

Tivdak[®] (tisotumab vedotin-tftv) for Injection 40 mg Appeals Request Guide

Preparing a Prior Authorization Appeal Letter

The following information is presented for informational purposes only and is not intended to provide reimbursement or legal advice. Laws, regulations, and policies concerning reimbursement are complex and are updated frequently. While we have made an effort to be current as of the issue date of this document, the information may not be as current or comprehensive when you view it. Providers are encouraged to contact third-party payers for specific information on their prior authorization policies. For more information, call Seagen Secure at 855-4SECURE (855-473-2873).

If the patient's initial claim or Prior Authorization Request Letter is denied by the patient's health plan, the payer may require a Prior Authorization Appeal Letter. Depending on the plan, there may be varying levels of appeals.

Follow the patient's plan requirements when requesting Tivdak[®] (tisotumab vedotin-tftv) for injection; otherwise, treatment may be delayed.

A **Prior Authorization Appeal Letter** originates from the prescribing healthcare provider (HCP).^{*} It should be submitted with 2 additional items—the patient's medical records and a Letter of Medical Necessity (LMN).

Prior Authorization: Appeal Considerations

- ✓ Include the patient's full name, plan identification number, and date of birth
- ✓ Add the prescribing HCP's National Provider Identifier (NPI) number and specialty
- ✓ Disclose that you are familiar with the plan's policy. Clearly document the basis for the plan's denial within the letter, along with the case identification number from the initial denial letter
- ✓ Provide a copy of the patient's records with the following details:
 - The patient's history, diagnosis and International Classification of Diseases (ICD) code(s), and present-day condition and symptoms
 - Indicate the severity of the patient's condition, if applicable
- ✓ Document prior treatments and the duration of each
 - Describe the rationale for why each treatment was discontinued
- ✓ Provide the clinical rationale for treatment; this information may be found in the Tivdak Prescribing Information and/or clinical peer-reviewed literature
- ✓ Summarize your recommendation at the end of the letter
- ✓ Include an LMN

^{*}For Medicare beneficiaries, specific requirements must be met for the HCP to be considered a legal representative of the patient in an appeal. For additional information, please visit <https://www.cms.gov/Medicare/Appeals-and-Grievances/MedPrescriptDrugApplGriev/downloads/partdmanualchapter18.pdf>.

Please see Indication and Important Safety Information on pages 3 and 4.
Please see full Prescribing Information, including BOXED WARNING for TIVDAK.

Sample Appeal Letter

If the Prior Authorization Request Letter is denied by the patient's health plan, an HCP may elect to submit an Appeal Letter.*

[Date]
[Prior authorization department] Re: [Patient's name]
[Name of health plan] [Plan identification number]
[Mailing address] [Date of birth]

To whom it may concern:

I have reviewed and recognized your guidelines for the responsible management of medications within this class. I am requesting that you reassess your recent denial of Tivdak® (tisotumab vedotin-tftv) for injection prior authorization for [patient name]. I understand that the reason for your denial is [copy reason verbatim from the plan's denial letter]. However, I believe that Tivdak [dose, frequency] is the appropriate treatment for this patient. In support of my recommendation for Tivdak treatment, I have provided an overview of the patient's relevant clinical history below.

Indicate the patient's diagnosis and affirm conditions for use:
Tivdak is indicated for the treatment of adult patients with recurrent or metastatic cervical cancer with disease progression on or after chemotherapy.

[Insert rationale for prescribing Tivdak here, including your professional opinion of the patient's likely prognosis without Tivdak treatment.]

Provide supporting references for your recommendation:
[Provide clinical rationale for treatment; this information may be found in the Tivdak Prescribing Information and/or clinical peer-reviewed literature.]

Please feel free to contact me, [HCP name], at [office phone number] or [patient's name] at [phone number] for any additional information you may require. I look forward to receiving your timely response and approval of this claim.

Sincerely,

[Physician's name and signature]
[Physician's medical specialty]
[Physician's NPI]
[Physician's practice name]
[Phone #]
[Fax #]

Encl: Medical records, supporting documentation, and clinical references, if applicable.

