tivdak®
tisotumab vedotin-tftv
for injection 40 mg

Dosing, Administration, and Eye Care Guide

FOR YOUR PRACTICE

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.

Select 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.

Please see additional Important Safety Information and full prescribing information, including BOXED WARNING for TIVDAK.

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 pages 1 and 3 and full prescribing information, including BOXED WARNING for TIVDAK.

Important Safety Information (continued)

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 (≥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 (4%), and hemorrhage (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%).

The most common (≥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.

The Tivdak® infusion

Recommended dosage[1,a]

Patient weight (kg) x 2.0 mg/kg = Tivdak dose (mg)

The recommended dosage guidelines are appropriate for patients up to a maximum of 200 mg for patients ≥100 kg.

[a]For patients who weigh >100 kg, the calculation of the dosage should be normalized to 100 kg (ie, 2.0 mg/kg x 100 kg = 200 mg). The equation above is based off of the recommended dose and does not include dose modifications. This calculation should not replace professional judgment or clinical experience.

Please see information about dose modifications for Tivdak on pages 16-19.

Tivdak is administered as an **intravenous infusion**
over 30 minutes
every 3 weeks
until disease progression or unacceptable toxicity[1]

The Tivdak infusion appointment takes approximately **60 minutes**
including administration of eye drops, application of cold packs, and a 30-minute infusion[1,2]

Dosage forms & storage[1]

Tivdak 40 mg for injection is supplied as a white to off-white lyophilized cake or powder in a single-dose vial for reconstitution. Tivdak vials are available in the following packages:

- Carton of one 40 mg single-dose vial [NDC 51144-003-01]

Store Tivdak vials refrigerated at 2 °C to 8 °C (36 °F to 46 °F) in the original carton to protect from light.

- Do not freeze
- Do not shake

Reconstitution in single-dose vial[1]

PREPARATION AND ADMINISTRATION

- **Administer Tivdak as an intravenous infusion only**
- Tivdak is a hazardous drug. Follow applicable special handling and disposal procedures[a]
- DO NOT mix Tivdak as an intravenous push or bolus
- DO NOT mix with, or administer as an infusion with, other medicinal products

Use appropriate aseptic technique for reconstitution and preparation of dosing solutions. Prior to administration, the Tivdak vial is reconstituted with Sterile Water for Injection, USP. The reconstituted solution is subsequently diluted in an intravenous infusion bag containing one of the following: 5% Dextrose Injection, USP, 0.9% Sodium Chloride Injection, USP, or Lactated Ringer's Injection, USP.

CALCULATE

- Calculate the recommended dose based on the patient's weight to determine the number of vials needed

RECONSTITUTE

- Reconstitute each 40 mg vial with 4.0 mL of Sterile Water for Injection, USP, resulting in 10 mg/mL Tivdak
- Slowly swirl each vial until the contents are completely dissolved. Allow the reconstituted vial(s) to settle

DO NOT SHAKE THE VIAL. Do not expose to direct sunlight

[a]Refer to OSHA website for more information: http://www.osha.gov/SLTC/hazardousdrugs/index.html

Please see additional information about reconstitution on the following page.

Please see Important Safety Information on pages 1-3 and full prescribing information, including BOXED WARNING for TIVDAK.

Reconstitution in single-dose vial (continued)[1]

INSPECT

- Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. The reconstituted solution should be clear to slightly opalescent, colorless to brownish-yellow and free of visible particles. Discard any vial with visible particles or discoloration

USE OR STORE

- Based upon the calculated dose amount, the reconstituted solution from the vial(s) should be added to the infusion bag immediately. This product does not contain a preservative. If not used immediately, reconstituted vials may be stored for up to 24 hours in refrigeration at 2 °C to 8 °C (36 °F to 46 °F) or at room temperature up to 25 °C (77 °F) for up to a maximum of 8 hours prior to dilution

DO NOT FREEZE. Do not expose to direct sunlight. Discard unused vials with reconstituted solution beyond the recommended storage time

