MIRVETUXIMAB SORAVTANSINE (Elahere)

INDICATION (ICD10) C56, C57

Check the most recent Blueteq eligibility criteria before prescribing. Blueteq registration required. (www.england.nhs.uk/publication/national-cancer-drugs-fund-list/) (MIR1)

1. Mirvetuximab soravtansine for treating folate receptor-alpha-positive (≥75% of tumour cells showing moderate (2+) and/or strong (3+) membrane staining using an approved assay) platinum-resistant (recurrence / progression less than 6 months after last dose of platinum containing chemotherapy) high-grade serous epithelial ovarian, fallopian tube or primary peritoneal cancer. PS 0 or 1.

REGIMEN

Day 1	**Premedication** 30 minutes prior to mirvetuximab soravtansine: Chlorphenamine 10mg IV bolus Dexamethasone 10mg IV bolus Paracetamol 1000mg tablet Ondansetron 8mg IV			
	MIRVETUXIMAB SORAVTANSINE	6mg/kg (use adjusted ideal body weight)	IV infusion	#ml glucose 5%

diluent volume for dose prescribed as per national standardised product specification
Must be diluted prior to administration with 5% glucose to a final concentration of 1mg/mL to 2mg/mL

To calculate AIBW (adjusted ideal body weight): all weights are measured / calculated in kg, height is measured in cm
IBW = ideal body weight IBW in kg (female) = (0.9 x height) – 92
AIBW in kg = IBW + 0.4(actual weight - IBW)

Intravenous infusion at a rate of 1mg/min. If well tolerated after 30 minutes, the infusion rate can be increased to 3mg/min. If well tolerated after 30 minutes at 3mg/min, the infusion rate can be increased to 5mg/min.
If no infusion-related reactions occur with the previous dose, subsequent infusions should be started at the maximally tolerated rate and may be increased up to a maximum infusion rate of 5 mg/min, as tolerated.

CYCLE FREQUENCY AND NUMBER OF CYCLES

Every 21 days until disease progression

ANTI-EMETICS

Low emetic risk day 1

CONCURRENT MEDICATION REQUIRED

Mirvetuximab soravtansine	Ensure premedication given before mirvetuximab soravtansine Lubricating eye drops

EXTRAVASATION AND TYPE OF LINE / FILTERS

Mirvetuximab soravtansine - irritant

Administer using a 0.2 or 0.22µm polyethersulfone (PES) 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
CA125	baseline and day 1 every cycle
Opthalmic exam including visual acuity and slit lamp exam	Baseline and if a patient develops any new or worsening ocular symptoms prior to the next dose. In patients with ≥grade 2 ocular adverse reactions, additional ophthalmic exams should be conducted at a minimum of every other cycle and as clinically indicated until resolution or return to baseline.
Virology	before cycle 1 if not previously checked
Weight	baseline and every cycle

MAIN TOXICITES AND ADVERSE REACTIONS

Mirvetuximab soravtansine	Haematological Infusion-related reactions / hypersensitivity Keratitis / keratopathy Opthalmic toxicity Peripheral neuropathy Pneumonitis

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

Mirvetuximab soravtansine	DM4 (the maytansoid antitubulin agent linked to mirvetuximab in the antibody drug conjugate) is a CYP 3A4 substrate. Concurrent use of mirvetuximab soravtansine with strong CYP 3A4 inhibitors may increase exposure to unconjugated DM4 and increase the toxicity of mirvetuximab soravtansine. Avoid concurrent use if possible. Monitor for increased toxicity if concurrent use cannot be avoided. Strong inducers of CYP 3A4 may reduce exposure to unconjugated DM4. Clinical significance is unknown.

DOSE MODIFICATIONS

Starting dose 6mg/kg AIBW
First dose reduction 5mg/kg AIBW
Second dose reduction 4mg/kg AIBW
Permanently discontinue in patients who cannot tolerate 4mg/kg AIBW

Haematological

Mirvetuximab soravtansine

Grade 3 or 4	Withhold dose until grade 1 or less, then resume at one lower dose level.

Non-haematological

Mirvetuximab soravtansine

Infusion related reactions / hypersensitivity

Grade 1	Maintain infusion rate
Grade 2	• Interrupt infusion and administer supportive treatment. • After recovery from symptoms, resume the infusion at 50% of the previous rate, and if no further symptoms appear, increase rate as appropriate until infusion is completed. • Administer additional pre-medication with dexamethasone 8 mg oral BD the day before infusion (or local equivalent) for future cycles.
Grade 3 or 4	• Immediately stop infusion and administer supportive treatment. • Advise patient to seek emergency treatment and immediately notify their healthcare professional if the infusion- related symptoms recur after discharge from the infusion area. • Permanently discontinue

Keratitis / keratopathy

≥ Grade 2 corneal adverse reactions (keratopathy) on slit lamp examination	Patients should be instructed to use steroid eye drops on the day of infusion and through the next 7 days of each subsequent cycle. Patients should be advised to wait at least 15 minutes after ophthalmic topical steroid administration before instilling lubricating eye drops. During treatment with ophthalmic topical steroids the measurement of intraocular pressure and an examination with slit lamp should be carried out regularly.
Non-confluent superficial keratitis/keratopathy	Monitor
Confluent superficial keratitis / keratopathy, a cornea epithelial defect, or 3-line or more loss in best corrected visual acuity	Withhold dose until improved to nonconfluent superficial keratitis/keratopathy or better or resolved, then maintain at same dose level. Consider dose reduction for patients with recurrent confluent keratitis/keratopathy despite best supportive care or in patients with ocular toxicity lasting longer than 14 days.
Corneal ulcer or stromal opacity or best corrected distance visual acuity 6/60 or worse	Withhold dose until improved to nonconfluent superficial keratitis/keratopathy or better or resolved, then reduce by one dose level.
Corneal perforation	Permanently discontinue

Other adverse reactions

Grade 3	Withhold dose until grade 1 or less, then resume at one lower dose level.
Grade 4	Permanently discontinue

Peripheral neuropathy

Grade 2	Withhold dose until grade 1 or less, then reduce by one dose level.
Grade 3 or 4	Permanently discontinue

Pneumonitis

Grade 1	Monitor
Grade 2	Withhold dose until grade 1 or less, then maintain at same dose level or consider dose reduction if recurrent, lasts longer than 28 days, or at physician discretion.
Grade 3 or 4	Permanently discontinue

Hepatic impairment
Mirvetuximab soravtansine
No dose adjustment is recommended for patients with mild hepatic impairment (total bilirubin ≤ULN and AST >ULN or total bilirubin >1 to 1.5 times ULN and any AST).
It should be avoided in patients with moderate to severe hepatic impairment (total bilirubin >1.5xULN with any AST).

Renal impairment
Mirvetuximab soravtansine
No dose adjustment is recommended for patients with mild to moderate renal impairment (creatinine clearance 30 to <90mL/min). It has not been evaluated in patients with severe renal impairment (CrCl 15 to <30mL/min) or end-stage renal disease and the potential need for dose adjustment in these patients cannot be determined

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
CT scan	X					At cycle 6, Inform consultant team if not booked
Ophthalmic exam	X					And as required
Informed consent	X					Verbal each cycle
Height	X					
Weight recorded	X	X	X	X	X	Every cycle