ELAHERE™
mirvetuximab soravtansine-gynx
injection 100 mg

DOSING AND ADMINISTRATION GUIDE FOR ELAHERE

THE FIRST AND ONLY FRα-TARGETED ADC FOR PLATINUM-RESISTANT OVARIAN CANCER[1]

ELAHERE is indicated for the treatment of adult patients with folate receptor-alpha (FRα) positive, platinum-resistant epithelial ovarian, fallopian tube, or primary peritoneal cancer, who have received one to three prior systemic treatment regimens. Select patients for therapy based on an FDA-approved test.

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 a confirmatory trial.

PROPHYLACTIC MEDICATIONS PRIOR TO INFUSION

Help reduce the incidence and severity of infusion-related reactions and emesis by following the ELAHERE premedication guidelines[1]

Premedication prior to each ELAHERE infusion			
Premedication	**Route of administration**	**Examples (or equivalent)**	**Administration time prior to ELAHERE infusion**
Corticosteroid	intravenous (IV)	dexamethasone 10 mg	At least 30 minutes prior
Antihistamine	oral or IV	diphenhydramine 25 mg to 50 mg	
Antipyretic	oral or IV	acetaminophen 325 mg to 650 mg	
Antiemetic	oral or IV	5-HT_3 serotonin receptor antagonist or appropriate alternatives	Before each dose and thereafter as needed
Consider additional premedications including corticosteroids the day prior to ELAHERE administration for patients who experience infusion-related reactions.			

ADC=antibody-drug conjugate.

SELECT IMPORTANT SAFETY INFORMATION

BOXED WARNING: OCULAR TOXICITY

- **ELAHERE can cause severe ocular toxicities, including visual impairment, keratopathy, dry eye, photophobia, eye pain, and uveitis.**
- **Conduct an ophthalmic exam including visual acuity and slit lamp exam prior to initiation of ELAHERE, every other cycle for the first 8 cycles, and as clinically indicated.**
- **Administer prophylactic artificial tears and ophthalmic topical steroids.**
- **Withhold ELAHERE for ocular toxicities until improvement and resume at the same or reduced dose.**
- **Discontinue ELAHERE for Grade 4 ocular toxicities.**

Please see Important Safety Information throughout and full Prescribing Information, including BOXED WARNING.

CALCULATING STARTING DOSE[1]

The recommended dose of ELAHERE is **6 mg/kg adjusted ideal body weight (AIBW) administered once every 3 weeks (21-day cycle)** as an IV infusion until disease progression or unacceptable toxicity.

The total dose of ELAHERE is calculated based on each patient's AIBW using the following formula:

$$\text{AIBW} = \text{IBW} + 0.4 \times (\text{actual weight}_{(\text{kg})} - \text{IBW})$$

Female IBW = (0.9 x height in cm) – 92

AIBW is equivalent to AdjBW.
In the SORAYA clinical study, the mean AIBW was 59.2 kg. Based on an AIBW of 59.2 kg, the dose would be 355 mg per cycle (4 vials).[1,2]
Dose modifications may help manage treatment-related toxicities.

INSTRUCTIONS FOR PREPARATION[1]

Calculate the dose (mg) (based on the patient's AIBW), total volume (mL) of solution required, and the number of vials of ELAHERE needed. More than one vial will be needed for a full dose

Remove the vials of ELAHERE from the refrigerator and allow to warm to room temperature

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. ELAHERE is a clear to slightly opalescent, colorless solution

Gently swirl and inspect each vial prior to withdrawing the calculated dose volume of ELAHERE for subsequent further dilution. **Do not shake** the vial

Using aseptic technique, withdraw the calculated dose volume of ELAHERE for subsequent further dilution

ELAHERE contains no preservative and is intended for single dose only. Discard any unused drug remaining in the vial

ADMINISTRATION[1]

Administer ELAHERE as an IV infusion only. Prior to administration, ELAHERE must be diluted with 5% Dextrose Injection, USP to a final concentration of 1 mg/mL to 2 mg/mL

Administer the first dose at the rate of 1 mg/min. If well tolerated after 30 minutes, the infusion rate can be increased to 3 mg/min. If well tolerated after 30 minutes, the infusion rate can be increased to 5 mg/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

AdjBW=adjusted body weight; IBW=ideal body weight.

