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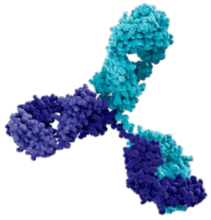
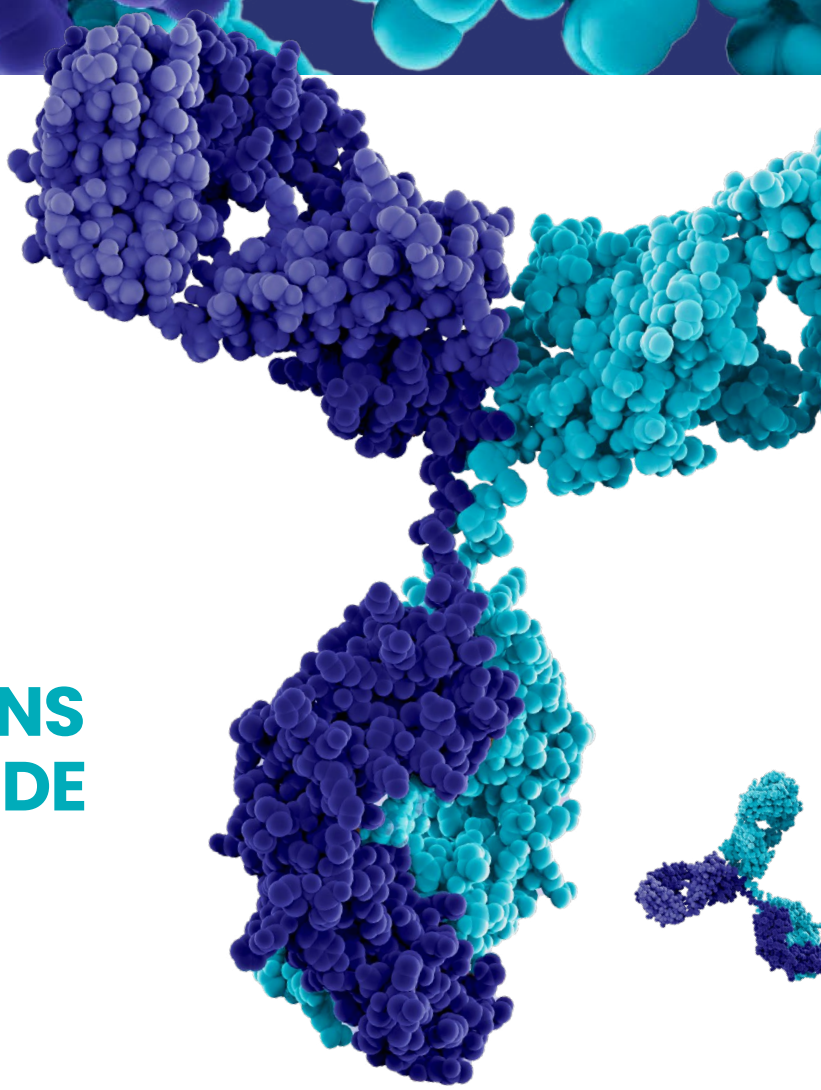
# ADVERSE REACTIONS MANAGEMENT GUIDE





**INDICATION**

EPKINLY is indicated for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL), not otherwise specified (NOS), including DLBCL arising from indolent lymphoma, and high-grade B-cell lymphoma (HGBL) after 2 or more lines of systemic therapy.

This indication is approved under accelerated approval based on 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(s).

**SELECT IMPORTANT SAFETY INFORMATION**

**BOXED WARNINGS:**

- **Cytokine release syndrome (CRS), including serious or life-threatening reactions, can occur in patients receiving EPKINLY. Initiate treatment with the EPKINLY step-up dosing schedule to reduce the incidence and severity of CRS. Withhold EPKINLY until CRS resolves or permanently discontinue based on severity.**
- **Immune effector cell–associated neurotoxicity syndrome (ICANS), including life-threatening and fatal reactions, can occur with EPKINLY. Monitor patients for neurological signs or symptoms of ICANS during treatment. Withhold EPKINLY until ICANS resolves or permanently discontinue based on severity.**

**Additional Warnings & Precautions:** Infections, Cytopenias, and Embryo-Fetal Toxicity.

**Please see additional Important Safety Information on pages 3-4 and throughout this brochure.**
**Please see full Prescribing Information.**

# Introduction

This guide was developed to help healthcare providers understand more about the adverse reactions that may occur in patients who are receiving EPKINLY. You play a critical role in caring for and monitoring patients, administering drug and managing dose modifications when needed, and providing supportive care, all of which may help your patients with relapsed or refractory diffuse large B-cell lymphoma (R/R DLBCL) stay on treatment with EPKINLY.[1]

## TABLE OF CONTENTS



NHL=non-Hodgkin lymphoma.

