

Pharmacist Guide

KIMMTRAK® Dosing, Preparation, and Adverse Event Management



INFORMATION AT A GLANCE

Use this guide when caring for patients prescribed KIMMTRAK. More details can be found inside.

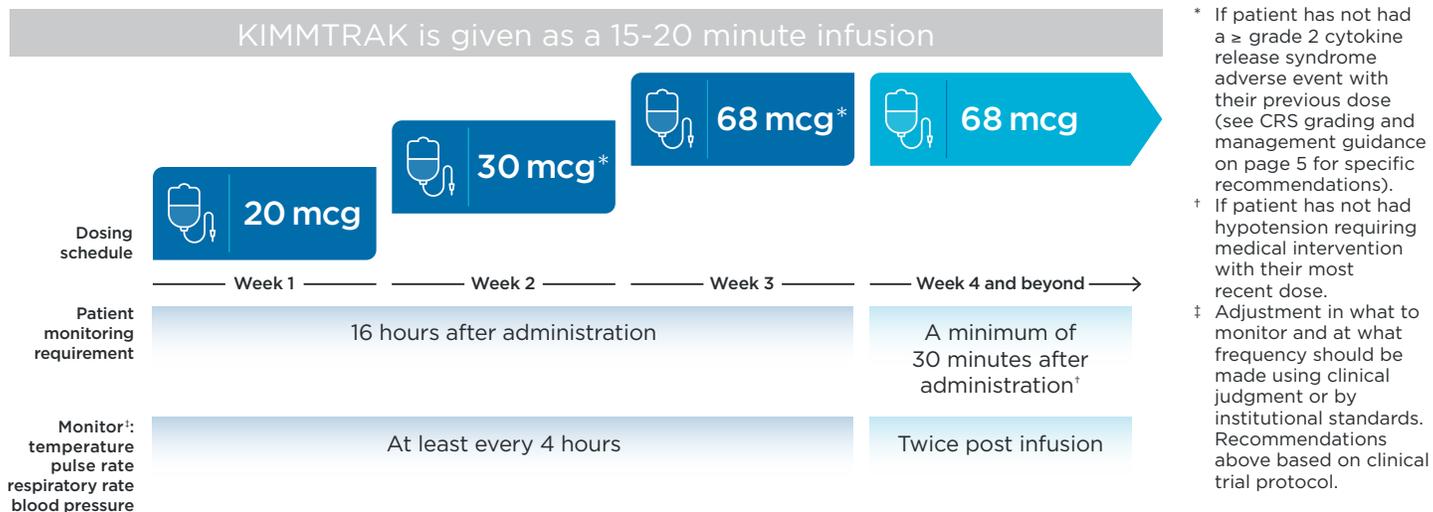
KIMMTRAK is indicated for the treatment of HLA-A*02:01-positive adult patients with unresectable or metastatic uveal melanoma.

Cytokine Release Syndrome (CRS) which may be serious or life-threatening, occurred in patients receiving KIMMTRAK. Monitor for at least 16 hours following the first three infusions and then as clinically indicated.

Please see the Important Safety Information, including **BOXED WARNING for CRS** on page 9 and click [here](#) for full Prescribing Information.

KIMMTRAK Dosing and Patient Monitoring¹

Adequate hydration/euvolemic status prior to starting KIMMTRAK is advised



What You Need to Prepare KIMMTRAK¹

Before you begin, have the following available:

- KIMMTRAK comes in a 100 mcg/0.5 mL clear, colorless to slightly yellowish solution in a 0.5 mL single-dose vial
- 1 mL sterile syringes with graduations of 2 decimal places (eg, TB syringe)
- Sterile needles: 18-gauge to 21-gauge sterile needles commonly used in aseptic compounding are recommended
- Albumin (Human); use concentration as per local availability. Examples include but are not restricted to the following strengths: 5%, 20%, or 25%

Human albumin is important to ensure that the active ingredient does not adhere to the bag and result in underdosing the patient.