Dilution in infusion bag[1]

TRANSFER

- Withdraw the calculated dose amount of reconstituted solution from the vial(s) and transfer into an infusion bag

DILUTE

- Dilute Tivdak with one of the following: 5% Dextrose Injection, USP, 0.9% Sodium Chloride Injection, USP, or Lactated Ringer's Injection, USP. The infusion bag size should allow enough diluent to achieve a final concentration of 0.7 mg/mL to 2.4 mg/mL Tivdak
- Mix diluted solution by gentle inversion

DO NOT SHAKE THE BAG. Do not expose to direct sunlight

INSPECT

- Visually inspect the infusion bag for any particulate matter or discoloration prior to use. The reconstituted solution should be clear to slightly opalescent, colorless to brownish-yellow and free of visible particles

Discard the infusion bag if particulate matter or discoloration is observed

DISCARD

- Discard any unused portion left in the single-dose vials

Administration[1]

EYE DROPS
- Confirm administration of corticosteroid and vasoconstrictor eye drops

COLD PACKS
- Apply cold packs fully over the eye area following administration of the vasoconstrictor eye drops and leave on during the infusion. Change cold packs as needed throughout infusion to ensure eye area remains cold

Additional information on Tivdak® Required Eye Care, including eye drop and cold pack administration, can be found on pages 20-22

INFUSION
- Immediately administer the infusion over 30 minutes through an intravenous line containing a 0.2 µm in-line filter

DELAYED INFUSION HANDLING
- If the infusion is not administered immediately, store the diluted Tivdak solution in refrigeration as specified in the table on page 9. Discard if storage time exceeds these limits

DO NOT FREEZE. Once removed from refrigeration, complete administration of the diluted infusion solution of Tivdak within 4 hours (including infusion time)

Please see additional information about administration on the following page.

Please see Important Safety Information on pages 1-3 and full prescribing information, including BOXED WARNING for TIVDAK.

Administration (continued)[1]

Diluted Tivdak Solution Refrigeration Storage Conditions

Diluent Used to Prepare Solution for Infusion	Diluted Tivdak Solution Storage Conditions (Including Infusion Time)
0.9% Sodium Chloride Injection, USP	Up to 18 hours at 2 °C to 8 °C (36 °F to 46 °F)
5% Dextrose Injection, USP	Up to 24 hours at 2 °C to 8 °C (36 °F to 46 °F)
Lactated Ringer's Injection, USP	Up to 12 hours at 2 °C to 8 °C (36 °F to 46 °F)

Adverse reactions reported in innovaTV 204[1,a]

Adverse Reactions Reported in ≥10% of Patients Treated With Tivdak® in innovaTV 204

Adverse Reaction	Tivdak (2.0 mg/kg) N=101	
	All Grades %	Grade 3-4 %
General		
Fatigue[b]	50	7
Pyrexia	16	1
Pruritus	13	1
Gastrointestinal disorders		
Nausea[c]	41	0
Diarrhea[d]	25	2
Constipation	23	2
Abdominal pain[e]	23	1
Vomiting	17	2
Nervous system disorders		
Peripheral neuropathy[f]	39	7
Skin and subcutaneous tissue disorders		
Alopecia	39	0
Rash[g]	25	0
Vascular disorders		
Epistaxis	39	0
Hemorrhage[h]	32	6

[a]These data reflect exposure to Tivdak in 101 patients with recurrent or metastatic cervical cancer who received at least one dose of Tivdak at 2 mg/kg intravenously every 3 weeks in the innovaTV 204 clinical trial.

[b]Fatigue includes fatigue and asthenia.

[c]Nausea includes nausea and retching.

[d]Diarrhea includes diarrhea, gastroenteritis, and colitis.

[e]Abdominal pain includes abdominal pain, abdominal pain upper, abdominal pain lower, abdominal distention, and abdominal discomfort.

