

Up Close with Epcoritamab

This section provides an overview of epcoritamab-bysp (EPKINLY®).



Indications



Dosing and Administration



CRS



Neurotoxicity (including ICANS)



Other Toxicities

Indications



Epcoritamab is a **bispecific CD20-directed CD3 T-cell engager** indicated for the treatment of adults with:

1. Diffuse large B-cell lymphoma (DLBCL) or High-grade B-cell Lymphoma

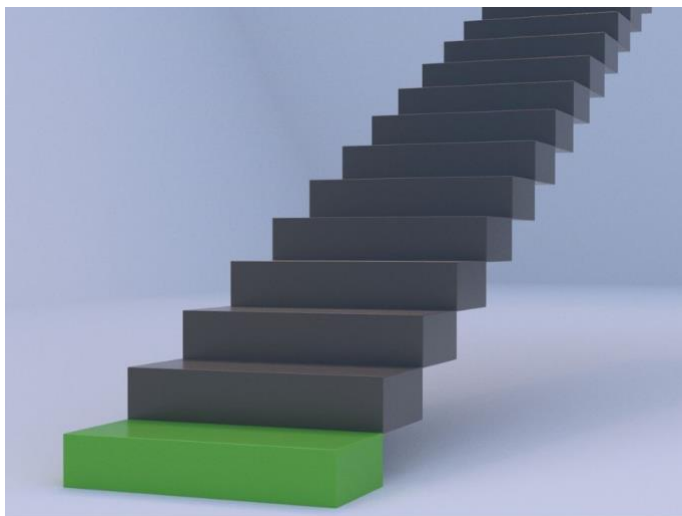
- Relapsed or refractory DLBCL, not otherwise specified, including DLBCL arising from indolent lymphoma and high-grade B-cell lymphoma after 2 or more lines of systemic therapy.

2. Follicular Lymphoma (FL)

- Relapsed or refractory FL after 2 or more lines of systemic therapy.
- Relapsed or refractory FL in combination with lenalidomide and rituximab (R²) for relapsed.

Note: These indications are approved under accelerated approval based on response rate and durability of response. Continued approval may be contingent upon verification of clinical benefit in confirmatory trials.

Dosing and Administration



Epcoritamab is administered **subcutaneously in 28-day cycles** until disease progression or unacceptable toxicity.

- Cycle 1 is given as a **step-up dosage schedule** to reduce the incidence and severity of cytokine release syndrome (CRS). The step-up dosage schedule varies by indication, where:
 - DLBCL or High-grade B-cell Lymphoma has 2 step-up doses
 - FL has 3 step-up doses

Epcoritamab 2-step up Dosage Schedule for Patients with DLBCL or High-grade B-cell Lymphoma				
Indication	Cycle of Treatment	Day of Treatment	Dose of Epcoritamab	
DLBCL or High-grade B-cell Lymphoma	Cycle 1	1	Step-up dose 1	0.16 mg
		8	Step-up dose 2	0.8 mg
		15	First full dose	48 mg
		22	48 mg	
	Cycle 2 and 3	1, 8, 15, and 22	48 mg	
	Cycle 4 to 9	1 and 15	48 mg	
	Cycle 10 and beyond	1	48 mg	

Recommendations for Restarting Therapy with Epcoritamab After Dosage Delay for Patients with DLBCL or High-grade B-cell Lymphoma		
Last Dose Administered	Time Since Last Dose Administered	Action for Next Dose(s)
0.16 mg (e.g., on Cycle 1 Day 1)	More than 8 days	Repeat Cycle 1 schedule starting at step-up dose 1 (0.16 mg). Following the repeat of Cycle 1 schedule, resume the planned treatment schedule.
0.8 mg (e.g., on Cycle 1 Day 8)	14 days or less	Administer 48 mg, then resume the planned treatment schedule.
	More than 14 days	Repeat Cycle 1 schedule starting at step-up dose 1 (0.16 mg). Following the repeat of Cycle 1 schedule, resume the planned treatment schedule.
48 mg (e.g., on Cycle 1 Day 15 onwards)	6 weeks or less	Administer 48 mg, then resume the planned treatment schedule.
	More than 6 weeks	Repeat Cycle 1 schedule starting at step-up dose 1 (0.16 mg). Following the repeat of Cycle 1 schedule, resume the planned treatment schedule.
*Administer pretreatment medication prior to epcoritamab dose and monitor patients accordingly.		

