TISOTUMAB VEDOTIN (Tivdak)

INDICATION (ICD10) C53

Check the most recent Blueteq eligibility criteria before prescribing. Blueteq registration required. (www.england.nhs.uk/publication/national-cancer-drugs-fund-list/) (TISV1)

1. Tisotumab vedotin for treating recurrent or metastatic (squamous, adenocarcinoma, or adenosquamous) cervical cancer that has progressed on or after either one or two systemic treatment for their recurrent/metastatic cervical cancer. PS 0 or 1.

REGIMEN

Day 1	**Premedication** Corticosteroid preservative free eye drops 1 drop BE tds starting 1 day prior to infusion. Vasoconstrictor preservative free eye drops 3 drops BE immediately prior to infusion. Lubricating eyedrops Cold packs following administration of eye drops apply prior to start of the infusion, during and for 30 minutes after the infusion.			
	TISOTUMAB VEDOTIN	2mg/kg (cap all doses at 100kg)	IV infusion	#ml sodium chloride 0.9% over 30 minutes

diluent volume for dose prescribed as per national standardised product specification

CYCLE FREQUENCY AND NUMBER OF CYCLES

Every 21 days until disease progression

ANTI-EMETICS

Low emetic risk day 1

CONCURRENT MEDICATION REQUIRED

Tisotumab vedotin	Ensure both types of eye drops and cold packs administered before tisotumab vedotin. Corticosteroid preservative free eye drops 1 drop BE tds starting 1 day prior to and to continue for 3 days after tisotumab vedotin. Lubricating eye drops multiple times per day continuously until 30 days after last dose of tisotumab vedotin.

EXTRAVASATION AND TYPE OF LINE / FILTERS

Tisotumab vedotin.- irritant

Administer using a 0.2µm in-line filter
Central or peripheral line

INVESTIGATIONS

Blood results required before SACT administration

FBC, U&E and LFTs Neutrophils x 10^9/L ≥1.0 provided patient is well Platelets ≥100x10^9/L	baseline and every cycle
GFR assessed using EDTA result (BMI <19 or >30 or calculated creatinine clearance at the Consultant's discretion	baseline and every cycle
Serum creatinine	baseline and every cycle
Ophthalmic exam (including visual acuity and slit lamp exam) (optometry)	Baseline and if worsening symptoms
Ophthalmic exam	Prior to each infusion, the treating healthcare provider should inspect the patient's eyes, including control of normal eye movement, and ask about any ocular signs or symptoms.
Virology	before cycle 1 if not previously checked
Weight	baseline and every cycle

MAIN TOXICITES AND ADVERSE REACTIONS

Tisotumab vedotin	Blood and lymphatic disorders eg anaemia, neutropenia Decreased appetite Eye disorders eg conjunctivitis, dry eye, keratitis etc Epistaxis Gastro intestinal eg nausea, vomiting, constipation, diarrhoea Peripheral neuropathy Skin disorders eg alopecia, rash, pruritic, dermatitis May affect driving / machinery use

INTERACTIONS WHICH MAY REQUIRE DOSE MODIFICATIONS (not exhaustive list check SPC/BNF/Stockleys)

Tisotumab vedotin	Caution is advised in case of treatment with strong CYP3A4 inhibitors. Patients should be closely monitored for adverse reactions when tisotumab vedotin is given concomitantly with strong CYP3A4 inhibitors (e.g., boceprevir, clarithromycin, cobicistat, indinavir, itraconazole, nefazodone, nelfinavir, posaconazole, ritonavir, saquinavir, telaprevir, telithromycin, voriconazole). The concomitant use of strong inducers of CYP3A4 eg rifampicin with tisotumab vedotin would likely decrease MMAE exposure, with no change in ADC exposure.

DOSE MODIFICATIONS

Starting dose 2mg/kg (maximum 200mg)
First dose reduction 1.3mg/kg (maximum 130mg)
Second dose reduction 0.9mg/kg (maximum 90mg)
Permanently discontinue in patients who cannot tolerate 0.9mg/kg

Non-haematological

Tisotumab vedotin

Conjunctival ulceration

Grade 1 or 2 First occurrence	Withhold dose until clinically stable, then resume treatment at the next lower dose level.
Grade 1 or 2 Second occurrence	Withhold dose until clinically stable, then resume treatment at the next lower dose level. If no stabilisation or improvement, permanently discontinue.
Grade 3 or 4. Any occurrence	Permanently discontinue.

Conjunctivitis and other ocular reactions

Grade 1 Any occurrence	Withhold dose until clinically stable, then resume treatment at the same dose
Grade 2 First occurrence	Withhold dose until grade ≤1, then resume treatment at the same dose..
Grade 2 Second occurrence	Withhold dose until grade ≤1, then resume treatment at the next lower dose level. If no resolution to grade ≤1, permanently discontinue.
Grade 2 Third occurrence	Permanently discontinue.
Grade 3 or 4 Any occurrence	Permanently discontinue.

Keratitis

Grade 1 Any occurrence	Withhold dose until clinically stable, then resume treatment at the same dose.
Grade 2 First occurrence	Withhold dose until grade ≤1, then resume treatment at the next lower dose level
Grade 2 Second occurrence	Withhold dose until grade ≤1, then resume treatment at the next lower dose level. If no resolution to grade ≤1, permanently discontinue.
Grade 2 Third occurrence	Permanently discontinue.
Grade 3 or 4 Any occurrence	Permanently discontinue.

Peripheral neuropathy

Grade 2 or 3 Any (initial or worsening of pre-existing condition)	Withhold dose until grade ≤1, then resume treatment at the next lower dose level.
Grade 4 Any occurrence	Permanently discontinue

Severe cutaneous reactions (including Stevens-Johnson syndrome (SJS)

Suspected any grade. Any occurrence	Immediately withhold dose and consult a specialist to confirm the diagnosis.
Confirmed grade 3 or 4 Any occurrence	Permanently discontinue

Hepatic impairment
Tisotumab vedotin
No dose adjustment is required in patients with mild hepatic impairment (total bilirubin of >1-1.5×ULN and any AST or total bilirubin ≤ULN and AST >ULN, as defined using the National Cancer Institute criteria for hepatic impairment). However, as the exposure is expected to increase in patients with mild hepatic impairment, caution is advised when treating patients with mild hepatic impairment.
Tisotumab vedotin has not been studied in patients with moderate or severe hepatic impairment.

Renal impairment
Tisotumab vedotin
No dose adjustment is required in patients with mild renal impairment (CrCL >60-90mL/min] or moderate (CrCL 30-60mL/min).
Tisotumab vedotin has not been studied in patients with severe renal impairment (CrCL 15-<30mL/min) or end-stage renal disease (CrCL <15mL/min).

REFERENCES
CDF

Assessments

	Pre	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Ongoing
Clinical assessment	X		Pre cycle		Pre cycle	Every cycle
SACT assessment (PS and toxicities)	X	X	X	X	X	Every cycle
FBC	X	X	X	X	X	Every cycle
U&E, calcium, magnesium & LFT	X	X	X	X	X	Every cycle
CrCl	X	X	X	X	X	Every cycle
Ocular exam	X	X	X	X	X	Every cycle
CT scan	X					At cycle 6, Inform consultant team if not booked
Informed consent	X					Verbal each cycle
Height	X					
Weight recorded	X	X	X	X	X	Every cycle