**Please see Important Safety Information, including Boxed Warnings for CRS and ICANS, on pages 3-4 and throughout this brochure.**
**Please see full Prescribing Information.**

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# IMPORTANT SAFETY INFORMATION

## BOXED WARNINGS

- **Cytokine release syndrome (CRS), including serious or life-threatening reactions, can occur in patients receiving EPKINLY. Initiate treatment with the EPKINLY step-up dosing schedule to reduce the incidence and severity of CRS. Withhold EPKINLY until CRS resolves or permanently discontinue based on severity.**
- **Immune effector cell–associated neurotoxicity syndrome (ICANS), including life-threatening and fatal reactions, can occur with EPKINLY. Monitor patients for neurological signs or symptoms of ICANS during treatment. Withhold EPKINLY until ICANS resolves or permanently discontinue based on severity.**

### Cytokine Release Syndrome (CRS)

- EPKINLY can cause CRS, including serious or life-threatening reactions. CRS occurred in 51% of patients at the recommended dose in the clinical trial (37% grade 1, 17% grade 2, and 2.5% grade 3). Recurrent CRS occurred in 16% of patients. Of all the CRS events, most (92%) occurred during cycle 1. In cycle 1, 9% of CRS events occurred after the 0.16 mg dose (cycle 1, day 1), 16% after the 0.8 mg dose (cycle 1, day 8), 61% after the 48 mg dose (cycle 1, day 15), and 6% after the 48 mg dose (cycle 1, day 22). The median time to onset of CRS from the most recently administered EPKINLY dose across all doses was 24 hours (range, 0-10 days). The median time to onset after the first full 48 mg dose was 21 hours (range, 0-7 days). CRS resolved in 98% of patients; the median duration of CRS events was 2 days (range, 1-27 days).
- Signs and symptoms of CRS can include pyrexia, hypotension, hypoxia, dyspnea, chills, and tachycardia. Concurrent neurological adverse reactions associated with CRS occurred in 2.5% of patients and included headache, confusional state, tremors, dizziness, and ataxia.
- Initiate EPKINLY according to the step-up dosing schedule. Administer pretreatment medications to reduce the risk of CRS and monitor patients for potential CRS. Following administration of the first 48 mg dose, patients should be hospitalized for 24 hours. At the first signs or symptoms of CRS, immediately evaluate patients for hospitalization, manage per current practice guidelines, and administer supportive care as appropriate. Withhold or discontinue EPKINLY based on the severity of CRS.
- Patients who experience CRS (or other adverse reactions that impair consciousness) should be evaluated and advised not to drive and to refrain from operating heavy or potentially dangerous machinery until resolution.

### Immune Effector Cell–Associated Neurotoxicity Syndrome (ICANS)

- EPKINLY can cause life-threatening and fatal ICANS. ICANS occurred in 6% (10/157) of patients in the clinical trial (4.5% grade 1, 1.3% grade 2, 0.6% fatal: 1 event). Of the 10 ICANS events, 9 occurred in cycle 1 of treatment. The median time to onset was 16.5 days (range, 8-141 days) from the start of treatment. Relative to the most recent administration, the median time to onset was 3 days (range, 1-13 days). The median duration of ICANS was 4 days (range, 0-8 days), with ICANS resolving in 90% of patients with supportive care.
- Signs and symptoms of ICANS can include confusional state, lethargy, tremors, dysgraphia, aphasia, and nonconvulsive status epilepticus. The onset of ICANS can be concurrent with CRS, following resolution of CRS, or in the absence of CRS.
- Monitor for potential ICANS. At the first signs or symptoms of ICANS, immediately evaluate patient and provide supportive therapy based on severity. Withhold or discontinue EPKINLY per recommendations and consider further management per current practice guidelines.
- Patients who experience signs or symptoms of ICANS or any other adverse reactions that impair cognition or consciousness should be evaluated, including potential neurology evaluation, and patients at increased risk should be advised not to drive and to refrain from operating heavy or potentially dangerous machinery until resolution.

**Please see additional Important Safety Information on page 4.**
**Please see full Prescribing Information.**

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# IMPORTANT SAFETY INFORMATION (continued)

**Infections**

- EPKINLY can cause serious and fatal infections. In the clinical trial, serious infections, including opportunistic infections, were reported in 15% of patients treated with EPKINLY at the recommended dose (14% grade 3 or 4, 1.3% fatal). The most common grade 3 or greater infections were sepsis, COVID-19, urinary tract infection, pneumonia, and upper respiratory tract infection.
- Monitor patients for signs and symptoms of infection prior to and during treatment with EPKINLY and treat appropriately. Avoid administration of EPKINLY in patients with active infections.
- Prior to starting EPKINLY, provide *Pneumocystis jirovecii* pneumonia (PJP) prophylaxis and consider prophylaxis against herpes virus.
- Withhold or consider permanent discontinuation of EPKINLY based on severity.