Option 1: Epcoritamab Monotherapy Dosing

Epcoritamab Monotherapy 3-step up Dosage Schedule for Patients with FL				
Indication	Cycle of Treatment	Day of Treatment	Dose of Epcoritamab	
Follicular Lymphoma	Cycle 1	1	Step-up dose 1	0.16 mg
		8	Step-up dose 2	0.8 mg
		15	First full dose	3 mg
		22	First full dose	48 mg
	Cycle 2 and 3	1, 8, 15, and 22	48 mg	
	Cycle 4 to 9	1 and 15	48 mg	
	Cycle 10 and beyond	1	48 mg	

Option 2: Epcoritamab + R² Combination Dosing

Epcoritamab Combination Therapy with R ² 3-step up Dosage Schedule for Patients with FL				
Indication	Cycle of Treatment	Day of Treatment	Dose of Epcoritamab	
Follicular Lymphoma	Cycle 1	1	Step-up dose 1	0.16 mg
		8	Step-up dose 2	0.8 mg
		15	First full dose	3 mg
		22	First full dose	48 mg
	Cycle 2 and 3	1, 8, 15, and 22	48 mg	
	Cycle 4 to 12	1	48 mg	
*Administer epcoritamab in combination with lenalidomide 20 mg (Days 1 to 21 in Cycles 1 to 12) and rituximab 375 mg/m ² (Cycles 1 to 5). Refer to the lenalidomide prescribing information and rituximab prescribing information for the respective dosage recommendations, including lenalidomide dosage recommendations for patients with renal insufficiency.				

Note: When epcoritamab is used in combination with R², dosing shifts to once per cycle beginning in Cycle 4, with administration only on Day 1 for Cycles 4 and beyond.

Recommendations for Restarting Therapy with Epcoritamab After Dosage Delay for Patients with FL		
Last Dose Administered	Time Since Last Dose Administered	Action for Next Dose(s)*
0.16 mg (e.g., on Cycle 1 Day 1)	More than 8 days	Repeat Cycle 1 schedule starting at step-up dose 1 (0.16 mg). Following the repeat of Cycle 1 schedule, resume the planned treatment schedule.
0.8 mg (e.g., on Cycle 1 Day 8)	More than 8 days	Repeat Cycle 1 schedule starting at step-up dose 1 (0.16 mg). Following the repeat of Cycle 1 schedule, resume the planned treatment schedule.
3 mg (e.g., on Cycle 1 Day 15)	14 days or less	Administer 48 mg, then resume the planned treatment schedule.
	More than 14 days	Repeat Cycle 1 schedule starting at step-up dose 1 (0.16 mg). Following the repeat of Cycle 1 schedule, resume the planned treatment schedule.
48 mg (e.g., on Cycle 1 Day 22 onwards)	6 weeks or less	Administer 48 mg, then resume the planned treatment schedule.
	More than 6 weeks	Repeat Cycle 1 schedule starting at step-up dose 1 (0.16 mg). Following the repeat of Cycle 1 schedule, resume the planned treatment schedule.
*Administer pretreatment medication prior to epcoritamab dose and monitor patients accordingly.		

Recommended Pre- and Post-Administration Medications

Cycle	Patients Requiring Medications	Medication	Administration
Cycle 1	All patients	<ul style="list-style-type: none"> Dexamethasone^a (15 mg oral or intravenous) or prednisolone (100 mg oral or intravenous) or equivalent 	<ul style="list-style-type: none"> 30-120 minutes prior to each weekly administration of epcoritamab And for three consecutive days following each weekly administration of epcoritamab in Cycle 1
		<ul style="list-style-type: none"> Diphenhydramine (50 mg oral or intravenous) or equivalent Acetaminophen (650 mg to 1,000 mg oral) 	<ul style="list-style-type: none"> 30-120 minutes prior to each weekly administration of epcoritamab
Cycle 2 and Beyond	Patients who experienced Grade 2 or 3 ^b CRS with previous dose	<ul style="list-style-type: none"> Dexamethasone^a (15 mg oral or intravenous) or prednisolone (100 mg oral or intravenous) or equivalent 	<ul style="list-style-type: none"> 30-120 minutes prior to next administration of epcoritamab after a Grade 2 or 3b CRS event And for three consecutive days following the next administration of epcoritamab until epcoritamab is given without subsequent CRS of Grade 2 or higher
^a Dexamethasone is the preferred corticosteroid when available ^b Patients will be permanently discontinued from epcoritamab after Grade 4 CRS			

Due to the risk of CRS and neurotoxicity, **all patients should be monitored** for signs and symptoms.

- DLBCL or High-grade B-cell Lymphoma:** Patients **should be hospitalized for 24 hours after administration** of the Cycle 1, Day 15 dosage of 48 mg.
 - Real-world application: Some sites administer all doses in the outpatient setting—even the first full dose for patients with DLBCL—by ensuring systems are in place for safe observation.
- FL:** Patients **do NOT require hospitalization** during any of the step-up doses.

Additional recommendations

- Provide *Pneumocystis jirovecii pneumonia* (PJP) prophylaxis prior to starting treatment with epcoritamab.
- Consider initiating prophylaxis against herpes virus prior to starting epcoritamab to prevent herpes zoster reactivation.
- Patients should be well hydrated.