- A 100 mL 0.9% Sodium Chloride Injection, USP infusion bag
 - The infusion bag should be constructed of polyolefins (PO) (such as polyethylene [PE] and polypropylene [PP]) or polyvinyl chloride (PVC)
- A sterile, non-pyrogenic, low protein binding 0.2 micron in-line filter infusion set for administration of the final infusion bag
- Inspect the parenteral drug products and infusion bags for particulate matter and discoloration

Reminders¹

- KIMMTRAK is not a hazardous drug under NIOSH
- **Before preparation and administration of KIMMTRAK, verify the dose of KIMMTRAK**
 - See directions within this guide or the KIMMTRAK Prescribing Information.
- **KIMMTRAK must be diluted prior to intravenous (IV) administration**
- If not used immediately, store the KIMMTRAK infusion bag in a refrigerator at 2 °C to 8 °C (36 °F to 46 °F) and **infuse within 24 hours from the time of preparation**

Scan and Watch!

Access a video showing the preparation of KIMMTRAK by scanning the QR code or visiting www.KIMMTRAKhcp.com.



KIMMTRAK Dosing¹

The recommended dosage of KIMMTRAK administered intravenously is 20 mcg on day 1, 30 mcg on day 8, 68 mcg on day 15, and 68 mcg once every week thereafter. In clinical trials, patients stopped treatment for disease progression, unless the patient was otherwise deriving benefit, or for unacceptable toxicity.

For at least the first 3 infusions, patients should be monitored during infusion and at least for 16 hours after infusion is complete.

- Based on clinical trials, 16 hours is the likely time frame for presentation of cytokine release syndrome (CRS) symptoms
- After infusion 3, and once the patient tolerates the most recent infusion without hypotension requiring medical intervention (eg, giving IV fluids), subsequent doses can be administered in appropriate ambulatory care settings (eg, infusion center)

Starting with the fourth infusion of KIMMTRAK, patients should be monitored for a minimum of 30 minutes following each infusion.

- Dose of KIMMTRAK is generally based on how many infusions have been received
- Verify patient dose prior to each infusion
- Patients must be monitored at baseline, during, and after each infusion for side effects

Preparation of KIMMTRAK¹

- KIMMTRAK is to be administered intravenously as IV infusion only
- **Before preparation and administration of KIMMTRAK, verify the dose of KIMMTRAK**
 - The recommended dosage of KIMMTRAK administered intravenously is 20 mcg on day 1, 30 mcg on day 8, 68 mcg on day 15, and 68 mcg once every week thereafter
- KIMMTRAK must be diluted prior to IV administration
- Each vial of KIMMTRAK is intended as single-dose only. DO NOT SHAKE the KIMMTRAK vial

What You Need to Prepare KIMMTRAK

Before you begin, have the following available:

- KIMMTRAK comes in a 100 mcg/0.5 mL clear, colorless to slightly yellowish solution in a 0.5 mL single-dose vial
- 1 mL sterile syringes with graduations of 2 decimal places (eg, TB syringe)
- Sterile needles: 18-gauge to 21-gauge sterile needles commonly used in aseptic compounding are recommended
- Albumin (Human); use concentration as per local availability. Examples include but are not restricted to the following strengths: 5%, 20%, or 25%

KIMMTRAK is not a hazardous drug under NIOSH

- A 100 mL 0.9% Sodium Chloride Injection, USP infusion bag
 - The infusion bag should be constructed of polyolefins (PO) (such as polyethylene [PE] and polypropylene [PP]) or polyvinyl chloride (PVC)
- A sterile, non-pyrogenic, low protein binding 0.2 micron in-line filter infusion set for administration of the final infusion bag
- Inspect the parenteral drug products and infusion bags for particulate matter and discoloration

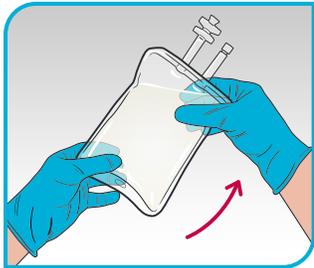
Human albumin is important to ensure that the active ingredient does not adhere to the bag and result in underdosing the patient.

