tivdak®
tisotumab vedotin-tftv
for injection 40 mg

Tivdak Premedication
and Required Eye Care

EYE CARE PROVIDER GUIDE

INDICATION

TIVDAK is indicated for the treatment of adult patients with recurrent or metastatic cervical cancer (r/mCC) with disease progression on or after chemotherapy.

IMPORTANT SAFETY INFORMATION

BOXED WARNING: OCULAR TOXICITY

TIVDAK can cause severe ocular toxicities resulting in changes in vision, including severe vision loss, and corneal ulceration. Conduct an ophthalmic exam, including an assessment of ocular symptoms, visual acuity, and slit lamp exam of the anterior segment of the eye prior to initiation of TIVDAK, prior to every cycle for the first nine cycles, and as clinically indicated. Adhere to the required premedication and eye care before, during, and after infusion. Withhold TIVDAK until improvement and resume, reduce the dose, or permanently discontinue, based on severity.

Please see additional Important Safety Information on pages 2-5 and full prescribing information, including BOXED WARNING for TIVDAK.

IMPORTANT SAFETY INFORMATION (continued)

Warnings and Precautions

Ocular adverse reactions: TIVDAK can cause severe ocular adverse reactions, including conjunctivitis, keratopathy (keratitis, punctate keratitis, and ulcerative keratitis), and dry eye (increased lacrimation, eye pain, eye discharge, pruritus, irritation, and foreign body sensation), that may lead to changes in vision and/or corneal ulceration.

Ocular adverse reactions occurred in 55% of patients with cervical cancer treated with TIVDAK across clinical trials. The most common were conjunctivitis (32%), dry eye (24%), keratopathy (17%), and blepharitis (5%). Grade 3 ocular adverse reactions occurred in 3.3% of patients, including severe ulcerative keratitis in 1.2% of patients. Nine patients (2.1%) experienced ulcerative keratitis (including one with perforation requiring corneal transplantation), six (1.4%) conjunctival ulcer, four (0.9%) corneal erosion, two (0.5%) conjunctival erosion, and two (0.5%) symblepharon.

In innovaTV 301, 8 patients (3.2%) experienced delayed ocular adverse reactions occurring more than 30 days after discontinuation of TIVDAK. These adverse reactions included 3 patients with ulcerative keratitis, and one patient (each) with keratitis, punctate keratitis and corneal erosion, blepharitis and conjunctival hyperemia, conjunctival scar, and conjunctivitis and xerophthalmia.

Refer patients to an eye care provider to conduct an ophthalmic exam prior to initiation of TIVDAK, prior to every cycle for the first nine cycles, and as clinically indicated. The exam should include visual acuity, slit lamp exam of the anterior segment of the eye, and an assessment of normal eye movement and ocular signs or symptoms which include dry or irritated eyes, eye secretions, or blurry vision.

Adhere to the required premedication and eye care before, during, and after infusion to reduce the risk of ocular adverse reactions. Monitor for ocular toxicity and promptly refer patients to an eye care provider for any new or worsening ocular signs and symptoms. Withhold, reduce, or permanently discontinue TIVDAK based on the severity or persistence of the ocular adverse reaction.

Peripheral neuropathy (PN) occurred in 39% of cervical cancer patients treated with TIVDAK across clinical trials; 6% of patients experienced Grade 3 PN. PN adverse reactions included peripheral sensory neuropathy (23%), PN (5%), paresthesia (3.8%), peripheral sensorimotor neuropathy (3.3%), muscular weakness (2.8%), and peripheral motor neuropathy (2.4%). 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.

IMPORTANT SAFETY INFORMATION (continued)

Hemorrhage occurred in 51% of cervical cancer patients treated with TIVDAK across clinical trials. The most common all grade hemorrhage adverse reaction was epistaxis (33%). Grade 3 hemorrhage occurred in 4% of patients.

Monitor patients for signs and symptoms of hemorrhage. For patients experiencing pulmonary or central nervous system 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 cervical cancer patients treated with TIVDAK across clinical trials, 4 patients (0.9%) 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 such 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.