Go deeper. For more information on dosing and administration, click [here](#).

⚠ CRS



What is it? Cytokine release syndrome (CRS) is a systemic inflammatory response that can occur when the immune system is activated and releases large amounts of cytokines—proteins that help regulate immune responses.

- **Signs and symptoms:** pyrexia, hypotension, hypoxia, dyspnea, chills, and tachycardia.
- CRS is frequently graded using the [American Society for Transplantation and Cellular Therapy \(ASTCT\) consensus criteria](#).

Why it matters. CRS occurred in ~50% of patients in the EPCORE NHL-1. Most CRS events occurred during **Cycle 1**, with the **highest events** occurring on the day of the **first full 48 mg dose**.

- **DLBCL or High-grade B-cell Lymphoma:** CRS occurred in **51% of patients** (37% grade 1, 17% grade 2, and 2.5% grade 3) and **recurred in 16% of patients**.
 - **Most events (92%)** occurred during **cycle 1**, with **61%** occurring **after the 48 mg dose on cycle 1, day 15**.
- **FL Monotherapy:** CRS occurred in **49% of patients** (45% grade 1, 9% grade 2) and **recurred in 23% of patients**.
 - **Most events (88%)** occurred during **cycle 1**, with **49%** occurring **after the 48 mg dose on cycle 1, day 22**.
- **FL R² Combination Therapy:** CRS occurred in **26% of patients** (21% grade 1, 5% grade 2) and **recurred in ~8% of patients**.
 - **Most events (88%)** occurred during **cycle 1**, with **18%** occurring **after the 48 mg dose on cycle 1, day 22**.

The **time to onset of CRS** varied by indication.

- **DLBCL or High-grade B-cell Lymphoma:** **Median time to CRS onset** across all doses was **24 hours** (range: 0-10 days) post-administration.
 - **First full 48 mg dose:** 21 hours (range: 0-7 days) post-administration.
- **FL Monotherapy:** **Median time to CRS onset** across all doses was **59 hours** (range: 0.1-7 days) post-administration.

- **First full 48 mg dose:** 61 hours (range: 0.1-7 days) post-administration.
- **FL R² Combination Therapy:** **Median time to CRS onset** across all doses was **34.9 hours** (range: 20.2-100.1 hours) post-administration.

The **duration of CRS** was **1-2 days**.

- **DLBCL or High-grade B-cell Lymphoma:** CRS lasted 2 days (range: 1-27 days).
- **FL Monotherapy:** CRS lasted 2 days (range: 1-14 days).
- **FL R² Combination Therapy:** CRS lasted 1 day (range: 11.3-72 hours).

Concurrent neurological adverse reactions associated with CRS occurred in <5% of patients.

- **DLBCL or High-grade B-cell Lymphoma:** 2.5% of patients.
- **FL Monotherapy:** 4.7% of patients.
- **FL R² Combination Therapy:** 0.8% of patients.

Note: The incidence of CRS was similar between epcoritamab monotherapy and the R² combination regimen, and CRS in the combination setting tended to be **less severe**.

The bottom line. CRS was primarily low-grade, predictable, and manageable.

Neurotoxicity (including ICANS)



What is it? Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS) is characterized by various neurologic symptoms resulting from the activation of the immune system and the resultant inflammatory processes.

- **Signs and symptoms:** encephalopathy, headaches, seizures, aphasia, motor deficits, ataxia, and tremor.
- ICANS is frequently graded using the [ASTCT consensus criteria](#).

Why it matters. ICANS occurred in **6%** of patients in the EPCORE NHL-1 trial.

- **DLBCL or High-grade B-cell Lymphoma:** ICANS occurred in **6%** (4.5% grade 1, 1.3% grade 2, 0.6% fatal). Of the 10 ICANS events, 9 occurred in cycle 1 of treatment.
- **FL:** ICANS occurred in **6%** of patients **receiving the 2-step up dosage schedule** in the clinical trial (3.9% grade 1, 2.4% grade 2). **Note:** The approved dosage schedule has 3-step up doses.

The **time to onset of ICANS** varied by indication.

- **DLBCL or High-grade B-cell Lymphoma:** Median time to ICANS onset from the start of treatment was **16.5 days** (range: 8-141 days).
 - **Median time from the most recent administration:** 3 days (range: 0-13 days).
- **FL:** Median time to ICANS onset from the start was **21.5 days** (range: 14-66 days) post-administration.
 - **Median time from the most recent administration:** 3 days (range: 0.4-7 days) post-administration.

ICANS resolved in most cases and lasted a few days.

- **DLBCL or High-grade B-cell Lymphoma:** Resolved in **90% of cases**; duration: **4 days** (range: 0-8 days).
- **FL:** Resolved in 100% of cases; duration: **2 days** (range: 1-7 days).