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ADMINISTRATION[1] (CONT'D)

ELAHERE is a hazardous drug. Follow applicable special handling and disposal procedures

DO NOT mix ELAHERE with other drugs or IV fluids

DO NOT mix ELAHERE with normal saline (0.9% Sodium Chloride Injection)

ADDITIONAL DOSING AND ADMINISTRATION INFORMATION[1]

Dilution

- ELAHERE is incompatible with 0.9% Sodium Chloride Injection. ELAHERE must not be mixed with any other drugs or IV fluids
- Determine the volume of 5% Dextrose Injection, USP required to achieve the final diluted drug concentration. Either remove excess 5% Dextrose Injection, USP from a prefilled IV bag, or add the calculated volume of 5% Dextrose Injection, USP to a sterile empty IV bag. Then add the calculated dose volume of ELAHERE to the IV bag
- Gently mix the diluted drug solution by slowly inverting the bag several times to assure uniform mixing. **Do not shake or agitate**
- If the diluted infusion solution is not used immediately, store solution either at ambient temperature [18 °C to 25 °C (64.4 °F to 77 °F)] for no more than 8 hours (including infusion time), or under refrigeration 2 °C to 8 °C (36 °F to 46 °F) for no more than 12 hours. If refrigerated, allow the infusion bag to reach room temperature prior to administration. After refrigeration, administer diluted infusion solutions within 8 hours (including infusion time)
- **Do not freeze** prepared infusion solution

Administration

- Inspect the ELAHERE IV infusion bag visually for particulate matter and discoloration prior to administration
- Administer premedications prior to ELAHERE administration
- Administer ELAHERE as an IV infusion only, using a 0.2 or 0.22 µm polyethersulfone (PES) in-line filter. Do not substitute other membrane materials
- Following the infusion, flush the IV line with 5% Dextrose Injection, USP to ensure delivery of the full dose. **Do not use any other IV fluids for flushing**

PROACTIVE MANAGEMENT OF OCULAR EVENTS[1-4]

Work with an eye care provider (ophthalmologist or optometrist) to manage ocular events that may occur

Patients should receive a baseline ophthalmic exam from an ophthalmologist or optometrist, including visual acuity and slit lamp exam, prior to treatment initiation, and follow-up exams during every other cycle for the first 8 cycles and as clinically indicated

Tell your patients to avoid use of contact lenses

The use of ophthalmic topical steroids is recommended. The initial prescription and renewals of any corticosteroid medication should be made only after examination with a slit lamp. Instruct patients to administer 1 drop of ophthalmic topical steroid in each eye 6 times daily starting the day prior to each infusion of ELAHERE until day 4; then administer 1 drop in each eye 4 times daily on days 5–8 of each cycle of ELAHERE

The use of preservative-free* lubricating eye drops at least 4 times daily and as needed is recommended during treatment with ELAHERE. Instruct patients to use lubricating eye drops and advise to wait at least 10 minutes after ophthalmic topical steroid administration before instilling lubricating eye drops

- The most common (≥5%) ocular adverse events were visual impairment (49%), keratopathy (36%), dry eye (26%), cataract (15%), photophobia (13%), and eye pain (12%)

DOSE MODIFICATIONS[1]

Dose modifications may help manage treatment-related toxicities. Adjust the schedule of administration to maintain a 3-week interval between doses.

Recommended dose reduction schedule for adverse events	
	ELAHERE dose level
Starting dose	6 mg/kg AIBW
First dose reduction	5 mg/kg AIBW
Second dose reduction	4 mg/kg AIBW[a]

[a]Permanently discontinue in patients who cannot tolerate 4 mg/kg AIBW.

*Preservative-free is not a requirement for all patients. Lubricating eye drops without preservatives are recommended for patients with sensitive eyes.

