See National Comprehensive Cancer Network® (NCCN®) recommendation on page 30

LYNOZYFIC™

(linvoseltamab-gcpt) Injection 5mg | 200mg

For eligible patients with R/R multiple myeloma after 4 prior lines of treatment[1]

INDICATION AND USAGE

LYNOZYFIC is a bispecific B-cell maturation antigen (BCMA)-directed CD3 T-cell engager indicated for the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least four prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody.

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 confirmatory trial(s).

5L+, fifth line or later; R/R, relapsed/refractory.

IMPORTANT SAFETY INFORMATION

WARNING: CYTOKINE RELEASE SYNDROME and NEUROLOGIC TOXICITY, including IMMUNE EFFECTOR CELL-ASSOCIATED NEUROTOXICITY SYNDROME

- **Cytokine release syndrome (CRS), including serious or life-threatening reactions, can occur in patients receiving LYNOZYFIC. Initiate treatment with LYNOZYFIC step-up dosing to reduce the risk of CRS. Manage CRS, withhold LYNOZYFIC until CRS resolves, and modify the next dose or permanently discontinue based on severity.**
- **Neurologic toxicity, including immune effector cell-associated neurotoxicity syndrome (ICANS), including serious or life-threatening reactions, can occur in patients receiving LYNOZYFIC. Monitor patients for signs or symptoms of neurologic toxicity, including ICANS during treatment. Manage neurologic toxicity, including ICANS, withhold LYNOZYFIC until neurologic toxicity, including ICANS resolves, and modify the next dose or permanently discontinue based on severity.**
- **Because of the risk of CRS and neurologic toxicity, including ICANS, LYNOZYFIC is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the LYNOZYFIC REMS.**

Please see additional IMPORTANT SAFETY INFORMATION throughout and full Prescribing Information, including Boxed WARNING, for LYNOZYFIC.

Despite treatment advances, there remains an unmet need for patients who relapse or become refractory to multiple lines of therapy

1

Multiple myeloma remains an incurable disease, and almost all patients eventually relapse or become resistant to their treatment.[2-4]

2

Durability of response usually declines with each successive line of multiple myeloma therapy.[2,5]

3

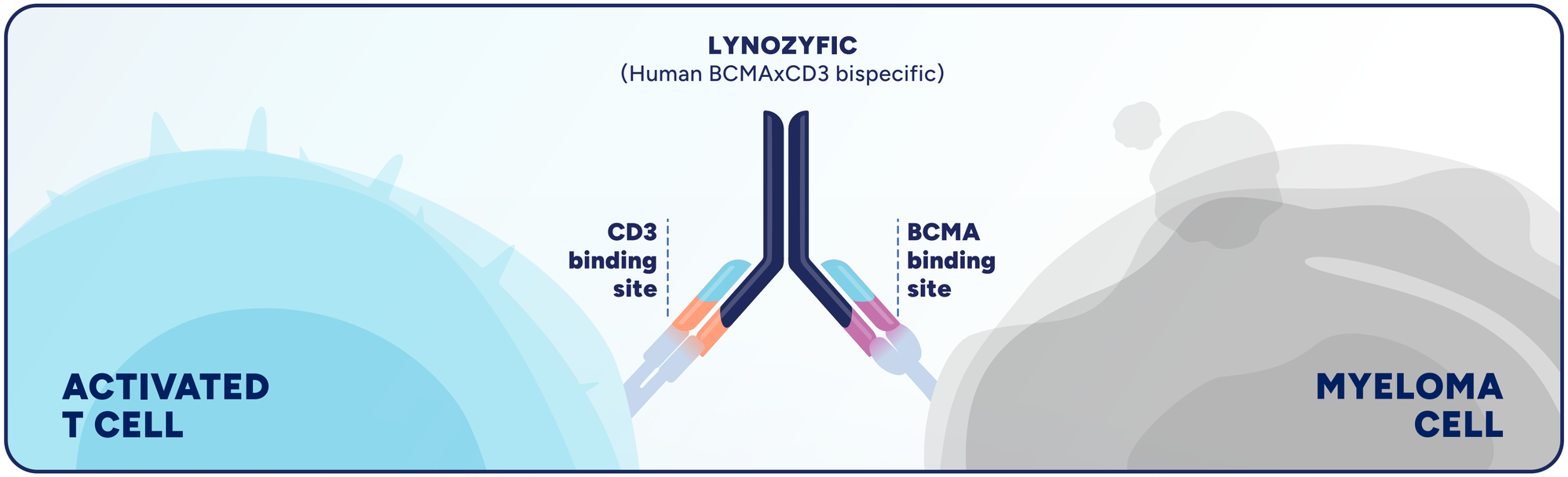
Patients with high-risk characteristics, such as aggressive disease progression or genetic abnormalities, have particularly poor outcomes.[6]