Note: ICANS was uncommon and primarily low-grade with epcoritamab monotherapy. ICANS data for the R² combination regimen were not available in the reviewed sources.

The bottom line. ICANS was uncommon and primarily low-grade.

Other Toxicities



Epcoritamab can cause other adverse reactions such as **infections, cytopenias, and embryo-fetal toxicity**.

Why it matters. In addition to the risks of CRS and neurotoxicity (including ICANS), care teams need to be on the lookout for other **epcoritamab**-associated toxicities.

Infections. Epcoritamab can cause serious and fatal infections.

- **DLBCL or High-grade B-cell Lymphoma: Serious infections** reported in **15%** (most common: 4.5% sepsis, 3.2% pneumonia). **Fatal infections** occurred in **1.3%** (1.3% COVID-19).
- **FL (receiving the 2-step up dosage schedule): Serious infections** reported in **40%** (most common: 20% COVID-19, 13% pneumonia, 3% urinary tract infections). **Fatal infections** occurred in **6%** (5% COVID-19, 0.8% pneumonia, 0.8% sepsis).

The bottom line. Care teams should **monitor patients for signs of infection before and during treatment**; treat appropriately.

- Avoid administration in patients with active infections; withhold or discontinue epcoritamab based on severity.
 - Provide PJP prophylaxis and consider herpes virus prophylaxis before starting epcoritamab.
 - Refer to the lenalidomide prescribing information for recommendations on prophylaxis for venous and arterial thrombotic events for the R² combination.
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Cytopenias. Epcoritamab can cause serious or severe cytopenias.

- **DLBCL or High-grade B-cell Lymphoma: Grade 3 or 4 events** occurred in **32%** (neutrophils decreased), **12%** (hemoglobin decreased), and **12%** (platelets decreased).
 - Febrile neutropenia occurred in 2.5%.
- **FL** (based on patients receiving the 2-step up dosage schedule, not the FDA-approved 3-step up dosage schedule): **Grade 3 or 4 events** occurred in **30%** (neutrophils decreased), **10%** (hemoglobin decreased), and **8%** (platelets decreased).
 - Febrile neutropenia occurred in 3.1%.

The bottom line. Care teams should **monitor complete blood counts throughout treatment.**

- **Withhold or discontinue epcoritamab based on cytopenia severity**; consider prophylactic granulocyte colony-stimulating factor.
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Embryo-Fetal Toxicity. Epcoritamab may cause fetal harm when administered to a pregnant woman.

- Advise **females of reproductive potential** to use effective contraception **during treatment and for 4 months after the last dose.**
 - Verify pregnancy status before initiating epcoritamab.
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Use in Specific Populations

- **Lactation:** Advise women not to breastfeed during treatment and for 4 months after the last dose.
- **Geriatric Use:**
 - In EPCORE NHL-1, 52% of patients with relapsed/refractory FL were ≥65 years old, and 13% were ≥75 years old.
 - Higher rate of fatal adverse reactions, mainly infections, including COVID-19, in patients ≥65 years old compared to younger adults.
 - No overall difference in efficacy was observed.
- **Pediatric Use:** At this time, no safety and effectiveness data has been established in pediatric patients.

Updated: 1/6/26

References

1. [EPKINLY™ \(epcoritamab-bysp\) \[package insert\]. Plainsboro, NJ: Genmab US, Inc.; North Chicago, IL: AbbVie Inc. 2024.](#)
2. [Falchi L, Nijland M, Huang H, et al. Epcoritamab, lenalidomide, and rituximab versus lenalidomide and rituximab for relapsed or refractory follicular lymphoma \(EPCORE FL-1\): a global, open-label, randomised, phase 3 trial. *Lancet*. Published online December 7, 2025. doi:10.1016/S0140-6736\(25\)02360-8.](#)
3. [Lee DW, Santomaso BD, Locke FL, et al. ASTCT consensus grading for cytokine release syndrome and neurologic toxicity associated with immune effector cells. *Biol Blood Marrow Transplant*. 2019;25\(4\):625-638. doi:10.1016/j.bbmt.2018.12.758](#)
4. [Linton KM, Vitolo U, Jurczak W, et al. Epcoritamab monotherapy in patients with relapsed or refractory follicular lymphoma \(EPCORE NHL-1\): a phase 2 cohort of a single-arm, multicentre study. *Lancet Haematol*. 2024;11\(8\):e593-e605. doi:10.1016/S2352-3026\(24\)00166-2](#)
5. [Hutchings M, Mous R, Clausen MR, et al. Dose escalation of subcutaneous epcoritamab in patients with relapsed or refractory B-cell non-Hodgkin lymphoma: an open-label, phase 1/2 study. *Lancet*. 2021;398\(10306\):1157-1169. doi:10.1016/S0140-6736\(21\)00889-8.](#)