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DOSE MODIFICATIONS[1] (CONT'D)

Dose modification guidelines for adverse events		
Adverse event	**Severity of adverse event[a]**	**Dosage modification**
Keratitis/keratopathy	Nonconfluent superficial keratitis	Monitor
	Confluent superficial keratitis, a cornea epithelial defect, or 3-line or more loss in best corrected visual acuity	Withhold dose until improved or resolved, then maintain at same dose level or consider dose reduction
	Corneal ulcer or stromal opacity or best corrected distance visual acuity 20/200 or worse	Withhold dose until improved or resolved, then reduce by one dose level
	Corneal perforation	Permanently discontinue
Uveitis	Grade 1: Rare cell in anterior chamber	Monitor
	Grade 2: 1–2+ cell or flare in anterior chamber	Withhold dose until Grade 1 or less, then maintain dose at same dose level
	Grade 3: 3+ cell or flare in anterior chamber	Withhold dose until Grade 1 or less, then reduce dose by one dose level
	Grade 4: Hypopyon	Permanently discontinue
Pneumonitis	Grade 1	Monitor
	Grade 2	Withhold dose until Grade 1 or less, then resume at same dose level or one lower dose level at the discretion of the healthcare provider
	Grade 3 or 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
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 premedication 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 provider if the infusion-related symptoms recur • Permanently discontinue
Other adverse events	Grade 3	Withhold dose until Grade 1 or less, then resume at one lower dose level
	Grade 4	Permanently discontinue

[a]Unless otherwise specified, National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) version 5.0.

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- **Administer prophylactic artificial tears and ophthalmic topical steroids.**
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WARNINGS and PRECAUTIONS

Ocular Disorders

ELAHERE can cause severe ocular adverse reactions, including visual impairment, keratopathy (corneal disorders), dry eye, photophobia, eye pain, and uveitis.

Ocular adverse reactions occurred in 61% of patients with ovarian cancer treated with ELAHERE. Nine percent (9%) of patients experienced Grade 3 ocular adverse reactions, including visual impairment, keratopathy/keratitis (corneal disorders), dry eye, photophobia, and eye pain; and one patient (0.2%) experienced Grade 4 keratopathy. The most common (≥5%) ocular adverse reactions were visual impairment (49%), keratopathy (36%), dry eye (26%), cataract (15%), photophobia (13%), and eye pain (12%).

The median time to onset for first ocular adverse reaction was 1.2 months (range: 0.03 to 12.9). Of the patients who experienced ocular events, 49% had complete resolution and 39% had partial improvement (defined as a decrease in severity by one or more grades from the worst grade) at last follow up. Ocular adverse reactions led to permanent discontinuation of ELAHERE in 0.6% of patients.

Premedication and use of lubricating and ophthalmic topical steroid eye drops during treatment with ELAHERE are recommended. Advise patients to avoid use of contact lenses during treatment with ELAHERE unless directed by a healthcare provider.

Refer patients to an eye care professional for an ophthalmic exam including visual acuity and slit lamp exam prior to treatment initiation, every other cycle for the first 8 cycles, and as clinically indicated. Promptly refer patients to an eye care professional for any new or worsening ocular signs and symptoms.

Monitor for ocular toxicity and withhold, reduce, or permanently discontinue ELAHERE based on severity and persistence of ocular adverse reactions.

Pneumonitis

Severe, life-threatening, or fatal interstitial lung disease (ILD), including pneumonitis, can occur in patients treated with ELAHERE. Pneumonitis occurred in 10% of patients treated with ELAHERE, including 0.8% with Grade 3 events, and 1 patient (0.2%) with a Grade 4 event. One patient (0.2%) died due to respiratory failure in the setting of pneumonitis and lung metastases.

Monitor patients for pulmonary signs and symptoms of pneumonitis. Infectious, neoplastic, and other causes for symptoms should be excluded through appropriate investigations.

Withhold ELAHERE for patients who develop persistent or recurrent Grade 2 pneumonitis until symptoms resolve to ≤Grade 1 and consider dose reduction. Permanently discontinue ELAHERE in all patients with Grade 3 or 4 pneumonitis. Patients who are asymptomatic may continue dosing of ELAHERE with close monitoring.