**Cytopenias**

- EPKINLY can cause serious or severe cytopenias, including neutropenia, anemia, and thrombocytopenia. Among patients who received the recommended dose in the clinical trial, grade 3 or 4 events occurred in 32% (decreased neutrophils), 12% (decreased hemoglobin), and 12% (decreased platelets). Febrile neutropenia occurred in 2.5%.
- Monitor complete blood counts throughout treatment. Based on severity of cytopenias, temporarily withhold or permanently discontinue EPKINLY. Consider prophylactic granulocyte colony-stimulating factor administration as applicable.

**Embryo-Fetal Toxicity**

- EPKINLY may cause fetal harm. Advise pregnant women of the potential risk to the fetus. Verify pregnancy status in females of reproductive potential prior to initiating EPKINLY. Advise females of reproductive potential to use effective contraception during treatment with EPKINLY and for 4 months after the last dose.

**Adverse Reactions**

- The most common (≥20%) adverse reactions were CRS, fatigue, musculoskeletal pain, injection site reactions, pyrexia, abdominal pain, nausea, and diarrhea. The most common grade 3 to 4 laboratory abnormalities (≥10%) were decreased lymphocyte count, decreased neutrophil count, decreased white blood cell count, decreased hemoglobin, and decreased platelets.

**Lactation**

- Advise women not to breastfeed during treatment and for 4 months after the last dose of EPKINLY.

**Please see additional Important Safety Information, including Boxed Warnings for CRS and ICANS, on page 3. Please see full Prescribing Information, including Boxed Warnings.**

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# Adverse reactions in the EPCORE™ NHL-1 trial[1]

The safety of EPKINLY was evaluated in EPCORE NHL-1, a single-arm trial of 157 patients with R/R LBCL after 2 or more lines of systemic therapy, including DLBCL NOS, DLBCL arising from indolent lymphoma, HGBL, and other B-cell lymphomas.

| Adverse Reactions (≥10%) | All Grades (%) | Grade 3 or 4[a] (%) |
|---|---|---|
| Cytokine release syndrome | 51 | 2.5 |
| Fatigue[b] | 29 | 2.5 |
| Musculoskeletal pain[b] | 28 | 1.3 |
| Injection site reactions[b] | 27 | 0 |
| Pyrexia | 24 | 0 |
| Abdominal pain[b] | 23 | 1.9 |
| Nausea | 20 | 1.3 |
| Diarrhea | 20 | 0 |
| Rash[b] | 15 | 0.6 |
| Edema[b] | 14 | 1.9 |
| Headache | 13 | 0.6 |
| Vomiting | 12 | 0.6 |
| Decreased appetite | 12 | 0.6 |
| Cardiac arrhythmias[b] | 10 | 0.6 |

[a]Only grade 3 adverse reactions occurred.
[b]Term includes other related terms. See Prescribing Information.

- Median duration of exposure was 5 cycles (range, 1-20 cycles)
- Serious adverse reactions occurred in 54% of patients (reactions occurring ≥2%: CRS, infections,* pleural effusion, febrile neutropenia, fever, and ICANS)
- Fatal adverse reactions occurred in 3.8% of patients (1.3% COVID-19, 0.6% hepatotoxicity, 0.6% ICANS, 0.6% myocardial infarction, 0.6% pulmonary embolism)
- Discontinuation due to an adverse reaction occurred in 3.8% of patients (reactions included COVID-19, CRS, ICANS, pleural effusion, and fatigue)
- Dosage interruptions due to an adverse reaction occurred in 34% of patients (reactions occurring ≥3%: CRS, neutropenia, sepsis, and thrombocytopenia)
- The most common grade 3 to 4 laboratory abnormalities (≥10%) were decreased lymphocyte count, decreased neutrophil count, decreased white blood cell count, decreased hemoglobin, and decreased platelets
- Clinically relevant adverse reactions in <10% of patients included ICANS, sepsis, pleural effusion, COVID-19, pneumonia, tumor flare, febrile neutropenia, upper respiratory tract infections, and tumor lysis syndrome

*Infections included sepsis, COVID-19, pneumonia, and upper respiratory tract infections.

