DRUG NAME: Mirvetuximab soravtansine

SYNONYM(S): IMGN853[1]

COMMON TRADE NAME(S): ELAHERE® (EU, USA)

CLASSIFICATION: miscellaneous

Special pediatric considerations are noted when applicable, otherwise adult provisions apply.

MECHANISM OF ACTION:

Mirvetuximab soravtansine is an antibody-drug conjugate (ADC) composed of an IgG1 anti-FRα monoclonal antibody linked to a maytansoid antitubulin agent (DM4) via a cleavable linker. Following binding to the target FRα antigen on the cell surface, mirvetuximab soravtansine is internalized and the linker cleaved through a proteolytic process. The cytotoxic payload (DM4) is released within the cell where it disrupts the microtubule network, ultimately resulting in cell cycle arrest and apoptotic cell death. Mirvetuximab soravtansine is cell cycle phase-specific, inducing cell cycle arrest in the G_2/M phase.[1,2]

USES:

Primary uses:

Ovarian cancer[2]

Other uses:

*Health Canada approved indication

SPECIAL PRECAUTIONS:

Caution:

- ***premedication with corticosteroid, antihistamine, antipyretic*** is recommended prior to each dose for prevention of infusion-related reactions[2]
- ***premedication with antiemetics*** is recommended prior to each dose[2]
- ***ophthalmic exams*** are recommended prior to starting treatment with mirvetuximab soravtansine[2]
- ***lubricating eye drops*** are recommended throughout treatment with mirvetuximab soravtansine[2]
- the ability to ***drive and/or operate machinery*** may be impaired during treatment (e.g., impairment secondary to visual disturbances, peripheral neuropathy, fatigue, or dizziness)[2]

SIDE EFFECTS:

The table includes adverse events that presented during drug treatment but may not necessarily have a causal relationship with the drug. Because clinical trials are conducted under very specific conditions, the adverse event rates observed may not reflect the rates observed in clinical practice. Adverse events are generally included if they were reported in more than 1% of patients in the product monograph or pivotal trials. When placebo-controlled trials are available, adverse events will generally be included if the incidence is ≥5% higher in the treatment group.

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ORGAN SITE	SIDE EFFECT
Clinically important side effects are in ***bold, italics***	
blood and lymphatic system/ febrile neutropenia	anemia (18-25%, severe 1-3%)
	leukocytopenia (23-26%, severe 1%)
	lymphocytopenia (27-35%, severe 3-7%)
	neutropenia (22-26%, severe 1-3%)
	thrombocytopenia (17-18%, severe 1-2%)
eye (see paragraph following **Side Effects** table)	***blurred vision*** (43-50%, severe 5-9%)
	cataract (4-18%, severe 3%)
	dry eye (27-29%, severe 2-3%)
	eye pain (10%)
	keratopathy (29-37%, severe 5-11%)
	photophobia (17-18%, severe 1%)
gastrointestinal	*emetogenic potential:* low[3]
	abdominal distension (11%)
	abdominal pain (30-36%, severe 3-7%)
	constipation (26-30%, severe 1%)
	diarrhea (29-39%, severe 1-3%)
	intestinal obstruction (3%)
	nausea (27-41%, severe 2%)
	small bowel obstruction (3%)
	vomiting (18-23%, severe 3%)
general disorders and administration site conditions	*extravasation hazard:* none[4]
	fatigue, asthenia (35-49%, severe 3%)
investigations	albumin decrease (21-31%, severe 1%)
	alkaline phosphatase increase (30%, severe 1%)
	ALT increase (38-39%, severe 2%)
	AST increase (16-57%, severe 2%)
	bicarbonate decrease (11%)
	creatinine increase (10-16%)
metabolism and nutrition	appetite decrease (18-22%, severe 1%)
	hypercalcemia (12%)
	hypokalemia (15%, severe 1-4%)
	hypomagnesemia (21-27%, severe 1-2%)
	hyponatremia (16%)
	arthralgia (16-17%)

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ORGAN SITE	SIDE EFFECT
Clinically important side effects are in ***bold, italics***	
musculoskeletal and connective tissue	musculoskeletal pain (31%, severe 1%)
	myalgia (10%)
nervous system (see paragraph following **Side Effects** table)	headache (14%)
	hypoesthesia (1%)
	neurotoxicity (3%)
	paresthesia (6%)
	peripheral motor neuropathy (1%)
	peripheral neuropathy (20%, severe 2-4%)
	peripheral sensorimotor neuropathy (<1%)
	peripheral sensory neuropathy (9%)
	polyneuropathy (<1%)
respiratory, thoracic and mediastinal	dyspnea (12%)
	pneumonitis (4-10%, severe 1%); see paragraph following **Side Effects** table
	pleural effusion (2%)

Adapted from standard reference[2,5] unless specified otherwise.