[f]Peripheral neuropathy includes neuropathy peripheral, peripheral sensorimotor neuropathy, polyneuropathy, peripheral sensory neuropathy, paresthesia, hypoesthesia, burning sensation, neuralgia, sensory loss, peripheral motor neuropathy, muscular weakness, gait disturbance, and hyperesthesia.

[g]Rash includes rash, rash maculo-papular, rash macular, dermatitis acneiform, dermatitis allergic, and erythema.

[h]Hemorrhage includes vaginal hemorrhage, hematuria, rectal hemorrhage, cystitis hemorrhagic, lower gastrointestinal hemorrhage, urinary bladder hemorrhage, hematochezia, anal hemorrhage, gingival bleeding, post procedural hemorrhage, radiation associated with hemorrhage, metrorrhagia, large intestinal hemorrhage, paranasal sinus hemorrhage, and hemoptysis.

Please see additional information about adverse reactions on the following page.

Please see Important Safety Information on pages 1-3 and full prescribing information, including BOXED WARNING for TIVDAK.

Adverse reactions reported in innovaTV 204 (continued)[1,a]

Adverse Reactions Reported in ≥10% of Patients Treated With Tivdak in innovaTV 204 (continued)

Adverse Reaction	Tivdak (2.0 mg/kg) N=101	
	All Grades %	Grade 3-4 %
Eye disorders		
Conjunctival adverse reactions[b]	37	0
Dry eye[c]	29	0
Corneal adverse reactions[d]	21	3
Periorbital adverse reactions[e]	16	0
Musculoskeletal and connective tissue disorders		
Myalgia[f]	21	0
Arthralgia	16	0
Pain in extremity[g]	13	1
Metabolism and nutrition disorders		
Decreased appetite	16	1
Infections		
Urinary tract infection[h]	14	2
Investigations		
Weight decreased	12	0

[a]These data reflect exposure to Tivdak in 101 patients with recurrent or metastatic cervical cancer who received at least one dose of Tivdak at 2 mg/kg intravenously every 3 weeks in the innovaTV 204 clinical trial.

[b]Conjunctival adverse reactions includes conjunctivitis, conjunctival abrasion, conjunctival erosion, conjunctival hyperemia, conjunctival scar, noninfective conjunctivitis, ocular hyperemia, and conjunctival hemorrhage.

[c]Dry eye includes dry eye and lacrimation increased.

[d]Corneal adverse reactions includes keratitis, punctate keratitis, ulcerative keratitis, corneal erosion, corneal scar, keratopathy, and corneal bleeding.

[e]Periorbital adverse reactions includes blepharitis, meibomianitis, eye pruritus, entropion, trichiasis, chalazion, and meibomian gland dysfunction.

[f]Myalgia includes myalgia, musculoskeletal discomfort, and musculoskeletal pain.

[g]Pain in extremity includes pain in extremity and limb discomfort.

[h]Urinary tract infection includes urinary tract infection, urinary tract infection bacterial, and cystitis.

Ocular adverse reactions[1]

ACROSS CLINICAL TRIALS

PREVALENCE

- Ocular adverse reactions occurred in 60% of patients with cervical cancer treated with Tivdak® across clinical trials[a]
- The most common ocular adverse reactions were conjunctival adverse reactions (40%), dry eye (29%), corneal adverse reactions (21%), and blepharitis (8%)[a]
- Grade 3 ocular adverse reactions occurred in 3.8% of patients, including severe ulcerative keratitis in 3.2% of patients[a]
- 1 patient experienced ulcerative keratitis with perforation requiring corneal transplantation[a]
- Cases of symblepharon were reported in patients with other tumor types treated with Tivdak at the recommended dose[a]
- 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[b]
- Ocular adverse reactions led to discontinuation of Tivdak in 6% of patients with cervical cancer[a]
- The most common (≥3%) adverse reactions leading to dose reduction were conjunctival adverse reactions (9%) and corneal adverse reactions (8%)[b]

ONSET[a]

- The median time to onset of the first ocular adverse reaction was 1.2 months (range: 0-6.5)

MONITOR[a]

- Monitor and promptly refer patients to an eye care provider for new or worsening ocular signs and symptoms

[a]These data reflect exposure to Tivdak in 158 patients with recurrent or metastatic cervical cancer who received at least one dose of Tivdak at 2 mg/kg intravenously every 3 weeks in 4 clinical trials.