**Please see additional Important Safety Information, including Boxed Warnings for CRS and ICANS, on pages 3-4 and throughout this brochure.**
**Please see full Prescribing Information.**

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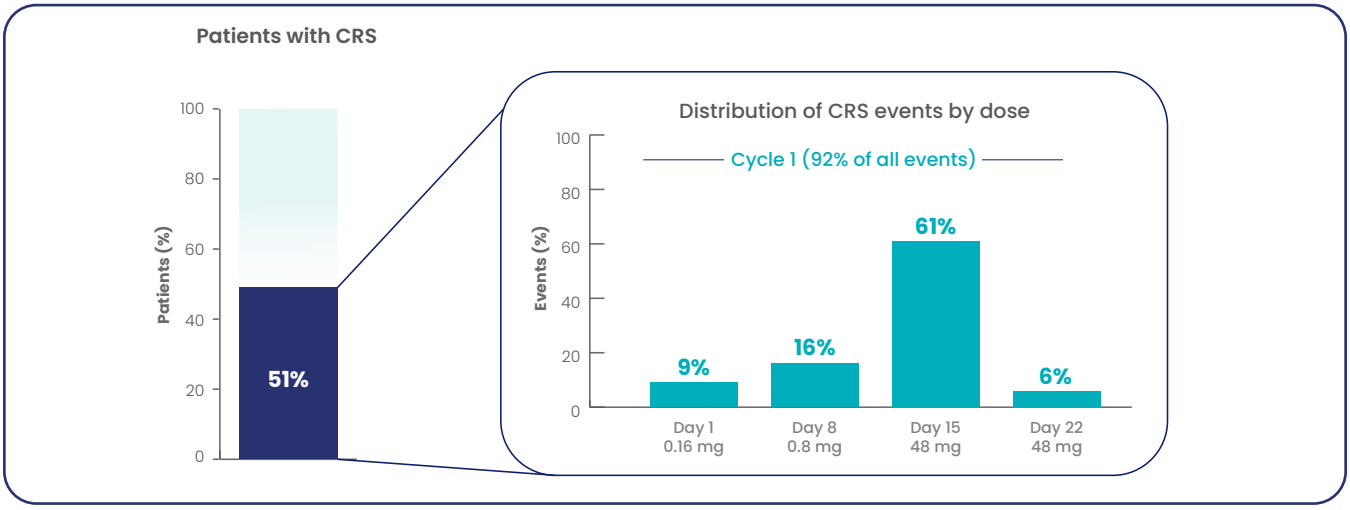
# Managing cytokine release syndrome (CRS)[1]

## CRS events by dosing period in the EPCORE NHL-1 clinical trial

**Most CRS events (92%) occurred in cycle 1 and were associated with the first full dose**

- CRS occurred in 51% of patients receiving the recommended dose in the clinical trial. Recurrent CRS occurred in 16% of patients




- The median time to onset of CRS from the most recently administered EPKINLY dose across all doses was 24 hours (range, 0-10 days)
  - The median time to onset after the first full 48-mg dose was 21 hours (range, 0-7 days)
- CRS resolved in 98% of patients; the median duration of CRS events was 2 days (range, 1-27 days)

## CRS events by grade

| Any grade | Grade 1 | Grade 2 | Grade 3 | Grade 4 |
|---|---|---|---|---|
| 51% | 37% | 17% | 2.5% | 0% |

**See CRS management guidance on pages 8-9.**

## SELECT IMPORTANT SAFETY INFORMATION

BOXED WARNINGS

- **Cytokine release syndrome (CRS), including serious or life-threatening reactions, can occur in patients receiving EPKINLY. Initiate treatment with the EPKINLY step-up dosing schedule to reduce the incidence and severity of CRS. Withhold EPKINLY until CRS resolves or permanently discontinue based on severity.**

**Please see additional Important Safety Information, including Boxed Warnings for CRS and ICANS, on pages 3-4 and throughout this brochure.**
**Please see full Prescribing Information.**

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## EPKINLY administration[1]

- EPKINLY should only be administered by a qualified healthcare professional with appropriate medical support to manage severe reactions such as CRS
- Administer EPKINLY subcutaneously according to the step-up dosage schedule and administer pretreatment medications to reduce the incidence and severity of CRS:
  - Cycle 1: 0.16 mg (Step-up dose 1) on day 1, 0.8 mg (Step-up dose 2) on day 8, 48 mg (full dose) on days 15 and 22
  - Cycles 2-3: 48 mg weekly
  - Cycles 4-9: 48 mg every 2 weeks
  - Cycles 10+: 48 mg every 4 weeks

## Recommended premedications

Between 30 and 120 minutes prior to administration of EPKINLY, administer the following medications:

- Cycle 1: For all patients, administer prior to each weekly administration of EPKINLY
  - **Prednisolone** (100 mg oral or IV) or **dexamethasone** (15 mg oral or IV) or equivalent (and for 3 consecutive days following each weekly administration)
  - **Diphenhydramine** (50 mg oral or IV) or equivalent
  - **Acetaminophen** (650-1000 mg oral)
- Cycles 2+: For patients who experienced grade 2 or 3* CRS with previous dose, administer prior to next administration until EPKINLY is given without subsequent CRS of grade 2 or higher
  - **Prednisolone** (100 mg oral or IV) or **dexamethasone** (15 mg oral or IV) or equivalent (and for 3 consecutive days following administration of EPKINLY)

*Patients will be permanently discontinued from EPKINLY after a grade 4 CRS event.