IMPORTANT SAFETY INFORMATION (CONT'D)

Peripheral Neuropathy (PN)

PN occurred in 36% of patients with ovarian cancer treated with ELAHERE across clinical trials; 2% of patients experienced Grade 3 PN. PN adverse reactions included peripheral neuropathy (19%), peripheral sensory neuropathy (9%), paraesthesia (6%), neurotoxicity (3%), hypoaesthesia (2%), peripheral motor neuropathy (1%), neuralgia (0.4%), polyneuropathy (0.2%) and oral hypoesthesia (0.2%).

Monitor patients for signs and symptoms of neuropathy. For patients experiencing new or worsening PN, withhold dosage, dose reduce, or permanently discontinue ELAHERE based on the severity of PN.

Embryo-Fetal Toxicity

Based on its mechanism of action, ELAHERE can cause embryo-fetal harm when administered to a pregnant woman because it contains a genotoxic compound (DM4) and affects actively dividing cells.

Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with ELAHERE and for 7 months after the last dose.

ADVERSE REACTIONS

Serious adverse reactions occurred in 31% of patients. The most common (≥2%) serious adverse reactions were intestinal obstruction (8%), ascites (4%), infection (3%), and pleural effusion (3%). Fatal adverse reactions occurred in 2% of patients, including small intestinal obstruction (1%) and pneumonitis (1%).

Permanent discontinuation of ELAHERE due to adverse reactions occurred in 11% of patients. The most common (≥2%) adverse reactions leading to permanent discontinuation were intestinal obstruction (2%) and thrombocytopenia (2%). One patient (0.9%) permanently discontinued ELAHERE due to visual impairment (unilateral decrease to BCVA ≤20/200 that resolved to baseline after discontinuation).

Dosage delays of ELAHERE due to an adverse reaction occurred in 39% of patients. Adverse reactions which required dosage delays in ≥3% of patients included visual impairment (15%), keratopathy (11%), neutropenia (6%), dry eye (5%), cataracts (3%) and increased gamma-glutamyltransferase (3%).

Dose reductions of ELAHERE due to an adverse reaction occurred in 20% of patients. Adverse reactions which required dose reductions in ≥3% of patients included visual impairment (9%) and keratopathy (7%).

The most common (≥20%) adverse reactions, including laboratory abnormalities, were vision impairment, fatigue, increased aspartate aminotransferase, nausea, increased alanine aminotransferase, keratopathy, abdominal pain, decreased lymphocytes, peripheral neuropathy, diarrhea, decreased albumin, constipation, increased alkaline phosphatase, dry eye, decreased magnesium, decreased leukocytes, decreased neutrophils, and decreased hemoglobin.

DRUG INTERACTIONS

Strong CYP3A4 Inhibitors

DM4 is a CYP3A4 substrate. Concomitant use of ELAHERE with strong CYP3A4 inhibitors may increase unconjugated DM4 exposure, which may increase the risk of ELAHERE adverse reactions. Closely monitor patients for adverse reactions with ELAHERE when used concomitantly with strong CYP3A4 inhibitors.

USE IN SPECIAL POPULATIONS

Lactation

Advise women not to breastfeed during treatment with ELAHERE and for at least 1 month after the last dose.

Pediatric Use

Safety and effectiveness of ELAHERE have not been established in pediatric patients.

Hepatic Impairment

Avoid use of ELAHERE in patients with moderate or severe hepatic impairment (total bilirubin >1.5 ULN).

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References: 1. ELAHERE. Package insert. ImmunoGen, Inc.; 2022. **2.** Data on file. ImmunoGen, Inc. Waltham, MA. **3.** Moore KN, Martin LP, Matulonis UA, et al. IMGN853 (mirvetuximab soravtansine), a folate receptor alpha (FRα)-targeting antibody-drug conjugate (ADC): single agent activity in platinum-resistant epithelial ovarian cancer (EOC) patients. Poster presented at: American Society of Clinical Oncology (ASCO) Annual Meeting; June 3–7, 2016; Chicago, Illinois. **4.** Moore KN, Martin LP, O'Malley DM, et al. Safety and activity of mirvetuximab soravtansine (IMGN853), a folate receptor alpha-targeting antibody-drug conjugate, in platinum-resistant ovarian, fallopian tube, or primary peritoneal cancer: a phase I expansion study. *J Clin Oncol*. 2017;35(10):1112–1118.

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