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 (r/mCC) with disease progression on or after chemotherapy.

SELECT 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 2-4 and full prescribing information, including BOXED WARNING for TIVDAK.

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.

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.

Please see additional Important Safety Information on pages 1, 3, and 4 and full prescribing information, including BOXED WARNING for TIVDAK.

Hemorrhage (continued) 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.

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%).

Please see additional Important Safety Information on pages 1, 2, and 4 and full prescribing information, including BOXED WARNING for TIVDAK.

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%).

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 dose[1]*:

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

up to a maximum of 200 mg for patients >100 kg.

*The recommended dosing guidelines are appropriate for patients who weigh ≤100 kg. For patients who weigh >100 kg, the calculation of the dose should be normalized to 100 kg (ie, 2.0 mg/kg x 100 kg = 200 mg). This equation is based on the recommended dose and does not include dose modifications. It should not replace professional judgment or clinical experience.

Please see information about dose modifications for Tivdak on pages 19-22.

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

Please see Important Safety Information on pages 1-4 and full prescribing information, including BOXED WARNING for TIVDAK.

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*
- DO NOT administer 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.

*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 1-4 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 during the entire infusion

Additional information on Tivdak Premedication and Required Eye Care, including eye drop and cold pack administration, can be found on pages 23-25.

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 10. 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 1-4 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 301[1]

Tivdak has a BOXED WARNING for ocular toxicity; WARNINGS & PRECAUTIONS for ocular adverse reactions, peripheral neuropathy, hemorrhage, pneumonitis, severe cutaneous adverse reactions (including Stevens-Johnson syndrome (SJS)), and embryo-fetal toxicity; and ADVERSE REACTIONS, which may require discontinuation of Tivdak.

Adverse reactions reported in ≥10% of patients treated with Tivdak in innovaTV 301

Adverse reaction	Tivdak n=250		IC chemotherapy n=239	
	All grades %	Grade 3-4 %	All grades %	Grade 3-4 %
Nervous system disorders				
Peripheral neuropathy*	38	6	4.2	0.4
Eye disorders				
Conjunctival adverse reactions†	37	0	1.7	0
Corneal adverse reactions‡	21	3.2	0	0
Dry eye§	21	0	1.7	0
Gastrointestinal disorders				
Nausea‖	33	0.4	40	2.1
Constipation	25	1.2	16	0
Diarrhea¶	22	1.6	15	1.3
Abdominal pain#	18	4	15	2.5
Vomiting	18	1.6	18	1.3

*Peripheral neuropathy includes peripheral sensory neuropathy, paresthesia, muscular weakness, peripheral sensorimotor neuropathy, peripheral motor neuropathy, neurotoxicity, gait disturbance, neuralgia, hypoaesthesia, neuropathy peripheral, and skin burning sensation.
†Conjunctival adverse reactions includes conjunctivitis, conjunctivitis bacterial, conjunctivitis viral, episcleritis, ocular hyperemia, conjunctival hemorrhage, conjunctival hyperemia, conjunctival ulcer, conjunctivitis allergic, conjunctival disorder, symblepharon, conjunctival erosion, conjunctival oedema, conjunctivochalasis, and conjunctival scar.
‡Corneal adverse reactions includes keratitis, punctate keratitis, corneal erosion, ulcerative keratitis, corneal degeneration, corneal opacity, and keratopathy.
§Dry eye includes dry eye, eye discharge, eye pruritus, eye pain, eye irritation, and lacrimation increased.
‖Nausea includes nausea and retching.
¶Diarrhea includes diarrhea and gastroenteritis.
#Abdominal pain includes abdominal pain, abdominal pain upper, abdominal discomfort, and abdominal pain lower.

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 additional information about adverse reactions on the following page.

Please see Important Safety Information on pages 1-4 and full prescribing information, including BOXED WARNING for TIVDAK.

Adverse reactions reported in innovaTV 301 (continued)[1]

Tivdak has a BOXED WARNING for ocular toxicity; WARNINGS & PRECAUTIONS for ocular adverse reactions, peripheral neuropathy, hemorrhage, pneumonitis, severe cutaneous adverse reactions (including Stevens-Johnson syndrome (SJS)), and embryo-fetal toxicity; and ADVERSE REACTIONS, which may require discontinuation of Tivdak.

