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Tisotumab Vedotin-tftv (Tivdak)

Clinical Policy Bulletins | Medical Clinical Policy Bulletins

Number: 0998

Policy

Note: Requires Precertification:

Precertification of tisotumab vedotin-tftv (Tivdak) is required of all Aetna participating providers and members in applicable plan designs. For precertification of tisotumab vedotin-tftv (Tivdak), call (866) 752-7021 (commercial), (866) 503-0857 (Medicare), or fax (888) 267-3277.

I. **Criteria for Initial Approval**

Cervical Cancer

Aetna considers tisotumab vedotin-tftv (Tivdak) medically necessary for treatment of recurrent or metastatic cervical cancer with disease progression on or after chemotherapy, as a single agent.

Aetna considers all other indications as experimental and investigational.

II. **Continuation of Therapy**

Policy History

Effective: 01/01/2022

Next Review: 09/22/2022

Definitions

Additional Information

Clinical Policy Bulletin Notes

Aetna considers continuation of tisotumab vedotin-tftv (Tivdak) therapy medically necessary for an indication listed in Section I when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

Dosage and Administration

Tisotumab vedotin-tftv (Tivdak) is supplied as 40 mg as a lyophilized cake or powder in a single-dose vial for reconstitution for intravenous infusion only. Do not administer as an intravenous push or bolus. Do not mix with, or administer as an infusion with, other medicinal products.

The recommended dosing for tisotumab vedotin-tftv (Tivdak) is as follows:

Cervical Cancer

- Administer 2 mg/kg (up to a maximum of 200 mg) via intravenous infusion over 30 minutes every 3 weeks until disease progression or unacceptable toxicity.

Source: Seagen, 2021b

Background

U.S. Food and Drug Administration (FDA)-Approved Indications

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

Tisotumab vedotin-tftv is available as Tivdak (Seagen Inc.) and is a tissue factor (TF)-directed antibody drug conjugate (ADC). The antibody consists of a human anti-TF IgGI-kappa antibody conjugated to the microtubule-disrupting agent monomethyl auristatin E (MMAE) via a protease-cleavable vc (valine-citruline). Additionally, this antibody is directed against cell surface TF. TF is the main initiator of the extrinsic

blood coagulation cascade. From a nonclinical data basis, the anticancer activity of tisotumab vedotin-tftv is from the resultant binding of the ADC to TF expressing cancer cells, subsequent internalization of the ADC-TF complex, and release of MMAE via proteolytic cleavage. MMAE disrupts the microtubule organization of actively dividing cells, leading to cell cycle stoppage and apoptotic cell death. Based on in vitro information, tisotumab vedotin-tftv also exerts antibody-dependent cellular phagocytosis and antibody-dependent cellular cytotoxicity.

Per the prescribing information, tisotumab vedotin-tftv (Tivdak) carries the following warnings and precautions:

- Ocular adverse reactions (black box warning): Per clinical trials, ocular adverse reactions were noted in 60% of patients with cervical cancer receiving Tivdak. The most frequent ocular adverse reactions were conjunctival adverse reactions (40%), dry eye (29%), corneal adverse reactions (21%), and blepharitis (8%). Grade 3 ocular adverse reactions were noted in 3.8% of patients, including severe ulcerative keratitis in 3.2% of patients.
- Peripheral neuropathy: Per clinical trials, peripheral neuropathy was noted in 42% of patients with cervical cancer receiving Tivdak. Additionally, 8% of patients experienced Grade 3 peripheral neuropathy.
- Hemorrhage: Per clinical trials, hemorrhage was noted in 62% of patients with cervical cancer receiving Tivdak. The most frequent all grade hemorrhage adverse reactions were epistaxis (44%), hematuria (10%), and vaginal hemorrhage (10%). Grade 3 hemorrhage was noted in 5% of patients.
- Pneumonitis: Severe, life-threatening, or fatal pneumonitis can result in patients receiving antibody drug conjugates containing vedotin including Tivdak. Per clinical trials, 2 patients (1.3%) experienced pneumonitis, including 1 patient resulting in a fatality.
- Embryo-fetal toxicity.