Severe cutaneous adverse reactions (SCAR), including events of fatal or life-threatening Stevens-Johnson syndrome (SJS), can occur in patients treated with TIVDAK. SCAR occurred in 1.6% of cervical cancer patients treated with TIVDAK across clinical trials. Grade ≥3 SCAR occurred in 0.5% of patients, including 1 patient who had a fatal outcome.

Monitor patients for signs or symptoms of SCAR, 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 SCAR 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 SCAR, 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.

IMPORTANT SAFETY INFORMATION (continued)

Adverse Reactions

Across clinical trials of TIVDAK in 425 patients with r/mCC, the most common (≥25%) adverse reactions, including laboratory abnormalities, were hemoglobin decreased (45%), PN (39%), conjunctival adverse reactions (38%), nausea (37%), fatigue (36%), aspartate aminotransferase increased (33%), epistaxis (33%), alopecia (31%), alanine aminotransferase increased (30%), and hemorrhage (28%).

innovaTV 301 Study: 250 patients with r/mCC with disease progression on or after systemic therapy

Serious adverse reactions occurred in 33% of patients receiving TIVDAK; the most common (≥2%) were urinary tract infection (4.8%), small intestinal obstruction (2.4%), sepsis, abdominal pain, and hemorrhage (each 2%). **Fatal adverse reactions** occurred in 1.6% of patients who received TIVDAK, including acute kidney injury, pneumonia, sepsis, and SJS (each 0.4%).

Adverse reactions leading to permanent discontinuation occurred in 15% of patients receiving TIVDAK; the most common (≥3%) were PN and ocular adverse reactions (each 6%). **Adverse reactions leading to dose interruption** occurred in 39% of patients receiving TIVDAK; the most common (≥3%) were ocular adverse reactions (16%) and PN (6%). **Adverse reactions leading to dose reduction** occurred in 30% of patients receiving TIVDAK; the most common (≥3%) were PN and ocular adverse reactions (each 10%). The ocular adverse reactions included conjunctival disorders (4.8%), keratopathy (4%), and dry eye (0.8%).

innovaTV 204 Study: 101 patients with r/mCC with disease progression on or after chemotherapy

Serious adverse reactions occurred in 43% of patients; the most common (≥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 (≥3%) were PN (5%) and corneal adverse reactions (4%). **Adverse reactions leading to dose interruption** occurred in 47% of patients; the most common (≥3%) were PN (8%), conjunctival adverse reactions, and hemorrhage (each 4%). **Adverse reactions leading to dose reduction** occurred in 23% of patients; the most common (≥3%) were conjunctival adverse reactions (9%) and corneal adverse reactions (8%).

IMPORTANT SAFETY INFORMATION (continued)

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.

Overview[1]

Tivdak has a BOXED WARNING and can cause severe ocular toxicities resulting in changes in vision, including severe vision loss, and corneal ulceration.

Tivdak Premedication and Required Eye Care may help reduce the risk of ocular adverse reactions.

As an eye care provider, **you will play a pivotal role** in the ocular care of recurrent or metastatic cervical cancer patients being considered for or treated with Tivdak. It is important to partner closely with your patient's oncologist.

In order to **monitor eye health** and reduce the risk of ocular adverse reactions, you, the patient, and the oncologist will adhere to **Tivdak Premedication and Required Eye Care**, details of which are described in this brochure.

In the event of an ocular adverse reaction, your patient may need to **visit you for diagnosis of the condition, assessment, and treatment of symptoms.**

This guide is designed to assist you and your staff.

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Prevalence of ocular adverse reactions[1]

Tivdak can cause severe ocular adverse reactions, including conjunctivitis, keratopathy (keratitis, punctate keratitis, and ulcerative keratitis), and dry eye (increased lacrimation, eye pain, eye discharge, pruritus, irritation, and foreign body sensation), that may lead to changes in vision and/or corneal ulceration.