[b]These data reflect exposure to Tivdak in 101 patients with recurrent or metastatic cervical cancer who received Tivdak 2 mg/kg intravenously every 3 weeks in the innovaTV 204 clinical trial.

Please see additional information about ocular adverse reactions on the following page.

Please see information about dose modifications for Tivdak on pages 18-21.

Please see Important Safety Information on pages 1-3 and full prescribing information, including BOXED WARNING for TIVDAK.

Ocular adverse reactions (continued)

ACROSS CLINICAL TRIALS

RESOLUTION ACROSS CLINICAL TRIALS[1,a]

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

COMPLETE RESOLUTION		PARTIAL IMPROVEMENT
55%	OR	**30%**

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

Time to resolution in the innovaTV 204 trial (N=101)[2,3,b]

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

The **median time to resolution** of each ocular adverse reaction was **0.7 months** (IQR: 0.3-1.6)[c]

At the 30-day follow-up after the last dose of Tivdak, 118 out of 138 ocular adverse reactions were resolved (86%)

Adhere to premedication and required eye care to reduce the risk of ocular adverse reactions (see pages 20-22)[1,2]

[a]These data reflect exposure to Tivdak in 158 patients with recurrent or metastatic cervical cancer who received at least one dose of Tivdak at 2 mg/kg intravenously every 3 weeks in 4 clinical trials.

[b]These data reflect exposure to Tivdak in 101 patients with recurrent or metastatic cervical cancer who received Tivdak 2 mg/kg intravenously every 3 weeks in the innovaTV 204 clinical trial.

[c]IQR=interquartile range.

Please see information about dose modifications for Tivdak on pages 18-21.

Please see Important Safety Information on pages 1-3 and full prescribing information, including BOXED WARNING for TIVDAK.

Peripheral neuropathy

ACROSS CLINICAL TRIALS

PREVALENCE[1,a]

- Peripheral neuropathy occurred in 42% of patients with cervical cancer treated with Tivdak® across clinical trials; 8% of patients experienced Grade 3 peripheral neuropathy
- Peripheral neuropathy 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%)
- 1 patient with another tumor type treated with Tivdak at the recommended dose developed Guillain-Barre syndrome
- Peripheral neuropathy led to discontinuation of Tivdak in 8% of patients with cervical cancer

ONSET[1,a]

- The median time to onset of peripheral neuropathy was 2.4 months (range: 0-11.3)

MONITOR[1,a]

- Monitor patients for general signs and symptoms of neuropathy, such as paresthesia, tingling or a burning sensation, neuropathic pain, muscle weakness, or dysesthesia

RESOLUTION[1,3]

At last follow-up, patients who experienced peripheral neuropathy had[a]

COMPLETE RESOLUTION		PARTIAL IMPROVEMENT
17%	OR	**17%**

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

In the innovaTV 204 trial, the **median time to resolution** of each peripheral neuropathy event was **0.6 months** (IQR: 0.5-1.2)[b]

[a]These data reflect exposure to Tivdak in 158 patients with recurrent or metastatic cervical cancer who received at least one dose of Tivdak at 2 mg/kg intravenously every 3 weeks in 4 clinical trials.

[b]These data reflect exposure to Tivdak in 101 patients with recurrent or metastatic cervical cancer who received Tivdak at 2 mg/kg intravenously every 3 weeks in the innovaTV 204 clinical trial.

Please see information about dose modifications for Tivdak on pages 18-21.

Please see Important Safety Information on pages 1-3 and full prescribing information, including BOXED WARNING for TIVDAK.