To dilute KIMMTRAK:

Step 1 - Prepare the infusion bag, using aseptic technique

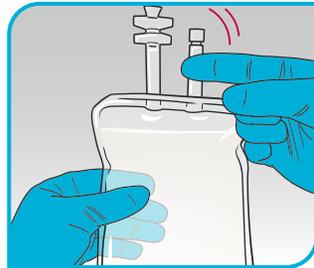
Using a 1 mL syringe with graduations of 2 decimal places and a sterile needle, withdraw the calculated volume of Albumin (Human) into the syringe and add to the 100 mL 0.9% Sodium Chloride Injection, USP bag to make a final Albumin (Human) concentration of 250 mcg/mL

Gently homogenize the prepared solution by completing the following steps:



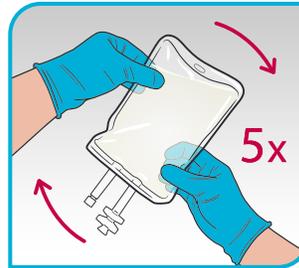
Step 1a

Invert the infusion bag so that the bag is upside down with the entry port positioned on top.



Step 1b

Tap the side of the port tubing to ensure that any residual solution is released into the bulk solution.



Step 1c

Mix the prepared solution by gently rotating the bag lengthwise at least 5 times.



Step 1d

DO NOT SHAKE the infusion bag.

Repeat the above steps an additional 3 times.

Before preparing KIMMTRAK, remember to verify the dose for the patient.

Homogenous mixing is essential to prevent adsorption of drug to the infusion bag and other components of the drug delivery system.

Step 2: Preparation of KIMMTRAK Solution for Infusion

- Do not shake the KIMMTRAK vial
- Using a 1 mL syringe with graduations of 2 decimal places and a sterile needle, withdraw the required volume of KIMMTRAK 100 mcg/0.5 mL as per the dose required (as shown in the table on right) and add to the prepared 100 mL infusion bag containing 0.9% Sodium Chloride Injection, USP plus Albumin (Human)
- Discard the single dose vial containing the unused portion of KIMMTRAK in accordance with local requirements. DO NOT prepare more than one dose from the vial
- Mix the infusion bag by following the same procedure as outlined in Steps 1a through 1d

Examples of Albumin (Human) Concentration and Volumes

Albumin (Human) concentration	Albumin (Human) volume for addition to a 100 mL 0.9% Sodium Chloride Injection, USP Infusion Bag to prepare a concentration of 250 mcg/mL Albumin (Human) in 0.9% Sodium Chloride Injection, USP
5% (50 g/L)	0.5 mL
20% (200 g/L)	0.13 mL
25% (250 g/L)	0.1 mL

KIMMTRAK Volumes Required for Addition to the Infusion Bag

Day of treatment	Dose (mcg) of KIMMTRAK	Volume (mL) of KIMMTRAK
Day 1	20	0.1
Day 8	30	0.15
Day 15 and weekly thereafter	68	0.34

Please see the Important Safety Information, including **BOXED WARNING for CRS** on page 9 and click [here](#) for full Prescribing Information.

