e.g., high-grade T1 and CIS) and that, if feasible, the dose of BCG may be split (1/3 or 1/2 dose) so that multiple patients may be treated with a single vial in the event of a shortage.
  - If BCG is unavailable, the NCCN recommends the following alternatives:
    - Intravesical chemotherapy agents as first-line and subsequent therapy (e.g., gemcitabine, mitomycin, epirubicin, valrubicin, docetaxel, sequential gemcitabine/docetaxel, gemcitabine/mitomycin);
    - Initial radical cystectomy if patient is a surgical candidate.

1. National Comprehensive Cancer Network Guidelines. Bladder Cancer Version 4.2024. Available at https://www.nccn.org/professionals/physician_gls/pdf/bladder.pdf. Accessed August 7, 2024.
2. American Urological Association. BCG Shortage Info. Feb 2019. Available at: https://www.auanet.org/about-us/bcg-shortage-info. Accessed August 7, 2024.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Bladder CIS	800 mg intravesically once every week for 6 weeks	800 mg/dose

VI. Product Availability

Single-use vials: 200 mg/5 mL

VII. References

1. Valstar Prescribing Information. Malvern, PA: Endo Pharmaceuticals Solutions Inc.; October 2019. Available at: http://valstarsolution.com/patient/. Accessed July 16, 2024.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed August 7, 2024.
3. Quan Y, Jeong CW, Kwak C, et al. Dose, duration, and strain of bacillus Calmette-Guerin in the treatment of nonmuscle invasive bladder cancer. Medicine (Baltimore). 2017; 96(2):e8300.

4. National Comprehensive Cancer Network. Bladder Cancer Version 4.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/bladder.pdf. Accessed August 7, 2024.
5. American Urological Association: Important message about the BCG shortage: Important message about the BCG shortage. Accessed August 7, 2024.

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
J9357	Injection, valrubicin, intravesical, 200 mg

Reviews, Revisions, and Approvals	Date	LDH Approval Date
Policy created.	05.09.23	08.28.23
Reviewed and updated references.	02.27.24	05.23.24
Clarified that policy applies to generic valrubicin; added criterion for brand Valstar requests, that member must use generic valrubicin; references reviewed and updated.	11.19.24	

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. LHCC 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.

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 LHCC administrative policies and procedures.

CLINICAL POLICY
Valrubicin

This clinical policy is effective as of the date determined by LHCC. 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. LHCC 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.

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