Medical Policy

Healthcare Services Department

Policy Name	Policy Number	Scope
Tisotumab vedotin-tftv (Tivdak®)	MP-RX-FP-145-24	☒ MMM MA ☒ MMM Multihealth

Service Category

☐ Anesthesia
☐ Surgery
☐ Radiology Procedures
☐ Pathology and Laboratory Procedures
☐ Medicine Services and Procedures
☐ Evaluation and Management Services
☐ DME/Prosthetics or Supplies
☒ Part B Drugs

Service Description

This document addresses the use of *Tisotumab vedotin-tftv (Tivdak®),* a tissue factor-directed antibody and microtubule inhibitor conjugate approved by the Food and Drug Administration (FDA) for the treatment of adult patients with recurrent or metastatic cervical cancer with disease progression on or after chemotherapy.

Background Information

Tivdak is an anticancer antibody-drug conjugate that is made up of an antibody and monomethyl auristatin E (MMAE), a cytotoxic component of the drug. It works binding to tissue factors expressed on cervical tumours and releasing MMAE upon cell entry to mediate its cytotoxic activity. It works by binding to tissue factors expressed on cervical tumours and releasing MMAE upon cell entry to mediate its cytotoxic activity.

The FDA approved indication for Tivdak is for the treatment of adults with recurrent or metastatic cervical cancer with disease progression on or after chemotherapy. The National Comprehensive Cancer Network compendia also provides a 2A recommendation for this use in the Cervical Cancer and Vaginal Cancer Clinical Practice Guidelines, stating use as second-line or subsequent therapy in recurrent or metastatic disease as a single agent.

Tivdak has a black box warning for ocular toxicity resulting in changes in vision, including severe vision loss, and corneal ulceration.

Tivdak is the first antibody-drug conjugate to treat adults with recurrent or metastatic cervical cancer and works by targeting tissue factor on cervical cancer cells, resulting in slowing of cell growth or cellular death. In clinical trials, Tivdak was administered to subjects with no more than two prior systemic regimens in the recurrent or metastatic setting, including at least one prior platinum-based (cisplatin, injection or carboplatin, injection) chemotherapy regimen. Approximately 70% of the women had received prior bevacizumab. Treatment for cervical cancer typically includes surgery, radiation, chemotherapy, vascular endothelial growth factor (VEGF) inhibitor bevacizumab, and PD-1 inhibitor pembrolizumab. The chemotherapy most often used to treat recurrent or metastatic cervical cancer includes cisplatin, carboplatin, paclitaxel and topotecan injections.

Definitions and Measures

- Chemotherapy: Medical treatment of a disease, particularly cancer, with drugs or other chemicals. Disease Progression: Cancer that continues to grow or spread.
- Line of Therapy:

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- First-line therapy: The first or primary treatment for the diagnosis, which may include surgery, chemotherapy, radiation therapy or a combination of these therapies.
- Second-line therapy: Treatment given when initial treatment (first-line therapy) is not effective or there is disease progression.
- Third-line therapy: Treatment given when both initial (first-line therapy) and subsequent treatment (second-line therapy) are not effective or there is disease progression.

- Metastasis: The spread of cancer from one part of the body to another; a metastatic tumor contains cells that are like those in the original (primary) tumor and have spread.

Approved Indications

A. 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.

Other Uses

i. Vaginal cancer

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS	Description
J9273	Injection, tisotumab vedotin-tftv, 1 mg [Tivdak]

ICD-10	Description
C52	Malignant neoplasm of vagina
C53.0 – C53.9	Malignant neoplasm of cervix uteri

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Medical Necessity Guidelines

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Tisotumab vedotin-tftv (Tivdak®)

A. Criteria For Initial Approval (*Provider must submit documentation [such as office chart notes, lab results, pathology reports, imaging studies, and any other pertinent clinical information] supporting the patient's diagnosis for the drug and confirming that the patient has met **all** approval criteria.)*

i. Individual has a diagnosis of recurrent or metastatic cervical cancer or vaginal cancer (NCCN 2A); **AND**
ii. Individual is using as single agent; **AND**
iii. Individual is using as second-line or subsequent therapy after confirmed disease progression on chemotherapy (Label, NCCN 2A); **AND**
iv. Individual has a current ECOG performance status of 0 to 1.

B. Criteria For Continuation of Therapy

i. MMM considers continuation of Tisotumab vedotin-tftv (Tivdak®) therapy medically necessary in members requesting reauthorization for an indication listed in Section A above (Criteria for Initial Approval) when there is no evidence of unacceptable toxicity or disease progression while on the current regimen. The following information should be submitted for reauthorization:
    A. A current oncology note documenting the patient's response to treatment showing no progression of disease.
    B. Current imaging studies and other objective measures, as appropriate, showing no progression of disease when compared with previous results.

C. Authorization Duration

i. Initial Approval Duration: Up to 6 months
ii. Reauthorization Approval Duration: Up to 6 months

D. Conditions Not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive):
Tivdak (tisotumab vedotin-tftv) may not be approved for the following:

i. Individual has moderate or severe hepatic impairment (defined as total bilirubin greater than 1.5 x ULN);

OR

ii. When the above criteria are not met and for all other indications.

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Limits or Restrictions

A. Therapeutic Alternatives

The list below includes preferred alternative therapies recommended in the approval criteria and may be subject to prior authorization.

i. N/A

B. Quantity Limitations

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. The chart below includes dosing recommendations as per the FDA-approved prescribing information.

Drug	Recommended Dosing Schedule
Tivdak (tisotumab vedotin-tftv) inj 40 mg SDV	- 2mg/kg IV every 3 weeks until disease progression or unacceptable toxicity.
Exceptions	
• Maximum dose of 200 mg for patients ≥100 kg. • Conduct an ophthalmic exam prior to initiation of Tivdak, prior to every cycle for the first nine cycles, and as clinically indicated. The ophthalmic exam should include visual acuity, slit lamp exam of the anterior segment of the eye, and an assessment of normal eye movement. Refer to package insert for dosage modifications for adverse reactions.	

Reference Information

1. Clinical Pharmacology powered by ClinicalKey. Tampa (FL): Elsevier. 2023. Available from: http://www.clinicalkey.com. Updated periodically.
2. Coleman RL, Lorusso D, Gennigens C, et al. Efficacy and safety of tisotumab vedotin in previously treated recurrent or metastatic cervical cancer (innovaTV 204/GOG-3023/ENGOT-cx6): a multicentre, open-label, single-arm, phase 2 study. Lancet Oncol. 2021;22(5):609-619. doi:10.1016/S1470-2045(21)00056-5.
3. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Accessed: October 10, 2023.
4. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
5. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2023; Updated periodically.
6. NCCN Clinical Practice Guidelines in Oncology™. © 2023 National Comprehensive Cancer Network, Inc. For additional information visit the NCCN website: http://www.nccn.org/index.asp. Accessed on October 10, 2023.

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a. Cervical Cancer. V1.2024. Revised September 20, 2023.
b. Vaginal Cancer. V2.2025. Revised August 8, 2024.

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.

Policy History

Revision Type	Summary of Changes	P&T Approval Date	UM/CMPC Approval Date
Annual Review 12/27/2024	Added NCCN 2A recommendation for use in vaginal cancer. Added dosage forms and strenghts to quantity limits table, and required ophtalmic eye care per FDA label. Minor wording and formattin changes. Updated references. Coding Reviewed: Added ICD10-CM C52; merged ICD10s C53.0 – C53.9.	3/20/2025	4/2/2025
Policy Inception 01/30/2024	New Medical Policy creation	4/18/2024	6/28/2024