Severe and life-threatening ***interstitial lung disease,*** including ***pneumonitis,*** has been reported with mirvetuximab soravtansine. Some fatalities have been recorded. Median time to onset is 18 weeks (range 1.6 to 97 weeks). Monitor for hypoxia, cough, and dyspnea, and interstitial infiltrates on radiologic exams. Withhold mirvetuximab soravtansine for persistent or recurrent grade 2 pneumonitis and consider dose reduction. Permanently discontinue mirvetuximab soravtansine for grade 3 or 4 pneumonitis. Asymptomatic patients may continue receiving mirvetuximab soravtansine if closely monitored.[2,5]

Ocular adverse events (e.g., blurred vision, keratopathy, dry eye) have been observed with antibody-drug conjugates and may be a result of an off-target effect.[1] Median time to onset of ocular events is 5 weeks (range 0.1 to 69 weeks). Most patients experience either partial improvement or complete resolution of their symptoms. Lubricating eye drops are recommended throughout treatment. Contact lens use should be avoided. Ophthalmic exams are recommended prior to starting treatment with mirvetuximab soravtansine and if any new or worsening ocular symptoms occur prior to the next dose. The frequency of ophthalmic exams should be increased following toxicity and continue until resolution of symptoms or return to baseline (suggested minimum frequency every 2 weeks). Patients experiencing ***corneal adverse reactions*** such as keratopathy may require secondary prophylaxis with ophthalmic topical steroids in subsequent cycles. For patients with grade 2 or greater corneal toxicity, instruct patients to use steroid eye drops for each subsequent infusion, administering the drops on the day of the infusion plus the next 7 days after the infusion in each treatment cycle. Regular measurement of intraocular pressure and ophthalmic exams are recommended if topical steroids are used. When using steroid eye drops, instruct patients to wait at least 15 minutes after the steroid eye drops before administering lubricating eye drops. Depending on the severity and persistence of the adverse reaction, mirvetuximab soravtansine may be withheld, dose reduced, or permanently discontinued to manage symptoms. Patients experiencing visual disturbances should be instructed not to drive or operate machinery until symptoms have resolved.[2,5]

Peripheral neuropathies, including sensory/motor neuropathy and paresthesias, are reported in approximately one-third of patients. Grade 3 reactions are reported in 2-4% of patients. Median time to onset is 6 weeks (range 0.1 to 127 weeks). Monitor patients for paresthesia, neuropathic pain, muscle weakness, or dysesthesia. New or worsening symptoms are managed by dose reduction and/or withholding or permanently discontinuing mirvetuximab

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soravtansine. One-quarter of patients who experience peripheral neuropathy report complete resolution of their symptoms; however, others report only partial improvement after treatment discontinuation.[2,5]

INTERACTIONS:

DM4 is a CYP 3A4 substrate. Concurrent use 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.[2]

SUPPLY AND STORAGE:

Injection: AbbVie Deutschland GmbH & Co. KG supplies mirvetuximab soravtansine as 100 mg ready-to-use, single-use (preservative free) vials in a concentration of 5 mg/mL. Refrigerate. Protect from light.[2]

For basic information on the current brand used at BC Cancer, see Chemotherapy Preparation and Stability Chart in Appendix.

SOLUTION PREPARATION AND COMPATIBILITY:

For basic information on the current brand used at BC Cancer, see Chemotherapy Preparation and Stability Chart in Appendix.

Additional information:
- administer using 0.2 or 0.22 micron in-line filter[2]
- use non-DEHP bags and IV tubing[2]
- not compatible with normal saline; dilute with D5W only[2]

Compatibility: consult detailed reference

PARENTERAL ADMINISTRATION:

BC Cancer administration guideline noted in ***bold***, ***italics***

Subcutaneous	do not use
Intramuscular	do not use
Direct intravenous	do not use

Intermittent infusion[2]	• ***first dose: initial rate of 1 mg/min***
	  ○ if tolerated at 1 mg/min, rate may be increased to 3 mg/min after 30 min
	  ○ if tolerated at 3 mg/min, rate may be increased to 5 mg/min after 30 min
	• ***subsequent doses:*** maximally tolerated rate of previous dose
	• ***max rate of 5 mg/min***
	• use non-DEHP administration sets
	• administer using 0.2-0.22 micron in-line filters

Continuous infusion	do not use
Intraperitoneal	no information found
Intrapleural	no information found
Intrathecal	no information found

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BC Cancer administration guideline noted in ***bold***, ***italics***

Intra-arterial	no information found
Intravesical	no information found

DOSAGE GUIDELINES:

Refer to protocol by which patient is being treated. Numerous dosing schedules exist and depend on disease, response and concomitant therapy. Guidelines for dosing also include consideration of absolute neutrophil count (ANC). Dosage may be reduced, delayed or discontinued in patients with bone marrow depression due to cytotoxic/radiation therapy or with other toxicities.

Adults:

BC Cancer usual dose noted in ***bold, italics***

	Cycle Length:	
Intravenous:	***3 weeks***[2]:	***6 mg/kg AIBW IV for one dose on day 1*** (total dose per cycle 6 mg/kg AIBW)

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)

REFERENCES:

1. ImmunoGen Inc. Mirvetuximab Soravtansine (IMGN853) Investigator's Brochure - Edition 12.0. Waltham, Massachusetts, USA; June 3, 2024.
2. AbbVie Deutschland GmbH & Co. KG. ELAHERE® Summary of Product Characteristics. Ludwigshafen, Germany; April 18th, 2024.
3. BC Cancer Supportive Care Tumour Group. (SCNAUSEA) BC Cancer Guidelines for Prevention and Treatment of Chemotherapy-Induced Nausea and Vomiting in Adults. Vancouver, British Columbia: BC Cancer; September 1 , 2022.
4. BC Cancer Provincial Systemic Therapy Program. Provincial Systemic Therapy Program Policy III-20: Prevention and Management of Extravasation of Chemotherapy. Vancouver, British Columbia: BC Cancer; March 1 , 2021.
5. ImmunoGen Inc. ELAHERE® full prescribing information. Waltham, Massachusetts, USA; March 22, 2024.

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