



Clinical Policy: Tisotumab Vedotin-tftv (Tivdak)

Reference Number: LA.PHAR.561

Effective Date: 09.29.23

Last Review Date: ~~02.27.24~~ 09.17.24

Line of Business: Medicaid

[Coding Implications](#)

[Revision Log](#)

Formatted Table

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

****Please note: This policy is for medical benefit****

Formatted: Font: Bold

Description

Tisotumab vedotin-tftv (TivdakTM®) is a tissue factor-directed antibody and microtubule inhibitor conjugate.

FDA Approved Indication(s)

Tivdak is indicated for the treatment of adult patients with recurrent or metastatic cervical cancer with disease progression on or after chemotherapy.

~~This indication is approved under accelerated approval based on tumor response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.~~

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 Tivdak is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Cervical Cancer, ~~Vaginal Cancer (off-label)~~ (must meet all):

1. Diagnosis of cervical cancer or vaginal cancer;
2. Disease is recurrent or metastatic;
3. Prescribed by or in consultation with an oncologist;
4. Age ≥ 18 years;
5. Failure of single-agent or combination chemotherapy regimen (*see Appendix B for examples*);
6. Prescribed as single-agent therapy;
7. Documentation of member's current weight in kilograms;
8. Request meets one of the following (a or b):*
 - a. Dose does not exceed 2 mg/kg (up to a maximum dose of 200 mg for members ≥ 100 kg) every 3 weeks;
 - 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

CLINICAL POLICY

Tisotumab Vedotin-tftv

Approval duration: 6 months

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. ~~Cervical Cancer~~ All Indications in Section I (must meet all):

1. Currently receiving medication via Louisiana Healthcare Connections benefit, or documentation supports that member is currently receiving Tivdak for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. Prescribed as single-agent therapy;
4. Member is receiving at least 0.9 mg/kg every 3 weeks;
5. Documentation of member's current weight in kilograms;
6. If request is for a dose increase, request meets one of the following (a or b):*
 - a. New dose does not exceed 2 mg/kg (up to a maximum dose of 200 mg for patients ≥ 100 kg) every 3 weeks;
 - 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: 12 months

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. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration

Appendix B: Therapeutic Alternatives

CLINICAL POLICY

Tisotumab Vedotin-tftv

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
paclitaxel/cisplatin ± bevacizumab (Avastin [®] , Mvasi [®] , Zirabev [™])	<ul style="list-style-type: none"> • Paclitaxel: 135 mg/m² or 175 mg/m² IV on Day 1 • Cisplatin: 50 mg/m² IV on Day 1 or 2 • With or without bevacizumab: 15 mg/kg IV on day <p>Repeat every 3 weeks until disease progression or unacceptable toxicity</p>	Varies
paclitaxel/carboplatin ± bevacizumab (Avastin [®] , Mvasi [®] , Zirabev [™])	<ul style="list-style-type: none"> • Paclitaxel 135 mg/m² IV over 3 hours • Carboplatin target AUC 5 IV • With or without bevacizumab: 15 mg/kg IV on day <p>Repeat every 3 weeks until disease progression or unacceptable toxicity</p>	Varies
topotecan (Hycamtin [®]) /paclitaxel ± bevacizumab (Avastin [®] , Mvasi [®] , Zirabev [™])	<ul style="list-style-type: none"> • Paclitaxel: 175 mg/m² on day 1 • Topotecan: 0.75 mg/m² on days 1, 2, and 3 • With or without bevacizumab: 15 mg/kg IV on day <p>Repeat every 3 weeks until disease progression or unacceptable toxicity</p>	Varies
paclitaxel/cisplatin	<ul style="list-style-type: none"> • Paclitaxel: 135 mg/m² over 24 hours • Cisplatin: 50 mg/m² on day 1 <p>Repeat every 3 weeks for a maximum of 6 cycles in non-responders or until disease progression or unacceptable toxicity</p>	Varies
paclitaxel/carboplatin	<ul style="list-style-type: none"> • Paclitaxel 135 mg/m² IV over 3 hours on day 1 until disease progression or unacceptable toxicity • Carboplatin: Target AUC 5 IV every 3 weeks for 6 to 9 cycles 	Varies
cisplatin/topotecan (Hycamtin [®])	<ul style="list-style-type: none"> • Cisplatin: 50 mg/m² IV on day 1 • Topotecan: 0.75 mg/m²/day IV for days 1, 2, and 3 	Varies

CLINICAL POLICY

Tisotumab Vedotin-tftv

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	Repeat every 3 weeks for a maximum of 6 cycles in nonresponders or until disease progression or unacceptable toxicity	
paclitaxel/topotecan (Hycamtin®)	<ul style="list-style-type: none"> • Paclitaxel: 175 mg/m² on day 1 • Topotecan: 0.75 mg/m² on days 1, 2, and 3 Repeat every 3 weeks until disease progression or unacceptable toxicity	Varies
Keytruda® (pembrolizumab) + paclitaxel/cisplatin ± bevacizumab (Avastin®, Mvasi®, Zirabev™) for PD-L1-positive tumors	Varies	Varies
cisplatin	40 mg/m ² over 4 hours to radiation therapy on days 1, 8, 15, 22, 29, and 36	Varies
carboplatin	400 mg/m ² on day 1 every 28 days	Varies
paclitaxel	Varies	Varies