KIMMTRAK
(tebentafusp-tebn)
Injection for Intravenous Use 100 mcg/0.5 mL

Prior to administering KIMMTRAK:

- No standard premedications are required
- Ensure patients are euvolemic prior to initiating the infusions. Administer IV fluids based on clinical evaluation, baseline vital signs, and the volume status of the patient, as assessed by the treating physician, to minimize the risk of hypotension associated with cytokine release syndrome (CRS)
- Patients who may be sensitive to manifestations of CRS, such as hypotension, tachycardia, or hypoxia, or the use of intravenous fluids to manage CRS, should be carefully assessed prior to starting KIMMTRAK. Ensure patients are euvolemic prior to initiating KIMMTRAK infusions
- For patients on maintenance systemic corticosteroids, consider adjusting the corticosteroid dose given the risk of hypotension

To administer KIMMTRAK:

- Immediately administer the diluted solution via intravenous infusion over 15-20 minutes through a dedicated IV line
 - A sterile, non-pyrogenic, low protein binding 0.2 micron in-line filter infusion set should be used
 - Administer the entire contents of the KIMMTRAK infusion bag to the patient
- Upon completion of KIMMTRAK infusion, flush the infusion line with adequate volume of sterile 0.9% Sodium Chloride Injection, USP to ensure that the entire contents of the infusion bag are administered
 - DO NOT mix KIMMTRAK with drugs other than albumin used during preparation or administer other drugs through the same IV line. Compatibility with other medications and fluids has not been established

KIMMTRAK Storage

- Store KIMMTRAK vials in the original carton refrigerated at 2 °C to 8 °C (36 °F to 46 °F) and protect from light until time of use
 - Do not freeze. DO NOT SHAKE
- KIMMTRAK does not contain a preservative
 - KIMMTRAK is stable for 4 hours if kept at room temperature. Administer the prepared infusion bag within 4 hours from the time of preparation including the duration of infusion (if kept at room temperature)
 - If not used immediately, store the KIMMTRAK infusion bag in a refrigerator at 2 °C to 8 °C (36 °F to 46 °F) **and infuse within 24 hours from the time of preparation**, which includes the storage time in the refrigerator, the time allowed for equilibration of the infusion bag to room temperature, and the duration of the infusion
 - Once removed from the refrigerator, do not refrigerate the KIMMTRAK infusion bag again
 - DO NOT freeze
 - Discard unused KIMMTRAK solution beyond the recommended storage time

Scan and Watch!



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Reminders

- **KIMMTRAK is not a hazardous drug under NIOSH**
- **Before preparation and administration of KIMMTRAK, verify the dose of KIMMTRAK**
 - The recommended dosage of KIMMTRAK administered intravenously is 20 mcg on day 1, 30 mcg on day 8, 68 mcg on day 15, and 68 mcg once every week thereafter

Patient Monitoring¹

Cytokine release syndrome (CRS), skin reactions, and elevated liver enzymes have occurred following KIMMTRAK infusion.

During the infusion and after KIMMTRAK administration, patients must be monitored for side effects.

A rise in temperature is generally the first sign of CRS, occurring earlier than drops in blood pressure. Once fever is detected, patients should be monitored more closely for changes in other vital signs like pulse rate, respiratory rate, and blood pressure. Consider managing symptoms early to help prevent CRS from escalating.

CRS (T cell activation)

- Fever
- Hypotension
- Hypoxia
- Chills
- Nausea
- Vomiting
- Rash
- Elevated Transaminases
- Fatigue
- Headache

Some of these symptoms may be associated with CRS OR may be isolated events.

Skin Reactions (gp100 expression in normal melanocytes)

- Rash
- Pruritus
- Skin hypopigmentation
- Edema
- Dry Skin
- Erythema
- Hair color changes

Elevated Liver Enzymes

Prior to the start of and during KIMMTRAK, monitor:

- Alanine aminotransferase (ALT)
- Aspartate aminotransferase (AST)
- Total blood bilirubin



NDC 80446-401-01

Low 3.3% discontinuation rate due to treatment-related adverse events¹

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KIMMTRAK
(tebentafusp-tebn)
Injection for Intravenous Use 100 mcg/0.5 mL

Possible Adverse Reactions¹

In clinical trials, CRS, skin reactions, and elevated liver enzymes have occurred following KIMMTRAK infusion. These events decreased in frequency and severity following each subsequent KIMMTRAK infusion