## Monitor patients

- Due to the risk of CRS and ICANS, patients should be hospitalized for 24 hours after administration of the cycle 1, day 15 dosage of 48 mg
- Signs and symptoms of CRS can include pyrexia, hypotension, hypoxia, dyspnea, chills, and tachycardia
- Concurrent neurological adverse reactions associated with CRS occurred in 2.5% of patients and included headache, confusional state, tremors, dizziness, and ataxia
- At the first signs or symptoms of CRS, immediately evaluate patients for hospitalization, manage per current practice guidelines, and administer supportive care as appropriate. Withhold or discontinue EPKINLY based on the severity of CRS

## Counsel patients about CRS

- Inform patients and their care partners of the risk of CRS
- Advise them to immediately contact their healthcare provider should signs and symptoms associated with CRS occur. These can include pyrexia, hypotension, hypoxia, chills, tachycardia, headache, and dyspnea
- Advise patients that they should be hospitalized for 24 hours after administration of the cycle 1, day 15 dosage of 48 mg
- Advise patients who experience symptoms that impair consciousness not to drive and refrain from operating heavy or potentially dangerous machinery until events resolve

IV=intravenous.

**Please see additional Important Safety Information, including Boxed Warnings for CRS and ICANS, on pages 3-4 and throughout this brochure.**
**Please see full Prescribing Information.**

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## What to do if CRS is suspected[1]

- Identify CRS based on clinical presentation. Evaluate for and treat other causes of fever, hypotension, and hypoxia
- Withhold EPKINLY until CRS resolves
- Manage according to the recommendations in the following table (from Section 2.6 Table 4 of full Prescribing Information) and consider further management per current practice guidelines
- Administer supportive therapy for CRS, which may include intensive care for severe or life-threatening CRS

## Recommendations for management of CRS

| Grade 1[a] | Actions |
|---|---|
| Temperature ≥100.4°F (38°C)[b] | **Withhold EPKINLY**<br>• Manage per current practice guidelines<br>• Ensure CRS symptoms are resolved prior to next dose of EPKINLY[c] |

| Grade 2[a] | Actions |
|---|---|
| Temperature ≥100.4°F (38°C)[b]<br>**with**<br>Hypotension not requiring vasopressors<br>**and/or**<br>Hypoxia requiring low-flow oxygen[e] by nasal cannula or blow-by | **Withhold EPKINLY**<br>• Manage per current practice guidelines<br>• Ensure CRS symptoms are resolved prior to next dose of EPKINLY[c]<br>• Administer premedication[d] prior to next dose of EPKINLY<br>• For the next dose of EPKINLY, monitor more frequently and consider hospitalization |

[a]Based on ASTCT 2019 grading for CRS.
[b]Premedication may mask fever, therefore if clinical presentation is consistent with CRS, follow these management guidelines.
[c]Refer to Table 2 in Section 2.3 of the Prescribing Information for information on restarting EPKINLY after dosage delays.
[d]If grade 2 or 3 CRS occurs with the second full dose (48 mg) or beyond, administer CRS premedications with each subsequent dose until an EPKINLY dose is given without subsequent CRS of grade 2 or higher. Refer to Table 3 in Section 2.4 of the Prescribing Information for additional information on premedication.
[e]Low-flow oxygen defined as oxygen delivered at <6 L/minute; high-flow oxygen defined as oxygen delivered at ≥6 L/minute.

ASTCT=American Society for Transplantation and Cellular Therapy.

**Please see additional Important Safety Information, including Boxed Warnings for CRS and ICANS, on pages 3-4 and throughout this brochure.**
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| Grade 3[a] | Actions |
|---|---|
| Temperature ≥100.4°F (38°C)[b]<br>**with**<br>Hypotension requiring a vasopressor (with or without vasopressin)<br>**and/or**<br>Hypoxia requiring high-flow oxygen[e] by nasal cannula, face mask, non-rebreather mask, or Venturi mask | **Withhold EPKINLY**<br>• Manage per current practice guidelines, which may include intensive care<br>• Ensure CRS symptoms are resolved prior to next dose of EPKINLY[c]<br>• Administer premedication[d] prior to next dose of EPKINLY<br>• Hospitalize for next dose of EPKINLY<br>**Recurrent grade 3 CRS**<br>**Permanently discontinue EPKINLY**<br>• Manage CRS per current practice guidelines and provide supportive therapy, which may include intensive care |

| Grade 4[a] | Actions |
|---|---|
| Temperature ≥100.4°F (38°C)[b]<br>**with**<br>Hypotension requiring multiple vasopressors (excluding vasopressin)<br>**and/or**<br>Hypoxia requiring oxygen by positive pressure (eg, CPAP, BiPAP, intubation, and mechanical ventilation) | **Permanently discontinue EPKINLY**<br>• Manage CRS per current practice guidelines and provide supportive therapy, which may include intensive care |

BiPAP=bilevel positive airway pressure; CPAP=continuous positive airway pressure.