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): ~~None~~none reported
- Boxed warning(s): ~~Ocular~~ocular toxicity

IV. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Cervical cancer	2 mg/kg IV over 30 minutes every 3 weeks until disease progression or unacceptable toxicity	2 mg/kg, 200 mg for members ≥ 100 kg 100 kg

Formatted Table

V. Product Availability

Intravenous powder for solution, single-dose vial: 40 mg

VI. References

1. Tivdak Prescribing Information. Bothell, WA: Seagen Inc.; ~~July 2023~~April 2024. Available at: <https://www.tivdakhcp.com>. Accessed ~~August 9, 2023~~May 8, 2024.
2. A Trial of Tisotumab Vedotin in Cervical Cancer. ClinicalTrials.gov Identifier: NCT03438396. Available at: <https://clinicaltrials.gov/ct2/show/NCT03438396>. Accessed October 18, 2021.

Formatted: Indent: Hanging: 0.31", Keep with next

CLINICAL POLICY

Tisotumab Vedotin-tftv

3. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed ~~August 9, 2023~~ May 8, 2024.
4. National Comprehensive Cancer Network. Cervical Cancer Version ~~1.2022~~ 3.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/cervical.pdf. Accessed ~~August 9, 2023~~ May 8, 2024.
- 4.5. National Comprehensive Cancer Network. Vaginal Cancer Version 1.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/vaginal.pdf. Accessed May 8, 2024.
- 5.6. Kitagwa R, Katsumata N, Shibata T, et al. Paclitaxel Plus Carboplatin Versus Paclitaxel Plus Cisplatin in Metastatic or Recurrent Cervical Cancer: The Open-Label Randomized Phase III Trial. J Clin Oncol 2015; 33(19):2129-2135.
- 6.7. Tewari KS, Sill MW, Penson RT, et al. Bevacizumab for advanced cervical cancer: final overall survival and adverse event analysis of a randomised, controlled, open-label, phase 3 trial (Gynecologic Oncology Group 240). Lancet. 2017;390(10103):1654-1663.
- 7.8. Monk BJ, Sill MW, McMeekin DS, et al. Phase III trial of four cisplatin-containing doublet combinations in stage IVB, recurrent, or persistent cervical carcinoma: a Gynecologic Oncology Group study. J Clin Oncol. 2009;27(28):4649-4655.
- 8.9. Redondo A, Colombo N, McCormack M, et al. Primary results from CECILIA, a global single-arm phase II study evaluating bevacizumab, carboplatin, and paclitaxel for advanced cervical cancer. Gynecol Oncol. 2020;159(1):142-149. doi:10.1016/j.ygyno.2020.07.026.
- 9.10. Long HJ 3rd, Bundy BN, Grendys EC Jr, et al. Randomized phase III trial of cisplatin with or without topotecan in carcinoma of the uterine cervix: a Gynecologic Oncology Group Study. J Clin Oncol. 2005;23(21):4626-4633.
- 10.11. Rose PG, Ali S, Watkins E, et al. Long-term follow-up of a randomized trial comparing concurrent single agent cisplatin, cisplatin-based combination chemotherapy, or hydroxyurea during pelvic irradiation for locally advanced cervical cancer: a Gynecologic Oncology Group Study. J Clin Oncol. 2007;25(19):2804-2810. doi:10.1200/JCO.2006.09.4532.
- 11.12. Weiss GR, Green S, Hannigan EV, et al. A phase II trial of carboplatin for recurrent or metastatic squamous carcinoma of the uterine cervix: a Southwest Oncology Group study. Gynecol Oncol. 1990;39(3):332-336.

Formatted: Font color: Auto

Coding Implications

HCPSC Codes	Description
J9273	Injection, tisotumab vedotin-tftv, 1 mg

Reviews, Revisions, and Approvals	Date	LDH Approval Date
Policy created	05.01.23	08.28.23
Annual review: no significant changes; references reviewed and updated.	02.27.24	05.23.24

CLINICAL POLICY

Tisotumab Vedotin-tftv

Reviews, Revisions, and Approvals	Date	LDH Approval Date
<u>Converted FDA approved indication for cervical cancer from accelerated approval to full approval per PI; added off-label vaginal cancer indication per NCCN; references reviewed and updated.</u>	<u>09.17.24</u>	

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.

Formatted: Underline

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.

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.

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.

CLINICAL POLICY

Tisotumab Vedotin-tftv

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

This clinical policy is the property of LHCC. 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.

©2024 Louisiana Healthcare Connections. All rights reserved. All materials are exclusively owned by Louisiana Healthcare Connections and are protected by United States copyright law and international copyright law. No part of this publication may be reproduced, copied, modified, distributed, displayed, stored in a retrieval system, transmitted in any form or by any means, or otherwise published without the prior written permission of Louisiana Healthcare Connections. You may not alter or remove any trademark, copyright or other notice contained herein. Louisiana Healthcare Connections is a registered trademark exclusively owned by Louisiana Healthcare Connections.