- Ocular adverse reactions occurred in 55% of patients with cervical cancer treated with Tivdak across clinical trials*
- The most common ocular adverse reactions were conjunctivitis (32%), dry eye (24%), keratopathy (17%), and blepharitis (5%)*
- Grade 3 ocular adverse reactions occurred in 3.3% of patients, including severe ulcerative keratitis in 1.2% of patients*
- Nine patients (2.1%) experienced ulcerative keratitis (including 1 with perforation requiring corneal transplantation), 6 (1.4%) conjunctival ulcer, 4 (0.9%) corneal erosion, 2 (0.5%) conjunctival erosion, and 2 (0.5%) symblepharon*
- The median time to onset of the first ocular adverse reaction was 1.2 months (range: 0-17.1). Ocular adverse reactions led to discontinuation of Tivdak in 6% of patients with cervical cancer*
- In innovaTV 301, the most common ocular adverse reactions leading to dose reduction were conjunctival disorders (4.8%), keratopathy (4%), and dry eye (0.8%)†
- In innovaTV 301, 8 (3.2%) patients experienced delayed ocular adverse reactions occurring more than 30 days after discontinuation of Tivdak†

There are no contraindications for Tivdak. Patients were excluded from the innovaTV 301 trial if they had active ocular surface disease, any prior episode of cicatricial conjunctivitis or ocular Stevens-Johnson syndrome (SJS), Grade ≥2 peripheral neuropathy, or clinically significant bleeding issues or risks.

*These data reflect exposure to Tivdak in 425 patients with recurrent or metastatic cervical cancer who received at least 1 dose of Tivdak at 2 mg/kg intravenously every 3 weeks in 6 clinical trials.
†These data reflect exposure to Tivdak in 250 patients with recurrent or metastatic cervical cancer who received at least 1 dose of Tivdak at 2 mg/kg intravenously every 3 weeks in the innovaTV 301 clinical trial.

Please see Important Safety Information on pages 1-5 and full prescribing information, including BOXED WARNING for TIVDAK.

Resolution of ocular adverse reactions[1]*

At last follow-up, patients who experienced ocular adverse reactions had either

COMPLETE RESOLUTION	OR	PARTIAL IMPROVEMENT
59%		**31%**

Partial improvement was defined as a decrease in severity by 1 or more grades from the worst grade.

Additional data: time to resolution of ocular adverse reactions[2†]

Time to resolution of ocular adverse reactions was exploratory. Data are provided as supportive clinical information.

- The median time to resolution of ocular adverse reactions was 0.59 months (range: 0.1-12.6) for Tivdak vs 0.26 months (range: 0.2-3.7) for IC chemotherapy

IC=investigator's choice.
*These data reflect exposure to Tivdak in 425 patients with recurrent or metastatic cervical cancer who received at least 1 dose of Tivdak at 2 mg/kg intravenously every 3 weeks in 6 clinical trials.
†These data reflect exposure to Tivdak in 250 patients with recurrent or metastatic cervical cancer who received at least 1 dose of Tivdak at 2 mg/kg intravenously every 3 weeks in the innovaTV 301 clinical trial.

Required exams and reminders[1]

CONDUCT AN OPHTHALMIC EXAM

- An oncologist will refer their Tivdak patient to you for an ophthalmic exam prior to initiation of Tivdak, the first 9 infusion cycles of Tivdak, and as clinically indicated
- This exam should include visual acuity, slit lamp exam of the anterior segment of the eye, and an assessment of normal eye movement

AVOID CONTACT LENSES AND IRRITANTS

- Advise patients to avoid wearing contact lenses throughout treatment unless otherwise specified
- Advise patients to avoid putting any irritants near their eyes throughout treatment

Topical eye drops[1,3]

Three different topical eye drops will need to be prescribed to the patient prior to starting Tivdak treatment. Coordinate with the patient's oncologist to manage the eye drop prescriptions.

CORTICOSTEROID EYE DROPS*

May address possible conjunctival inflammation. Patients will be referred to you for a slit lamp exam before the initial prescription and all renewals of any corticosteroid medication.