**Please see additional Important Safety Information, including Boxed Warnings for CRS and ICANS, on pages 3-4 and throughout this brochure.**
**Please see full Prescribing Information.**

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# Managing immune effector cell–associated neurotoxicity syndrome (ICANS)[1]

## ICANS events in the EPCORE NHL-1 clinical trial

- ICANS occurred in 6% (10/157) of patients, of the 10 events, 9 occurred within cycle 1
- Median time to onset was 3 days (range, 1-13 days) relative to the most recent administration
- Median time to onset was 16.5 days (range, 8-141 days) from the start of treatment
- Median duration of ICANS was 4 days (range, 0-8 days)

## ICANS events by grade

| Grade 1 | Grade 2 | Grade 3 | Grade 4 | Grade 5 |
|---|---|---|---|---|
| 4.5% | 1.3% | 0% | 0% | 0.6% (fatal) |

- ICANS resolved in 90% (9/10) of patients with supportive care

**See ICANS management guidance on pages 12-13.**

## SELECT IMPORTANT SAFETY INFORMATION

BOXED WARNINGS

- **Immune effector cell–associated neurotoxicity syndrome (ICANS), including life-threatening and fatal reactions, can occur with EPKINLY. Monitor patients for neurological signs or symptoms of ICANS during treatment. Withhold EPKINLY until ICANS resolves or permanently discontinue based on severity.**

**Please see additional Important Safety Information, including Boxed Warnings for CRS and ICANS, on pages 3-4 and throughout this brochure.**
**Please see full Prescribing Information.**

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## EPKINLY administration[1]

- EPKINLY should only be administered by a qualified healthcare professional with appropriate medical support to manage severe reactions such as ICANS
- Administer EPKINLY subcutaneously according to the step-up dosage schedule:
  - Cycle 1: 0.16 mg (Step-up dose 1) on day 1, 0.8 mg (Step-up dose 2) on day 8, 48 mg (full dose) on days 15 and 22
  - Cycles 2-3: 48 mg weekly
  - Cycles 4-9: 48 mg every 2 weeks
  - Cycles 10+: 48 mg every 4 weeks

## Monitor patients

- Due to the risk of CRS and ICANS, patients should be hospitalized for 24 hours after administration of the cycle 1, day 15 dosage of 48 mg
- Signs and symptoms of ICANS can include confusional state, lethargy, tremor, dysgraphia, aphasia, and nonconvulsive status epilepticus
- The onset of ICANS can be concurrent with CRS, following resolution of CRS, or in the absence of CRS
- At the first signs or symptoms of ICANS, immediately evaluate patient and provide supportive therapy based on severity. Withhold or discontinue EPKINLY per recommendations and consider further management per current practice guidelines

## Counsel patients about ICANS

- Advise patients and their care partners of the risks of ICANS, and to immediately contact their healthcare provider for signs and symptoms of ICANS. The onset of events may be delayed and can include:

- confusional state
- lethargy
- tremor
- dysgraphia
- aphasia
- nonconvulsive status epilepticus

- Advise patients who experience symptoms of ICANS that impair consciousness to refrain from driving or operating heavy or potentially dangerous machinery until symptoms of ICANS resolve

## What to do if ICANS is suspected

- At first sign of ICANS, withhold EPKINLY and consider neurology evaluation. Rule out other causes of neurologic symptoms. Provide supportive therapy, which may include intensive care, for ICANS
- Manage according to the recommendations in the table (from Section 2.6 Table 5 of full Prescribing Information) on the next page and consider further management per current practice guidelines

**Please see additional Important Safety Information, including Boxed Warnings for CRS and ICANS, on pages 3-4 and throughout this brochure.**
**Please see full Prescribing Information.**

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## Recommendations for management of ICANS[1]

| Grade 1[a,b] | Actions |
|---|---|
| **ICE score 7–9[c]**<br>**or**<br>**Depressed level of consciousness[d]:**<br>• Awakens spontaneously | **Withhold EPKINLY until ICANS resolves[e]**<br>• Monitor neurologic symptoms and consider consultation with neurologist and other specialists for further evaluation and management, including consideration for starting nonsedating, antiseizure medicines for seizure prophylaxis |

| Grade 2[a,b] | Actions |
|---|---|
| **ICE score 3–6[c]**<br>**or**<br>**Depressed level of consciousness[d]:**<br>• Awakens to voice | **Withhold EPKINLY until ICANS resolves[e]**<br>• Administer dexamethasone[f] 10 mg intravenously every 6 hours. Continue dexamethasone use until resolution to grade 1 or less, then taper<br>• Monitor neurologic symptoms and consider consultation with neurologist and other specialists for further evaluation and management, including consideration for starting nonsedating, antiseizure medicines for seizure prophylaxis |