Adverse reactions reported in ≥10% of patients treated with Tivdak in innovaTV 301

Adverse reaction	Tivdak n=250		IC chemotherapy n=239	
	All grades %	Grade 3-4 %	All grades %	Grade 3-4 %
General				
Fatigue*	28	6	32	6
Pyrexia	17	0.4	21	0.8
Pruritus	10	0.4	2.9	0
Vascular disorders				
Epistaxis	26	0	2.5	0
Hemorrhage†	21	2	11	2.5
Metabolism and nutrition disorders				
Decreased appetite	24	0.8	18	0.4
Decreased weight	10	0.4	5	0
Skin and subcutaneous tissue disorders				
Alopecia	24	0	2.9	0
Rash‡	17	1.6	16	1.3
Infections				
Urinary tract infection§	16	5	18	8

*Fatigue includes fatigue and asthenia.
†Hemorrhage includes hematuria, vaginal hemorrhage, rectal hemorrhage, hemoptysis, anal hemorrhage, hemorrhage, gastrointestinal hemorrhage, hemorrhagic shock, lower gastrointestinal hemorrhage, gingival bleeding, tumor hemorrhage, intra-abdominal hemorrhage, gastric hemorrhage, genital hemorrhage, uterine hemorrhage, urinary tract hemorrhage, hemorrhoidal hemorrhage.
‡Rash includes rash maculo-papular, eczema, rash macular, rash pustular, dermatitis acneiform, erythema, rash, urticaria, dermatitis, and rash erythematous.
§Urinary tract infection includes urinary tract infection, pyelonephritis acute, cystitis, and urinary tract infection bacterial.

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 1-4 and full prescribing information, including BOXED WARNING for TIVDAK.

Ocular adverse reactions[1]

ACROSS CLINICAL TRIALS

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.

PREVALENCE

- 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*
- 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%)†

ONSET

- The median time to onset of the first ocular adverse reaction was 1.2 months (range: 0-17.1)*
- In innovaTV 301, 8 (3.2%) patients experienced delayed ocular adverse reactions occurring more than 30 days after discontinuation of Tivdak†

MONITOR*

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

*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 additional information about ocular adverse reactions on the following page.

Please see information about dose modifications for Tivdak on pages 19-22.

Please see Important Safety Information on pages 1-4 and full prescribing information, including BOXED WARNING for TIVDAK.

Ocular adverse reactions (continued)

ACROSS CLINICAL TRIALS

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for injection 40 mg

RESOLUTION[1]*

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

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 FROM innovaTV 301[3†]

- 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

Adhere to Tivdak Premedication and Required Eye Care to reduce the risk of ocular adverse reactions (see pages 23-25).[1]

*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 information about dose modifications for Tivdak on pages 19-22.

Please see Important Safety Information on pages 1-4 and full prescribing information, including BOXED WARNING for TIVDAK.

Peripheral neuropathy[1]

ACROSS CLINICAL TRIALS

PREVALENCE[1]

- Peripheral neuropathy occurred in 39% of patients with cervical cancer treated with Tivdak across clinical trials; 6% of patients experienced Grade 3 peripheral neuropathy*
- Peripheral neuropathy adverse reactions included peripheral sensory neuropathy (23%), peripheral neuropathy (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*
- Peripheral neuropathy led to discontinuation of Tivdak in 7% of patients with cervical cancer*
- In innovaTV 301, the most common (≥3%) adverse reactions leading to dose reduction were peripheral neuropathy (10%) and ocular adverse reactions (10%)†

ONSET[1*]

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

MONITOR[1*]

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

RESOLUTION[1*]

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

COMPLETE RESOLUTION **18%** OR PARTIAL IMPROVEMENT **21%**

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

ADDITIONAL DATA FROM innovaTV 301[3†]

- Time to resolution of peripheral neuropathy was exploratory. Data are provided as supportive clinical information
- The median time to resolution of peripheral neuropathy was 1.12 months (range: 0-12.1) for Tivdak vs 1.31 months (range: 0.2-5.4) for IC chemotherapy

*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 information about dose modifications for Tivdak on pages 19-22.

Please see Important Safety Information on pages 1-4 and full prescribing information, including BOXED WARNING for TIVDAK.