Additional language from the boxes below can be placed after this paragraph to support the following scenarios:

Current User of Tivdak

If this Appeal Letter is for a patient who is currently taking Tivdak, which may be due to a change in payer coverage, sample copy may include the following:

[Describe the diagnosis and symptoms of the disease at the time when the patient was first prescribed Tivdak. In addition, include a summary of the patient's clinical response to Tivdak. It may be necessary to review past medical records to gather this information.]

Previous Therapy Requirement

If this Appeal Letter is intended to appeal a plan's requirement that a patient receive a certain number of lines of therapy, sample copy may include the following:

[Please provide statement(s) indicating why this requirement is inappropriate for this patient. Include documentation of previous courses of therapy and the patient's clinical response or intolerance to those treatments.]

Multiple Levels of Appeal

If this is the second or later appeal, sample copy may include the following:

[This is my (add level of request) prior authorization appeal. A copy of the most recent denial letter is attached for reference. The patient's medical records are also included in response to the denial.]

*Some plans may require an LMN to accompany the Appeal Letter.

**Please see Indication and Important Safety Information on pages 3 and 4.
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Indication

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.

Important Safety Information

BOXED WARNING: OCULAR TOXICITY

TIVDAK caused changes in the corneal epithelium and conjunctiva resulting in changes in vision, including severe vision loss, and corneal ulceration.

Conduct an ophthalmic exam at baseline, prior to each dose, and as clinically indicated. Adhere to premedication and required eye care before, during, and after infusion. Withhold TIVDAK until improvement and resume, reduce the dose, or permanently discontinue, based on severity.

Warnings and Precautions

Ocular adverse reactions occurred in 60% of patients with cervical cancer treated with TIVDAK across clinical trials. The most common were conjunctival adverse reactions (40%), dry eye (29%), corneal adverse reactions (21%), and blepharitis (8%). Grade 3 ocular adverse reactions occurred in 3.8% of patients, including severe ulcerative keratitis in 3.2% of patients. One patient experienced ulcerative keratitis with perforation requiring corneal transplantation. Cases of symblepharon were reported in patients with other tumor types treated with TIVDAK at the recommended dose.

In innovaTV 204, 4% of patients experienced visual acuity changes to 20/50 or worse including 1% of patients who experienced a visual acuity change to 20/200. Of the patients who experienced decreased visual acuity to 20/50 or worse, 75% resolved, including the patient who experienced decreased visual acuity to 20/200.

Refer patients to an eye care provider for an ophthalmic exam, including visual acuity and slit lamp exam, at baseline, prior to each dose, and as clinically indicated. Adhere to premedication and required eye care to reduce the risk of ocular adverse reactions. Promptly refer patients to an eye care provider for any new or worsening ocular signs and symptoms. Withhold dose, reduce the dose, or permanently discontinue TIVDAK based on the severity of the adverse reaction.

Peripheral neuropathy (PN) occurred in 42% of cervical cancer patients treated with TIVDAK across clinical trials; 8% of patients experienced Grade 3 PN. PN adverse reactions included peripheral neuropathy (20%), peripheral sensory neuropathy (11%), peripheral sensorimotor neuropathy (5%), motor neuropathy (3%), muscular weakness (3%), and demyelinating peripheral polyneuropathy (1%). One patient with another tumor type treated with TIVDAK at the recommended dose developed Guillain-Barre syndrome.

Monitor patients for signs and symptoms of neuropathy such as paresthesia, tingling or a burning sensation, neuropathic pain, muscle weakness, or dysesthesia. For new or worsening PN, withhold, then dose reduce, or permanently discontinue TIVDAK based on the severity of PN.

Hemorrhage occurred in 62% of cervical cancer patients treated with TIVDAK across clinical trials. The most common all grade hemorrhage adverse reactions were epistaxis (44%), hematuria (10%), and vaginal hemorrhage (10%). Grade 3 hemorrhage occurred in 5% of patients.

Monitor patients for signs and symptoms of hemorrhage. For patients experiencing pulmonary or central nervous system (CNS) hemorrhage, permanently discontinue TIVDAK. For Grade ≥ 2 hemorrhage in any other location, withhold until bleeding has resolved, blood hemoglobin is stable, there is no bleeding diathesis that could increase the risk of continuing therapy, and there is no anatomical or pathologic condition that can increase the risk of hemorrhage recurrence. After resolution, either resume treatment or permanently discontinue TIVDAK.