VASOCONSTRICTOR EYE DROPS

May reduce blood flow to the eye area, thereby potentially decreasing local ocular delivery of Tivdak.

LUBRICATING EYE DROPS (over the counter)

May add moisture to the eye, relieve dry eye discomfort, and reduce overall irritation.

See the full eye drop schedule on pages 11-12.

*The initial prescription and all renewals of any corticosteroid medication should be made only after examination with a slit lamp.

Monitoring and assessing[1,3]

- Monitor patients for new or worsening ocular signs and symptoms
- In the event of an ocular adverse reaction, the oncologist may refer the patient to you for diagnosis of the condition, assessment, and treatment of symptoms
- Depending on your assessment, the oncologist may maintain, withhold, reduce, or permanently discontinue Tivdak, based on recommended dose modification guidelines found in the Tivdak USPI

In the event of an ocular adverse reaction

EYE CARE PROVIDER		ONCOLOGIST
1 **Eye exam**	2 **Ocular adverse reaction assessment**	3 **Dose modification (if needed)**

EYE SELF-CHECK

- Encourage patients to monitor their eyes daily for any signs or symptoms of new or worsening ocular adverse reactions, including, but not limited to:
  - Dry eyes
  - Eye redness
  - Eye irritation
  - Light sensitivity
  - Blurred vision
  - Vision loss or impairment

Advise patients to call your office and their oncologist's office if they experience new or worsening ocular signs and symptoms.

Communicate with your patient's oncologist.
The Tisotumab vedotin-tftv Eye Care Consult Form may help you relay any updates or concerns you have.

The eye drop schedule[1,3]

With the help of a nurse, the patient will apply some of the eye drops at the infusion appointment. Between infusions, the patient will self-administer certain eye drops.

1 AT THE INFUSION APPOINTMENT

Timeline	Drops	Description
Prior to infusion	S	**CORTICOSTEROID EYE DROPS** **1 drop per eye** The care team should instruct the patient to apply corticosteroid drops (1 drop per eye, or as prescribed)
	V	**VASOCONSTRICTOR EYE DROPS** **3 drops per eye** The care team should instruct the patient to apply vasoconstrictor drops immediately prior to the infusion (3 drops per eye, or as prescribed)

The eye drop schedule (continued)[1,3]

2 AFTER THE INFUSION APPOINTMENT

Timeline	Drops	Description
For the remainder of infusion day	S	**CORTICOSTEROID EYE DROPS** **1 drop per eye, 2 more times** Patient will continue applying corticosteroid drops (1 drop per eye) two more times throughout the day, or as prescribed
Days 2-3 (72 hours post infusion)	S	**CORTICOSTEROID EYE DROPS** **1 drop per eye, 3x/day** Patient will apply corticosteroid drops (1 drop per eye) three times per day, or as prescribed

THROUGHOUT TREATMENT

Timeline	Drops	Description
Throughout treatment	L	**LUBRICATING EYE DROPS** **as needed** Patient should apply lubricating drops as needed for the duration of therapy and for 30 days after the last dose of Tivdak

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Want to know more about Tivdak?

Find more helpful resources for your practice and your patients at **tivdakHCP.com/support-and-resources**

EYE CARE CONSULT FORM
A form to streamline communication between the eye care provider and the oncologist

DOSING, ADMINISTRATION, AND EYE CARE GUIDE
A helpful guide to understanding and administering Tivdak

TIVDAKTEXTS BROCHURE
A guide to a text message support program designed to assist your patients throughout treatment

Please see Important Safety Information on pages 1-5 and full prescribing information, including BOXED WARNING for TIVDAK.

References: 1. TIVDAK [Prescribing Information]. Bothell, WA: Seagen Inc. April 2024. **2.** Data on file. Pfizer Inc., New York, NY. **3.** Kim SK, Ursell P, Coleman RL, Monk BJ, Vergote I. Mitigation and management strategies for ocular events associated with tisotumab vedotin. *Gynecol Oncol*. 2022;165(2):385-392.

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