- KIMMTRAK commonly causes mild to moderate **CRS**, which if not identified and treated appropriately, may become life-threatening or fatal
- Most patients typically experienced CRS following each of the first 3 infusions. The majority (84%) of episodes of CRS started the day of infusion

Discontinuation Rate	All Grades	Grade 1	Grade 2	Grades 3 or 4
1.2%	89%	12%	76%	0.8%

- A rise in temperature is generally the first sign of CRS, occurring earlier than drops in blood pressure. Once fever is detected, patients should be monitored more closely for changes in other vital signs like pulse rate, respiratory rate, and blood pressure. Consider managing symptoms early to help prevent CRS from escalating
- CRS symptoms were generally reversible and were mostly managed with IV fluids, NSAIDs, or a single dose of systemic corticosteroids

Systemic Corticosteroids*	Supplemental Oxygen*	Vasopressor*
23%	8%	0.8%

* For at least one infusion.

Skin Reactions: Typically occurred following each of the first 3 infusions. Median time to onset was one day, with most resolved to \leq grade 1 between doses.

Discontinuation Rate	All Grades	Grade 1	Grade 2	Grade 3	Grades 4 or 5
0.00%	91%	26%	44%	21%	NONE

- Rash occurred in 83% of patients. Rash was often described as closer to symptoms of a sunburn than a typical rash. It could cause all or more of the body to turn red, and the skin to be sore, itchy, and peel. It can manifest differently in different patients
- Monitor patients for skin reactions. If skin reactions occur, treat with antihistamines and topical or systemic steroids based on persistence and severity of symptoms
- Most systems resolved without any long-term sequelae. Withhold or permanently discontinue KIMMTRAK depending on the severity of skin reactions

Elevated Liver Enzymes: The majority (73%) of ALT or AST elevations occurred within the first 3 infusions. Most patients experiencing grade 3 or 4 ALT/AST elevations had improvement to \leq grade 1 within 7 days.

Discontinuation Rate	All Grades	Grades 3 or 4
0.4%	65%	8%

Incidence of Treatment-Related AEs by Week During Treatment with KIMMTRAK²



Please see the Important Safety Information, including **BOXED WARNING for CRS** on page 9 and click [here](#) for full Prescribing Information.

Adverse Event (AE) Management¹

No dosage reduction for KIMMTRAK is recommended. For specific dosage modifications please refer to Section 2.3, Table 1 in full Prescribing Information.

CRS Grading and Management Guidance

Temperature ≥ 38 °C (100.4 °F) with:	CTCAE Grade*	Hold KIMMTRAK?	Treat with corticosteroids?	Corticosteroid premedication 30 minutes prior to next dose?	Can escalate to next dose?
• No hypotension or hypoxia	≤ Grade 1	NO	NO	NO	YES
• Hypotension that responds to fluids (does not require vasopressors) • Or hypoxia requiring low flow nasal cannula (≤ 6 L/min) or blow by oxygen	Grade 2 lasting <2 hours	NO	NO	NO	YES
	lasting 2-3 hours or recurrent	NO	YES[†]	YES	YES
	lasting >3 hours & not responding to therapy	YES	YES[†]	YES	NO
• Hemodynamic instability requiring vasopressor (with or without vasopressin) • Or worsening hypoxia or respiratory distress requiring high flow nasal cannula (≥ 6 L/min) or face mask	Grade 3	YES	YES[†]	YES	NO
• Hemodynamic instability requiring multiple vasopressors (excluding vasopressin) • Worsening hypoxia or respiratory distress despite oxygen administration requiring positive pressure	Grade 4	Permanently discontinue KIMMTRAK and treat with corticosteroids[†]			

* Based on ASTCT consensus grading of CRS criteria (Lee et al. 2019).