Hemorrhage

ACROSS CLINICAL TRIALS

PREVALENCE[1*]

- Hemorrhage occurred in 51% of patients with cervical cancer treated with Tivdak across clinical trials
- The most common all-grade hemorrhage adverse reaction was epistaxis (33%)
- Most hemorrhage adverse reactions were Grade 1-2, with 4% Grade 3

ONSET[1*]

- The median time to onset of hemorrhage was 0.3 months (range: 0-10.4)

MONITOR[1*]

- Monitor patients for signs and symptoms of hemorrhage

RESOLUTION[1*]

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

COMPLETE RESOLUTION **71%**

OR

PARTIAL RESOLUTION **12%**

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

ADDITIONAL DATA FROM innovaTV 301[3†]

- Time to resolution of hemorrhage adverse reactions was exploratory. Data are provided as supportive clinical information
- The median time to resolution of hemorrhage adverse reactions was 0.26 months (range: 0-7.2) for Tivdak vs 0.16 months (range: 0-2.9) for IC chemotherapy

*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 information about dose modifications for Tivdak on pages 19-22.

Please see Important Safety Information on pages 1-4 and full prescribing information, including BOXED WARNING for TIVDAK.

Pneumonitis[1]*

ACROSS CLINICAL TRIALS

PREVALENCE

- Pneumonitis occurred in 4 patients (0.9%) 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

*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.

Please see information about dose modifications for Tivdak on pages 19-22.

Please see Important Safety Information on pages 1-4 and full prescribing information, including BOXED WARNING for TIVDAK.

Severe cutaneous adverse reactions[1]*

ACROSS CLINICAL TRIALS

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PREVALENCE

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

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

*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.

Please see information about dose modifications for Tivdak on pages 19-22.

Please see Important Safety Information on pages 1-4 and full prescribing information, including BOXED WARNING for TIVDAK.

Dose modifications for adverse reactions[1]*

Some patients may require dose 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†		
Nonconfluent superficial keratitis	Any	Monitor.
Confluent superficial keratitis, a corneal epithelial defect, or a 3 line or more loss in best corrected visual acuity	First occurrence	Withhold dose until resolution, or improvement to nonconfluent superficial keratitis, then resume treatment at the next lower dose level.
	Second occurrence	Permanently discontinue.
Ulcerative keratitis or perforation	Any	Permanently discontinue.
Conjunctival or corneal scarring or symblepharon†		
Any scarring or symblepharon	Any	Permanently discontinue.
Conjunctivitis and other ocular adverse reactions†		
Nonconfluent superficial punctate conjunctival defects, mild vasodilation	Any	Monitor.

*Please see the full prescribing information for more detail.
†Refer patients to an eye care provider promptly for an assessment of new or worsening ocular symptoms.

Please see additional information about dose modifications for Tivdak on pages 20-22.

Please see Important Safety Information on pages 1-4 and full prescribing information, including BOXED WARNING for TIVDAK.

Dose modifications for adverse reactions (continued)[1]*

Severity	Occurrence	Tivdak dose modification
Conjunctivitis and other ocular adverse reactions (continued)†		
Confluent superficial punctate conjunctival defects, moderate to severe vasodilation	First occurrence	Withhold dose until resolution or improvement to nonconfluent superficial punctate conjunctival defects, mild vasodilation, then resume treatment at the same dose.
	Second occurrence	Withhold dose until resolution or improvement to nonconfluent superficial punctate conjunctival defects, mild vasodilation, then resume treatment at the next lower dose level. If no resolution or improvement to nonconfluent superficial punctate conjunctival defects, mild vasodilation, permanently discontinue.
	Third occurrence	Permanently discontinue.
Conjunctival ulcer, conjunctival neovascularization, or fibrovascular scarring	Any	Permanently discontinue.
Peripheral neuropathy		
Grade 2	Any (initial or worsening of preexisting condition)	Withhold dose until Grade ≤1, then resume treatment at the next lower dose level.
Grade 3 or 4	Any	Permanently discontinue.

*Please see the full prescribing information for more detail.
†Refer patients to an eye care provider promptly for an assessment of new or worsening ocular symptoms.

Please see additional information about dose modifications for Tivdak on pages 19, 21, and 22.

Please see Important Safety Information on pages 1-4 and full prescribing information, including BOXED WARNING for TIVDAK.

Dose modifications for adverse reactions (continued)[1]*

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.

*Please see the full prescribing information for more detail.

Please see Important Safety Information on pages 1-4 and full prescribing information, including BOXED WARNING for TIVDAK.