Hemorrhage

ACROSS CLINICAL TRIALS

PREVALENCE[1,a]

- Hemorrhage occurred in 62% of patients with cervical cancer treated with Tivdak across clinical trials
- The most common all grade hemorrhage adverse reactions were epistaxis (44%), hematuria (10%), and vaginal hemorrhage (10%)
- Most hemorrhage adverse reactions were Grade 1-2, with 5% Grade 3

ONSET[1,a]

- The median time to onset of hemorrhage was 0.3 months (range: 0-6.5)

MONITOR[1,a]

- Monitor patients for signs and symptoms of hemorrhage

RESOLUTION[1,3]

At last follow-up, patients who experienced a hemorrhage adverse reaction had[a]

COMPLETE RESOLUTION		PARTIAL RESOLUTION
71%	OR	**11%**

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

In the innovaTV 204 trial, the **median time to resolution** of each hemorrhage adverse reaction was **0.5 months** (IQR: 0.1-1.4)[b]

[a]These data reflect exposure to Tivdak in 158 patients with recurrent or metastatic cervical cancer who received at least one dose of Tivdak at 2 mg/kg intravenously every 3 weeks in 4 clinical trials.

[b]These data reflect exposure to Tivdak in 101 patients with recurrent or metastatic cervical cancer who received Tivdak at 2 mg/kg intravenously every 3 weeks in the innovaTV 204 clinical trial.

Please see information about dose modifications for Tivdak on pages 18-21.

Please see Important Safety Information on pages 1-3 and full prescribing information, including BOXED WARNING for TIVDAK.

Pneumonitis[1,a]

ACROSS CLINICAL TRIALS

PREVALENCE

- Pneumonitis occurred in 2 patients (1.3%) with cervical cancer treated with Tivdak across clinical trials, including 1 patient who had a fatal outcome

MONITOR

- Monitor patients for pulmonary symptoms indicative 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

[a]These data reflect exposure to Tivdak in 158 patients with recurrent or metastatic cervical cancer who received at least one dose of Tivdak at 2 mg/kg intravenously every 3 weeks in 4 clinical trials.

Please see information about dose modifications for Tivdak on pages 18-21.

Please see Important Safety Information on pages 1-3 and full prescribing information, including BOXED WARNING for TIVDAK.

Severe cutaneous adverse reactions[1]

PREVALENCE

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

MONITOR

- 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

Please see information about dose modifications for Tivdak on pages 18-21.

Please see Important Safety Information on pages 1-3 and full prescribing information, including BOXED WARNING for TIVDAK.

Dosage modifications for adverse reactions[1,a]

Some patients may require dosage modifications or discontinuation of Tivdak® to manage adverse reactions. The recommended dose modifications for adverse reactions are provided below. Refer patients to an eye care provider promptly for an assessment of new or worsening ocular signs and symptoms.

Severity	Occurrence	Tivdak Dose Modification
Keratitis[b]		
Superficial punctate keratitis (SPK)	Any	Monitor.
Confluent superficial keratitis	First occurrence	Withhold dose until SPK or normal, then resume treatment at the next lower dose level.
	Second occurrence	Permanently discontinue.
Ulcerative keratitis or perforation	Any	Permanently discontinue.
Conjunctival ulceration[b]		
Any ulceration	First occurrence	Withhold dose until complete conjunctival re-epithelialization, then resume treatment at the next lower dose level.
	Second occurrence	Permanently discontinue.
Conjunctival or corneal scarring or symblepharon[b]		
Any scarring or symblepharon	Any	Permanently discontinue.

[a]Please see the full prescribing information for more detail.

[b]Refer patients to an eye care provider promptly for an assessment of new or worsening ocular symptoms.

Please see additional information about dose modifications on the following page.

Please see Important Safety Information on pages 1-3 and full prescribing information, including BOXED WARNING for TIVDAK.