[†] If hypotension is not rapidly resolved (ie, within 2–3 hours of onset) with intravenous crystalloid therapy, intravenous corticosteroid therapy of methylprednisolone 2 mg/kg initial dose or equivalent and/or tocilizumab 8 mg/kg IV (not to exceed 800 mg/infusion) per institutional guidelines should be administered until symptoms (eg, hypotension) resolve.³

Grade 1 = Mild

Grade 2 = Moderate

Grade 3 = Severe

Grade 4 = Potentially life threatening

Skin Reaction Management and Dose Modifications

Severity	KIMMTRAK Dosage Modifications
Grade 1 ^a	• Treat symptomatically with antihistamines, oral analgesics, and topical steroids, as needed
Grade 2 or 3 ^a	• Withhold KIMMTRAK until \leq grade 1 or baseline • Resume KIMMTRAK at same dose level (ie, do not escalate if grade 3 skin reactions occurred during initial dose escalation; resume escalation once dosage is tolerated) • For persistent reactions not responding to oral steroids, consider intravenous corticosteroid (eg, 2 mg/kg/day methylprednisolone or equivalent)
Grade 4 ^a	• Permanently discontinue KIMMTRAK • Administer intravenous corticosteroid (eg, 2 mg/kg/day methylprednisolone or equivalent)

^a Based on National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) version 4.03 (NCI CTCAEv4.03).

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Elevated Liver Enzymes Management and Dose Modifications

Severity	KIMMTRAK Dosage Modifications
Grade 3 or 4 ^a	<ul style="list-style-type: none">• Withhold KIMMTRAK until \leq grade 1 or baseline• Resume KIMMTRAK at same dose level if the elevated liver enzymes occur in the setting of grade 3 CRS; resume escalation if next administration is tolerated• If the elevated liver enzymes occur outside the setting of grade 3 CRS<ul style="list-style-type: none">- resume escalation if the current dose is less than 68 mcg,- or resume at same dose level if dose escalation has completed• Administer intravenous corticosteroids if no improvement within 24 hour

^a Based on National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) version 4.03 (NCI CTCAEv4.03).

Other Adverse Reactions* Management and Dose Modifications

Severity	KIMMTRAK Dosage Modifications
Grade 3 ^a	<ul style="list-style-type: none">• Withhold KIMMTRAK until \leq grade 1 or baseline• Resume KIMMTRAK at same dose level (ie, do not escalate if other grade 3 adverse reaction occurred during initial dose escalation; resume escalation once dosage is tolerated)
Grade 4 ^a	<ul style="list-style-type: none">• Permanently discontinue KIMMTRAK

* Other adverse reactions as found in Section 6.1, Table 4 of full Prescribing Information.

^a Based on National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) version 4.03 (NCI CTCAEv4.03).

Reminders for Patients¹

! Consider discussing with patients the frequency of monitoring and the possible side effects that can occur. Remind the patient to alert the provider or nursing staff if they have:

- Fever
- Tiredness or weakness
- Vomiting
- Chills
- Nausea
- Low blood pressure
- Dizziness and light headedness
- Headache
- Right-sided abdominal pain or yellowing of the skin or eyes (ie, abnormal liver blood tests)
- Wheezing and trouble breathing
- Rash
- Patchy or extensive redness, pain, itching or swelling of skin (rash)
- Redness, pain, or swelling around the eye, eyelid, or inner lining of the eyelid
- Dry skin and skin peeling

! Importance of patients keeping their infusion appointments

- Emphasize to patients the importance of keeping their weekly infusion schedule. To maximize the patient's opportunity to experience the overall survival benefit seen in clinical trials, patients must receive KIMMTRAK weekly, as prescribed
- Breaks in treatment, if needed, were allowed in the clinical trials for up to 2 weeks. Breaks for more than 2 weeks are not recommended
 - Side effects may occur at the same frequency and severity as a patient who is initiating treatment (first 3 infusions)
 - The impact on outcomes for breaks longer than 2 weeks has not been evaluated

! If KIMMTRAK is well tolerated during the first 3 infusions, the patient may be able to continue weekly treatments in an appropriate healthcare setting closer to home

- KIMMTRAK CONNECT[®] can help the patient find closer to home options



KIMMTRAKCONNECT.com
844-775-CARE (844-775-2273)



Please see the Important Safety Information, including **BOXED WARNING for CRS** on page 9 and click [here](#) for full Prescribing Information.