| Grade 3[a,b] | Actions |
|---|---|
| **ICE score 0–2[c]**<br>**or**<br>**Depressed level of consciousness[d]:**<br>• Awakens only to tactile stimulus<br>**or**<br>**Seizures,[d] either:**<br>• Any clinical seizure, focal or generalized, that resolves rapidly, or<br>• Nonconvulsive seizures on electroencephalogram (EEG) that resolve with intervention<br>**or**<br>**Raised intracranial pressure:** focal/local edema on neuroimaging[d] | **First occurrence of grade 3 ICANS**<br>**Withhold EPKINLY until ICANS resolves[e]**<br>• Administer dexamethasone[f] 10 mg intravenously every 6 hours. Continue dexamethasone use until resolution to grade 1 or less, then taper<br>• Monitor neurologic symptoms and consider consultation with neurologist and other specialists for further evaluation and management, including consideration for starting nonsedating, antiseizure medicines for seizure prophylaxis<br>• Provide supportive therapy, which may include intensive care<br>**Recurrent grade 3 ICANS**<br>**Permanently discontinue EPKINLY**<br>• Administer dexamethasone[f] 10 mg intravenously every 6 hours. Continue dexamethasone use until resolution to grade 1 or less, then taper<br>• Monitor neurologic symptoms and consider consultation with neurologist and other specialists for further evaluation and management, including consideration for starting nonsedating, antiseizure medicines for seizure prophylaxis<br>• Provide supportive therapy, which may include intensive care |

**Please see additional Important Safety Information, including Boxed Warnings for CRS and ICANS, on pages 3-4 and throughout this brochure.**
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| Grade 4[a,b] | Actions |
|---|---|
| **ICE score 0[c]**<br>**or**<br>**Depressed level of consciousness,[d] either:**<br>• Patient is unarousable or requires vigorous or repetitive tactile stimuli to arouse, or<br>• Stupor or coma<br>**or**<br>**Seizures,[d] either:**<br>• Life-threatening prolonged seizure (>5 minutes), or<br>• Repetitive clinical or electrical seizures without return to baseline in between<br>**or**<br>**Motor findings[d]:**<br>• Deep focal motor weakness, such as hemiparesis or paraparesis<br>**or**<br>**Raised intracranial pressure/cerebral edema,[d] with signs/symptoms such as:**<br>• Diffuse cerebral edema on neuroimaging, or<br>• Decerebrate or decorticate posturing, or<br>• Cranial nerve VI palsy, or<br>• Papilledema, or<br>• Cushing's triad | **Permanently discontinue EPKINLY**<br>• Administer dexamethasone[f] 10 mg intravenously every 6 hours. Continue dexamethasone use until resolution to grade 1 or less, then taper<br>• Alternatively, consider administration of methylprednisolone 1000 mg per day intravenously and continue methylprednisolone 1000 mg per day intravenously for 2 or more days<br>• Monitor neurologic symptoms and consider consultation with neurologist and other specialists for further evaluation and management, including consideration for starting nonsedating, antiseizure medicines for seizure prophylaxis<br>• Provide supportive therapy, which may include intensive care |

**For the ICE assessment tool, please see page 14.**

[a]Based on ASTCT 2019 grading for ICANS.
[b]Management is determined by the most severe event, not attributable to any other cause.
[c]See ICE assessment tool on next page. If patient is unarousable and unable to perform ICE Assessment (grade 4 ICANS) = 0 points.
[d]Not attributable to any other cause.
[e]See Table 2 in Section 2.3 of the Prescribing Information for recommendations on restarting EPKINLY after dosage delays.
[f]All references to dexamethasone administration are dexamethasone or equivalent.

ICE=immune effector cell–associated encephalopathy.

**Please see additional Important Safety Information, including Boxed Warnings for CRS and ICANS, on pages 3-4 and throughout this brochure.**
**Please see full Prescribing Information.**

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## Immune Effector Cell-Associated Encephalopathy (ICE) assessment tool[1,2]

| Cognitive domain | Task | Points |
|---|---|---|
| **Orientation** | Orientation to year<br>Orientation to month<br>Orientation to city<br>Orientation to hospital | 1<br>1<br>1<br>1 |
| **Naming** | Ability to name 3 common objects (eg, point to clock, pen, button) | 3 |
| **Following commands** | Ability to follow simple commands (eg, "Show me 2 fingers" or "Close your eyes and stick out your tongue") | 1 |
| **Writing** | Ability to write a standard sentence (eg, "Our national bird is the bald eagle") | 1 |
| **Attention** | Ability to count backward from 100 by 10 | 1 |
| **Maximum ICE score** | | **10** |