Dosage modifications for adverse reactions (continued)[1,a]

Severity	Occurrence	Tivdak Dose Modification
Conjunctivitis and other ocular adverse reactions[b]		
Grade 1	Any	Monitor.
Grade 2	First occurrence	Withhold dose until Grade ≤1, then resume treatment at the same dose.
	Second occurrence	Withhold dose until Grade ≤1, then resume treatment at the next lower dose level. If no resolution to Grade ≤1, permanently discontinue.
	Third occurrence	Permanently discontinue.
Grade 3 or 4	Any	Permanently discontinue.
Peripheral neuropathy		
Grade 2	Any (initial or worsening of pre-existing condition)	Withhold dose until Grade ≤1, then resume treatment at the next lower dose level.
Grade 3 or 4	Any	Permanently discontinue.

[a]Please see the full prescribing information for more detail.

[b]Refer patients to an eye care provider promptly for an assessment of new or worsening ocular symptoms.

Please see additional information about dose modifications on the following page.

Please see Important Safety Information on pages 1-3 and full prescribing information, including BOXED WARNING for TIVDAK.

Dosage modifications for adverse reactions (continued)[1,a]

Severity	Occurrence	Tivdak® Dose Modification
Hemorrhage		
Any grade pulmonary or CNS	Any	Permanently discontinue.
Grade 2 in any other location	Any	Withhold dose until resolved, then resume treatment at the same dose.
Grade 3 in any other location	First occurrence	Withhold dose until resolved, then resume treatment at the same dose.
	Second occurrence	Permanently discontinue.
Grade 4 in any other location	Any	Permanently discontinue.
Pneumonitis		
Grade 2	Any	Withhold dose until Grade ≤1 for persistent or recurrent pneumonitis, consider resuming treatment at next lower dose level.
Grade 3 or 4	Any	Permanently discontinue.
Severe cutaneous adverse reactions (including Stevens-Johnson syndrome (SJS))		
Suspected (any grade)	Any	Immediately withhold dose and consult a specialist to confirm the diagnosis.
Confirmed Grade 3 or 4	Any	Permanently discontinue.

[a]Please see the full prescribing information for more detail.

Recommended dose reduction schedule[1]

Starting Dose
Tivdak dose level
2.0 mg/kg up to a maximum of 200 mg

1st Dose Reduction
Tivdak dose level
1.3 mg/kg up to a maximum of 130 mg

2nd Dose Reduction
Tivdak dose level
0.9 mg/kg up to a maximum of 90 mg

Permanently discontinue in patients who cannot tolerate 0.9 mg/kg.

Tivdak® Required Eye Care[1,2]

BEFORE STARTING THE TIVDAK INFUSION

PARTNER WITH AN EYE CARE PROVIDER

Refer your patient to an eye care provider for an ophthalmic exam, including visual acuity and slit lamp exams. This exam should occur prior to their first infusion to establish baseline eye health, prior to each infusion of Tivdak, and as clinically indicated.

PRESCRIBE TOPICAL EYE DROPS

Remind patients to bring all their topical eye drops to each infusion appointment.

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

Tivdak Required Eye Care[1,2]

DURING AND AFTER INFUSION

Day 1: Infusion Day (once every 3 weeks)

Pre-Infusion (~10 min prior)

- **Corticosteroid Eye Drops** 1 drop per eye or as prescribed
- **Vasoconstrictor Eye Drops** 3 drops per eye immediately prior to infusion or as prescribed
- **Cold Packs** Rotate as needed to keep eye area cool for 60 minutes total

During Infusion (~30 min)

- **Infusion** 2.0-mg/kg intravenous infusion
- **Cold Packs** Rotate as needed to keep eye area cool for 60 minutes total

After Infusion (~20 min)

- **Cold Packs** Rotate as needed to keep eye area cool for 60 minutes total

Remainder of Day

- **Corticosteroid Eye Drops** 1 drop per eye 2x throughout the remainder of the day or as prescribed **(Instruct patients to self-administer)**

