CLINICAL GUIDELINES FOR MEDICAL NECESSITY

MEDICAL POLICY

Tisotumab Vedotin-tftv (Tivdak®)

Version: 1.0

Effective Date: 10/28/2025

NantHealth® | Eviti®

Please note the following:

For Medicare members/enrollees, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Please refer to the CMS website at http://www.cms.gov for additional information.

For Medicaid members/enrollees, circumstances when state Medicaid coverage provisions conflict with the coverage provisions within 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.

Tisotumab Vedotin-tftv (Tivdak®)

Discussion

Tisotumab vedotin-tftv is a tissue factor (TF)-directed antibody drug conjugate (ADC). The antibody is a human IgG1 directed against the cell surface TF. TF is the primary initiator of the extrinsic blood coagulation cascade. The small molecule MMAE is a microtubule-disrupting agent attached to the antibody via a protease-cleavable linker. The anticancer activity of tisotumab vedotin-tftv is due to the binding of the ADC to TF expressing cancer cells, followed by internalization of the ADC-TF complex, and release of MMAE via proteolytic cleavage. MMAE disrupts the microtubule network of actively dividing cells, leading to cell cycle arrest and apoptotic cell death.

The most common (≥25%) adverse reactions include laboratory abnormalities, such as decreased hemoglobin, peripheral neuropathy, conjunctival adverse reactions, nausea, fatigue, increased aspartate aminotransferase, epistaxis, alopecia, increased alanine aminotransferase, and hemorrhage. Clinically significant adverse reactions included peripheral neuropathy, hemorrhage, pneumonitis, severe ocular and cutaneous adverse reactions.[1]

Tisotumab vedotin-tftv is approved by the Food and Drug Administration (FDA) for cervical cancer. The National Comprehensive Cancer Network (NCCN) endorses tisotumab vedotin-tftv for cervical cancer and vaginal cancer.[2,3]

Definitions

- **Antibody-Drug Conjugate (ADC)** - The monoclonal antibody binds to specific proteins or receptors found on certain types of cells, including cancer cells. The linked drug enters these cells and kills them without harming other cells.[4]
- **Food and Drug Administration (FDA)** - The FDA is responsible for protecting the public health by assuring the safety, efficacy, and security of human and veterinary drugs, biological products, medical devices, our nation's food supply, cosmetics, and products that emit radiation.[5]
- **Monomethyl Auristatin E (MMAE)** - A potent microtubule disrupting agent, with potential antineoplastic activity. Upon intravenous administration of anti-c-Met/MMAE ADC MYTX-011, the monoclonal antibody moiety targets and binds to c-Met expressed on tumor cells. Upon binding and proteolytic cleavage, MMAE is released. MMAE binds to tubulin and inhibits its polymerization, and tumor cell apoptosis.[6]
- **National Comprehensive Cancer Network (NCCN)** - An alliance of more than 30 leading cancer centers devoted to patient care, research, and education. The NCCN guidelines are utilized for Radiation Therapy and Medical Oncology standards. NCCN consensus clinical standards are periodically updated and NantHealth, Inc. reviews these and updates its policies within a timely manner.[7]

Policy

Coverage will be considered for FDA approved indications and for NCCN category 1, 2A, or 2B recommendations when the following criteria are met:

Cervical Cancer

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

For **FDA** required criteria coverage:

3. Recurrent or metastatic disease with progression on or after chemotherapy;[1] OR

For **NCCN** required criteria coverage:

4. Second-line or subsequent therapy as a single agent for one of the following:
   a) Locoregional recurrence
   b) Stage IVB or recurrence with distant metastases; OR
5. Second-line or subsequent therapy in combination with pembrolizumab for PD-L1 positive tumors (combined positive score [CPS] ≥ 1) if no prior immuno-oncology therapy received for one of the following:
   a) Locoregional recurrence
   b) Stage IVB or recurrence with distant metastases.[2]

Vaginal Cancer

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

For **NCCN** required criteria coverage:

3. Second-line or subsequent therapy as a single agent for one of the following:
   a) Locoregional recurrence
   b) Stage IVB or recurrent distant metastases.[3]

Authorization Period and Renewal Criteria

1. Initial Authorization Period: 12 months
2. Renewal Criteria: No evidence of disease progression or unacceptable toxicity
3. Renewal Authorization Period: 12 months

Coding (CPT®, ICD-10, and HCPCS)

Procedure codes appearing in medical policy documents are only included as a general reference. This list may not be all-inclusive and is subject to updates. In addition, the codes listed are not a guarantee of payment. CPT codes are available through the AMA.

Code	Description
C52	Malignant neoplasm of vagina

C53.9	Malignant neoplasm of cervix uteri, unspecified
J9273	Injection, tisotumab vedotin-tftv

Revision and Review History

No.	Description	Date
1	Original Effective Date:	10/28/2025
2	Policy Annual Review Dates:	
3	Department Owner:	Medical Affairs
4	NH Advisory Committee Approval Dates:	10/28/2025
5	Revision Changes	

References

[1] Tivdak (Tisotumab Vedotin-tftv) [package insert]. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/761208s007lbl.pdf. Accessed September 24, 2025.

[2] National Comprehensive Cancer Network. NCCN Guidelines: Cervical Cancer. https://www.nccn.org/professionals/physician_gls/pdf/cervical.pdf. Accessed September 24, 2025.

[3] National Comprehensive Cancer Network. NCCN Guidelines: Vaginal Cancer. https://www.nccn.org/professionals/physician_gls/pdf/vaginal.pdf. Accessed September 24, 2025.

[4] Antibody-drug conjugate. National Cancer Institute. https://www.cancer.gov/publications/dictionaries/cancer-terms/def/antibody-drug-conjugate. Accessed September 24, 2025.

[5] U.S. Food & Drug Administration. https://www.fda.gov/about-fda/what-we-do. Accessed September 24, 2025.

[6] Anti-c-Met/MMAE ADC MYTX-011. National Cancer Institute. https://www.cancer.gov/publications/dictionaries/cancer-drug/def/anti-c-met-mmae-adc-mytx-011. Accessed September 24, 2025.

[7] National Comprehensive Cancer Network. https://www.nccn.org/home. Accessed September 24, 2025.