Pneumonitis that is severe, life-threatening, or fatal can occur in patients treated with antibody-drug conjugates containing vedotin, including TIVDAK. Among patients with cervical cancer treated with TIVDAK across clinical trials, 2 patients (1.3%) experienced pneumonitis, including 1 patient who had a fatal outcome.

Monitor patients for pulmonary symptoms of pneumonitis. Symptoms may include hypoxia, cough, dyspnea or interstitial infiltrates on radiologic exams. Infectious, neoplastic, and other causes for symptoms should be excluded through appropriate investigations. Withhold TIVDAK for patients who develop persistent or recurrent Grade 2 pneumonitis and consider dose reduction. Permanently discontinue TIVDAK in all patients with Grade 3 or 4 pneumonitis.

Please see additional Important Safety Information on page 4.

Please see full Prescribing Information, including BOXED WARNING for TIVDAK.



Important Safety Information (cont'd)

Severe cutaneous adverse reactions, including events of fatal or life-threatening Stevens-Johnson syndrome (SJS), can occur in patients treated with TIVDAK.

Monitor patients for signs or symptoms of severe cutaneous adverse reactions, which include target lesions, worsening skin reactions, blistering or peeling of the skin, painful sores in mouth, nose, throat, or genital area, fever or flu-like symptoms, and swollen lymph nodes. If signs or symptoms of severe cutaneous adverse reactions occur, withhold TIVDAK until the etiology of the reaction has been determined. Early consultation with a specialist is recommended to ensure greater diagnostic accuracy and appropriate management. Permanently discontinue TIVDAK for confirmed Grade 3 or 4 severe cutaneous adverse reactions, including SJS.

Embryo-fetal toxicity: TIVDAK can cause fetal harm when administered to a pregnant woman. Advise patients of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with TIVDAK and for 2 months after the last dose. Advise male patients with female partners of reproductive potential to use effective contraception during treatment with TIVDAK and for 4 months after the last dose.

Adverse Reactions

Serious adverse reactions occurred in 43% of patients; the most common ($\geq 3\%$) were ileus (6%), hemorrhage (5%), pneumonia (4%), PN, sepsis, constipation, and pyrexia (each 3%). Fatal adverse reactions occurred in 4% of patients who received TIVDAK, including septic shock, pneumonitis, sudden death, and multisystem organ failure (each 1%).

Adverse reactions leading to permanent discontinuation occurred in 13% of patients receiving TIVDAK; the

most common ($\geq 3\%$) were PN (5%) and corneal adverse reactions (4%). Adverse reactions leading to dose interruption occurred in 47% of patients; the most common ($\geq 3\%$) were PN (8%), conjunctival adverse reactions (4%), and hemorrhage (4%). Adverse reactions leading to dose reduction occurred in 23% of patients; the most common ($\geq 3\%$) were conjunctival adverse reactions (9%) and corneal adverse reactions (8%).

The most common ($\geq 25\%$) adverse reactions, including laboratory abnormalities, were hemoglobin decreased (52%), fatigue (50%), lymphocytes decreased (42%), nausea (41%), PN (39%), alopecia (39%), epistaxis (39%), conjunctival adverse reactions (37%), hemorrhage (32%), leukocytes decreased (30%), creatinine increased (29%), dry eye (29%), prothrombin international normalized ratio increased (26%), activated partial thromboplastin time prolonged (26%), diarrhea (25%), and rash (25%).

Drug Interactions

Strong CYP3A4 inhibitors: Concomitant use with strong CYP3A4 inhibitors may increase unconjugated monomethyl auristatin E (MMAE) exposure, which may increase the risk of TIVDAK adverse reactions. Closely monitor patients for TIVDAK adverse reactions.

Use in Specific Populations

Moderate or severe hepatic impairment: MMAE exposure and adverse reactions are increased. Avoid use.

Lactation: Advise lactating women not to breastfeed during TIVDAK treatment and for at least 3 weeks after the last dose.

Please see full Prescribing Information, including BOXED WARNING for TIVDAK.

Reference: TIVDAK (tisotumab-vedotin-tftv) [Prescribing Information]. Bothell, WA: Seagen Inc. July 2023.



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