The most common (≥25%) adverse reactions, including laboratory abnormalities, were decreased hemoglobin, fatigue, decreased lymphocytes, nausea, peripheral neuropathy, alopecia, epistaxis, conjunctival adverse reactions, hemorrhage, decreased leukocytes,

increased creatinine, dry eye, increased prothrombin international normalized ratio, prolonged activated partial thromboplastin time, diarrhea, and rash (Seagen, 2021b).

Cervical Cancer

On September 20, 2021, the U.S. Food and Drug Administration (FDA) granted accelerated approval to Tivdak (tisotumab vedotin-tftv) for the treatment of adult patients with recurrent o metastatic cervical cancer with disease progression on or after chemotherapy. The approval under the FDA's Accelerated Approval Program was based on tumor response and durability of the response. The approval was based on supporting data from the InnovaTV 204 study (Seagen, 2021a).

Coleman and colleagues (2021) in the InnovaTV 204 study, an open-label, multicenter, single-arm phase 2 trial, evaluated the efficacy and safety of tisotumab vedotin in 101 patients. The study inclusion consisted of patients aged 18 years or older who had recurrent or metastatic squamous cell, adenocarcinoma, or adenosquamous cervical cancer; disease progression on or after doublet chemotherapy with bevacizumab (if eligible by local standards); who had received two or fewer previous systemic regimens for recurrent or metastatic disease; had measurable disease based on Response Evaluation Criteria in Solid Tumors (RECIST; version 1.1); and had an Eastern Cooperative Oncology Group performance status of 0 or 1. Tisotumab vedotin was administered as 2 mg/kg (up to a maximum of 200 mg) intravenously once every 3 weeks until disease progression or unacceptable toxicity. The primary efficacy outcome measures were confirmed objective response rate (ORR) and duration of response (DOR). The median follow-up at the time of analysis was 10 months. The confirmed ORR was 24% (95% Confidence Interval [CI] 16-33), with 7% complete responses and 17% partial responses. The confirmed median DOR was 8.3 months (95% CI 4.2 - Not Reached [NR]). The most frequently encountered treatment-related adverse events included alopecia (38%), epistaxis (30%), nausea 27 (27%), conjunctivitis (26%), fatigue (26%) and dry eye (23%). Additionally, grade 3 or worse treatment-related adverse events were noted in 28% of patients and included neutropenia (3%), fatigue (2%), ulcerative keratitis (2%), and peripheral neuropathies (2% each with sensory, motor, sensorimotor, and peripheral neuropathy). Serious treatment-related adverse events were

noted in 13% of patients, the most frequent being peripheral sensorimotor neuropathy (2%) and pyrexia (2%). The investigators concluded that tisotumab vedotin demonstrated clinically meaningful and durable antitumor activity with a reasonable and tolerable safety profile in women with previously treated recurrent or metastatic cervical cancer.

CPT Codes / HCPCS Codes / ICD-10 Codes

Information in the [brackets] below has been added for clarification purposes. Codes requiring a 7th character are represented by "+":

Code	Code Description
Other CPT codes related to the CPB:	
96413	Chemotherapy administration, intravenous infusion technique; up to 1 hour, single or initial substance/drug
96415	Chemotherapy administration, intravenous infusion technique; each additional hour (List separately in addition to code for primary procedure)
HCPCS codes covered for indications listed in the CPB:	
Tisotumab vedotin-tftv (Tivdak) – no specific code	
ICD-10 codes covered if selection criteria are met:	
C53.0 - C53.9	Malignant neoplasm of cervix uteri

The above policy is based on the following references:

1. 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.
2. Seagen Inc. Seagen and Genmab announce FDA accelerated approval of Tivdak (tisotumab vedotin-tftv) in previously treated recurrent or metastatic cervical cancer. Press Release. Bothell, WA: Seagen; September 20, 2021a.

3. Seagen Inc. Tivdak (tisotumab vedotin-tftv) for injection, for intravenous use. Prescribing Information. Bothell, WA: Seagen; revised September 2021b.