# Managing other adverse reactions[1]

### Infection and cytopenia events in the EPCORE NHL-1 clinical trial

- EPKINLY can cause serious and fatal infections, and serious or severe cytopenias, including neutropenia, anemia, and thrombocytopenia
- Serious infections, including opportunistic infections, were reported in 15% of patients treated with EPKINLY at the recommended dose, with grade 3 or 4 infections in 14% and fatal infections in 1.3%
- The most common grade 3 or greater infections were sepsis, COVID-19, urinary tract infection, pneumonia, and upper respiratory tract infection
- In the clinical trial, grade 3 or 4 decreased neutrophils occurred in 32%, decreased hemoglobin in 12%, and decreased platelets in 12% of patients. Febrile neutropenia occurred in 2.5%

**Please see additional Important Safety Information, including Boxed Warnings for CRS and ICANS, on pages 3-4 and throughout this brochure.**
**Please see full Prescribing Information.**

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## Prior to and after administration[1]

- Avoid administration of EPKINLY in patients with active infections
- Provide *Pneumocystis jirovecii* pneumonia (PJP) prophylaxis prior to initiating treatment with EPKINLY
- Consider initiating prophylaxis against herpes virus prior to starting EPKINLY to prevent herpes zoster reactivation
- Monitor patients for signs and symptoms of infection, prior to and during treatment with EPKINLY and treat appropriately
- Monitor complete blood counts throughout treatment
- Based on the severity of cytopenias, temporarily withhold or permanently discontinue EPKINLY. Consider prophylactic granulocyte colony-stimulating factor administration as applicable

## Counsel patients

- Advise patients of the risk of serious infections, and to contact their healthcare provider for signs or symptoms of serious infection
- Discuss the signs and symptoms associated with cytopenias, including neutropenia and febrile neutropenia, anemia, and thrombocytopenia

## Recommended dosage modification for other adverse reactions

| Adverse reaction[a] | Severity[a] | Action |
|---|---|---|
| **Infections** | Grades 1-4 | **Withhold EPKINLY**<br>• In patients with active infection, until the infection resolves[b]<br>• For grade 4, consider permanent discontinuation of EPKINLY |
| **Neutropenia** | Absolute neutrophil count (ANC) <0.5 x $10^9$/L | **Withhold EPKINLY**<br>• Until ANC ≥0.5 x $10^9$/L |
| **Thrombocytopenia** | Platelet count <50 x $10^9$/L | **Withhold EPKINLY**<br>• Until platelet count ≥50 x $10^9$/L |
| **Other adverse reactions** | Grade 3 or higher | **Withhold EPKINLY**<br>• Until the toxicity resolves to grade 1 or baseline[b] |

[a]Based on National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE), version 5.0.
[b]See Table 2 in Section 2.3 of the Prescribing Information for recommendations on restarting EPKINLY after dosage delays.

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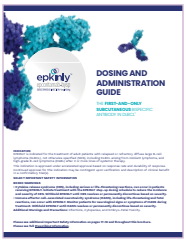
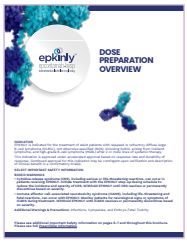
# Additional EPKINLY resources for healthcare providers




## Dosing and Administration Guide

A comprehensive resource containing information on the dosing schedule, premedications, dose modifications, administration, and storage and handling of EPKINLY



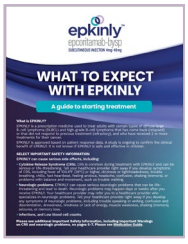

## Dose Preparation Overview

An easy-to-follow resource that provides step-by-step dilution and preparation instructions for EPKINLY

# EPKINLY resources for patients


## Patient Brochure

An overview of EPKINLY that informs patients and their care partners on what they need to know about starting treatment




## What to Expect With EPKINLY

A comprehensive resource containing useful information and tools designed to help patients understand their treatment

VISIT EPKINLYhcp.com FOR MORE INFORMATION

**Please see Important Safety Information, including Boxed Warnings for CRS and ICANS, on pages 3-4 and throughout this brochure. Please see full Prescribing Information.**

**References: 1.** EPKINLY [package insert]. Plainsboro, NJ: Genmab US, Inc. and North Chicago, IL: AbbVie Inc. 2023. **2.** Thieblemont C, Phillips T, Ghesquieres H, et al. Clinical trial protocol for: Epcoritamab, a novel, subcutaneous CD3xCD20 bispecific T-cell–engaging antibody, in relapsed or refractory large B-cell lymphoma: dose expansion in a phase I/II trial. *J Clin Oncol*. Published online December 22, 2022. doi:10.1200/JCO.22.01725

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