Tivdak® Required Eye Care[1,2]

DURING AND AFTER INFUSION (CONTINUED)

Post Infusion Day (patient-driven tasks)	DAY 2	DAY 3	ONGOING
Corticosteroid Drops 1 drop per eye, 3x per day for Days 2-3 (72 hours) after infusion or as prescribed	S	S	
Lubricating Drops Instruct patients to administer for the duration of therapy and for 30 days after the last dose of Tivdak	L	L	L
Eye Self-Check Encourage patients to monitor their eyes daily and call their eye care provider and/or your office in the event of new or worsening ocular signs and symptoms			
Avoid Contact Lenses Advise patients to avoid wearing contact lenses throughout treatment unless directed to do so by an eye care provider			

Eye care checklist[1,2]

A step-by-step checklist to help you adhere to Tivdak Required Eye Care

tivdak®
tisotumab vedotin-tftv
for injection 40 mg

BEFORE INFUSION DAY

Before starting treatment

☐ **Prescribe topical eye drops**
- Corticosteroid drops
- Vasoconstrictor drops
- Lubricating drops (OTC)

Prior to every infusion

☐ **Ophthalmic exams**
Refer patients to an eye care provider for an ophthalmic exam, including visual acuity and slit lamp exam, prior to their first infusion to establish baseline eye health, prior to each infusion of Tivdak, and as clinically indicated

DAY 1: INFUSION DAY

Promptly refer patients to an eye care provider for any new or worsening ocular signs and symptoms

~10 minutes before infusion

☐ **Eye drops**
- Administer 1 corticosteroid drop in each eye or as prescribed
- Administer 3 vasoconstrictor drops in each eye immediately prior to infusion or as prescribed

☐ **Cold packs**
Place cold packs fully over eye area prior to each infusion

During and after infusion

☐ **Infusion (~30 min)**
- Administer Tivdak 2.0 mg/kg as an intravenous infusion (up to a maximum of 200 mg for patients ≥ 100 kg)

☐ **Rotate cold packs**
- Rotate as needed to keep eye area cool for a total of 60 minutes

Remainder of day

☐ **Eye drops**
Instruct patients to administer 1 corticosteroid drop in each eye 2x throughout the remainder of the day or as prescribed

Advise patients to avoid wearing contact lenses or applying any irritants on or near the eyes throughout treatment with Tivdak, including between infusions

AFTER INFUSION DAY

For Days 2-3 (72 hours) following infusion

☐ **Corticosteroid eye drops**
1 drop per eye, 3x per day for Days 2-3 after infusion or as prescribed

Ongoing

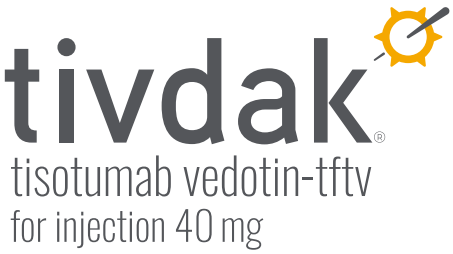
☐ **Lubricating eye drops**
Instruct patients to administer for the duration of therapy and for 30 days after the last dose of Tivdak

☐ **Eye self-check**
Encourage patients to monitor their eyes daily and call their eye care provider and/or your office in the event of new or worsening ocular signs and symptoms

☐ **Corticosteroid eye drop prescription renewal**
Refer patients to an eye care provider for a slit lamp exam before the initial prescription and all renewals of any corticosteroid medication

Instruct patients to call your office or their eye care provider if they experience changes or discomfort with their eyes

Please see Important Safety Information and full prescribing information, including BOXED WARNING for TIVDAK.



References: 1. TIVDAK [Prescribing Information]. Bothell, WA: Seagen Inc. July 2023. **2.** 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. **3.** 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.

Please see Important Safety Information on pages 1-3 and full prescribing information, including BOXED WARNING for TIVDAK.

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