Recommended dose reduction schedule[1]

Starting dose
Tivdak dose level
2.0 mg/kg (up to a maximum of 200 mg for patients ≥100 kg)

First dose reduction
Tivdak dose level
1.3 mg/kg (up to a maximum of 130 mg for patients ≥100 kg)

Second dose reduction
Tivdak dose level
0.9 mg/kg (up to a maximum of 90 mg for patients ≥100 kg)

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

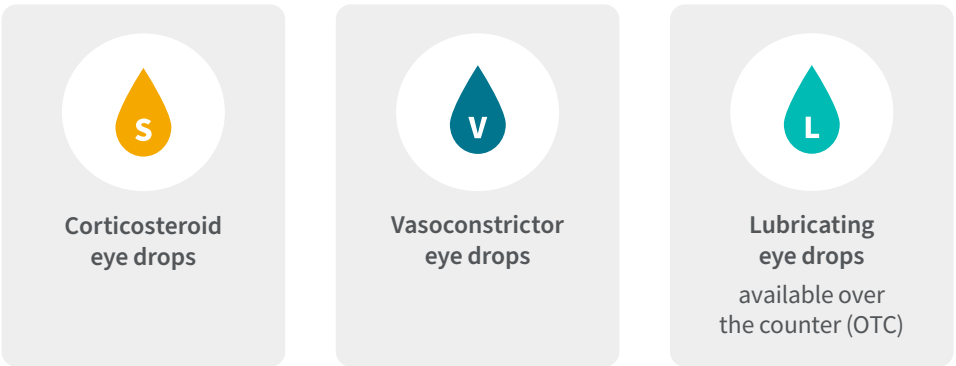
Tivdak Required Eye Care[1,2]

BEFORE STARTING THE TIVDAK INFUSION

PARTNER WITH AN EYE CARE PROVIDER

Refer your patient to an eye care provider (either an optometrist or ophthalmologist) to conduct an ophthalmic exam. This exam includes visual acuity, slit lamp exam of the anterior segment of the eye, and an assessment of normal eye movement. The exam will occur prior to initiation of Tivdak, prior to every cycle for the first 9 cycles, 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
tisotumab vedotin-tftv
for injection 40 mg

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)

Please see Important Safety Information on pages 1-4 and full prescribing information, including BOXED WARNING for TIVDAK.

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 Premedication and Required Eye Care

1 BEFORE THE INFUSION APPOINTMENT

Timeline	Description
Before the infusion	☐ Refer patient to an eye care provider (ECP) (either an optometrist or ophthalmologist) to conduct an ophthalmic exam prior to initiation of Tivdak, prior to every cycle for the first 9 cycles, and as clinically indicated. This exam includes visual acuity, slit lamp exam of the anterior segment of the eye, and an assessment of normal eye movement ☐ Either the oncologist or the ECP should prescribe 3 types of eye drops: corticosteroid, vasoconstrictor, and lubricating drops. Remind patient to bring all their topical eye drops to each infusion appointment

2 AT THE INFUSION APPOINTMENT

Prior to infusion	☐ The care team should instruct the patient to apply corticosteroid drops (1 drop per eye, or as prescribed) ☐ The care team should instruct the patient to apply vasoconstrictor drops immediately prior to the infusion (3 drops per eye, or as prescribed) ☐ The care team may assist the patient in placing cold packs over the eye area ~10 minutes prior to the infusion, during the infusion, and for 20 minutes after, keeping the eye area cool for a total of 60 minutes
Infusion	☐ Administer Tivdak (2.0 mg/kg) over 30 minutes through an intravenous line containing a 0.2 µm in-line filter

3 AFTER THE INFUSION APPOINTMENT

For the remainder of infusion day	☐ Instruct patient to continue applying corticosteroid drops (1 drop per eye) two more times throughout the day, or as prescribed
Days 2-3 (72 hours post infusion)	☐ Instruct patient to apply corticosteroid drops (1 drop per eye) three times per day, or as prescribed

THROUGHOUT TREATMENT

- ☐ Proactively monitor for new or worsening ocular adverse reactions throughout treatment with Tivdak, and encourage patient to check their eyes daily and report any symptoms
- ☐ Instruct patient to apply lubricating drops as needed for the duration of therapy and for 30 days after the last dose of Tivdak
- ☐ Advise patient to avoid contact lenses and eye irritants throughout treatment with Tivdak unless directed otherwise by an ECP

Please see Important Safety Information on pages 1-4 and full prescribing information, including BOXED WARNING for TIVDAK.

tivdak®
tisotumab vedotin-tftv
for injection 40 mg

References: 1. TIVDAK [Prescribing Information]. Bothell, WA: Seagen Inc. April 2024.
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. Data on file. Pfizer Inc., New York, NY.

Please see Important Safety Information on pages 1-4 and full prescribing information, including BOXED WARNING for TIVDAK.

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