Indication and Important Safety Information Including Boxed Warning

Indication

KIMMTRAK is a bispecific gp100 peptide-HLA-directed CD3 T cell engager indicated for the treatment of HLA-A*02:01-positive adult patients with unresectable or metastatic uveal melanoma.

Important Safety Information Including Boxed Warning

WARNING: CYTOKINE RELEASE SYNDROME

Cytokine Release Syndrome (CRS), which may be serious or life-threatening, occurred in patients receiving KIMMTRAK. Monitor for at least 16 hours following first three infusions and then as clinically indicated. Manifestations of CRS may include fever, hypotension, hypoxia, chills, nausea, vomiting, rash, elevated transaminases, fatigue, and headache. CRS occurred in 89% of patients who received KIMMTRAK with 0.8% being grade 3 or 4. Ensure immediate access to medications and resuscitative equipment to manage CRS. Ensure patients are euvolemic prior to initiating the infusions. Closely monitor patients for signs or symptoms of CRS following infusions of KIMMTRAK. Monitor fluid status, vital signs, and oxygenation level and provide appropriate therapy. Withhold or discontinue KIMMTRAK depending on persistence and severity of CRS.

Skin Reactions

Skin reactions, including rash, pruritus, and cutaneous edema occurred in 91% of patients treated with KIMMTRAK. Monitor patients for skin reactions. If skin reactions occur, treat with antihistamine and topical or systemic steroids based on persistence and severity of symptoms. Withhold or permanently discontinue KIMMTRAK depending on the severity of skin reactions.

Elevated Liver Enzymes

Elevations in liver enzymes occurred in 65% of patients treated with KIMMTRAK. Monitor alanine aminotransferase (ALT), aspartate aminotransferase (AST), and total blood bilirubin prior to the start of and during treatment with KIMMTRAK. Withhold KIMMTRAK according to severity.

Embryo-Fetal Toxicity

KIMMTRAK may cause fetal harm. Advise pregnant patients of potential risk to the fetus and patients of reproductive potential to use effective contraception during treatment with KIMMTRAK and 1 week after the last dose.

The most common adverse reactions ($\geq 30\%$) in patients who received KIMMTRAK were cytokine release syndrome, rash, pyrexia, pruritus, fatigue, nausea, chills, abdominal pain, edema, hypotension, dry skin, headache, and vomiting. The most common ($\geq 50\%$) laboratory abnormalities were decreased lymphocyte count, increased creatinine, increased glucose, increased AST, increased ALT, decreased hemoglobin, and decreased phosphate.

Please see [full Prescribing Information](#), including **BOXED WARNING for CRS**.



**For questions or to
report adverse events**

**For more information or to report suspected
adverse reactions, contact the Immunocore
Medical Information Center at 1-844-IMMUNO-1
(1-844-466-8661).**



For patient assistance, contact:



KIMMTRAKCONNECT®

**KIMMTRAKCONNECT.com
844-775-CARE (844-775-2273)**



References: 1. Kimmtrak. Package Insert. Immunocore Ltd; 2022. 2. Nathan P, Hassel JC, Rutkowski P, et al; IMCgp100-202 Investigators. Overall survival benefit with tebentafusp in metastatic uveal melanoma. *N Engl J Med.* 2021;385:1196-206. doi:10.1056/NEJMoa2103485 3. Protocol for: Nathan P, Hassel JC, Rutkowski P, et al; IMCgp100-202 Investigators. Overall survival benefit with tebentafusp in metastatic uveal melanoma. *N Engl J Med.* 2021;385:1196-206. doi:10.1056/NEJMoa2103485

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 **KIMMTRAK**
(tebentafusp-tebn)
Injection for Intravenous Use 100 mcg/0.5 mL