There is a need for effective later-line multiple myeloma treatments that deliver durable responses for a broad patient population and consider the patient experience.

LYNOZYFIC is an off-the-shelf, human BCMAxCD3 bispecific antibody[1,7]

LYNOZYFIC is designed to engage BCMA on MM cells and CD3 on cytotoxic T cells concurrently to trigger T-cell activation for tumor cell lysis and help eliminate malignant MM plasma cells[1]

BCMA is overexpressed on myeloma cells. BCMA may also be expressed to a lesser degree on normal plasma cells, and is minimally expressed on hematopoietic stem cells and in nonhematopoietic tissues.[8]



BCMA, B-cell maturation antigen; CD3, cluster of differentiation 3; MM, multiple myeloma.

IMPORTANT SAFETY INFORMATION (cont'd)

Warnings and Precautions

Cytokine Release Syndrome (CRS): LYNOZYFIC can cause CRS, which can be serious or life-threatening. In LINKER-MM1, CRS occurred in 46% (54/117) of patients who received LYNOZYFIC at the recommended dose, with Grade 1 CRS occurring in 35% (41/117) of patients, Grade 2 in 10% (12/117), and Grade 3 in 0.9% (1/117). Thirty-eight percent (45/117) of patients had CRS following step-up dose 1, including 1 patient who experienced Grade 3 CRS; 8% (9/117) had an initial CRS event following a subsequent dose. Seventeen percent (19/113) of patients developed CRS after step-up dose 2, 10% (11/111) developed CRS after the first full 200-mg dose of LYNOZYFIC, and 3.6% (4/110) developed CRS after the second full dose. Recurrent CRS occurred in 20% (23/117) of patients. The median time to onset of CRS from the end of infusion was 11 (range: -1 to 184) hours after the most recent dose, with a median duration of 15 (range: 1 to 76) hours.

Please see additional IMPORTANT SAFETY INFORMATION throughout and full Prescribing Information, including Boxed WARNING, for LYNOZYFIC.

The LINKER-MM1 study assessed the efficacy and safety of LYNOZYFIC in patients with R/R multiple myeloma[1]

LINKER-MM1 was a pivotal Phase 1/2, multicenter, open-label, multicohort trial of LYNOZYFIC[1]

Patients with triple-class exposed R/R multiple myeloma received 200 mg IV of LYNOZYFIC following step-up dosing period (N=117; Phase 1: n=12; Phase 2: n=105)[1,7]

Dosing switched to Q2W after 12 full QW doses, per protocol[1]

Phase 2 patients with ≥VGPR could extend their dose-free period to Q4W dosing at or after Week 24 and ≥17 full doses[1]

Major efficacy endpoint: ORR*
Select secondary efficacy endpoint: DoR[1,7,9]*

The efficacy population included 80 patients who had received at least 4 prior lines of therapy.[1]

Treatment until disease progression or unacceptable toxicity[1]

See the dosing schedule and hospitalization instructions.

Select eligibility criteria[1]:

- At least 3 prior therapies, including a PI, an IMiD, and an anti-CD38 Ab
- ECOG PS 0 or 1 and adequate baseline hematologic,† renal,‡ and hepatic§ function
- No known MM brain lesions or meningeal involvement, history of a neurodegenerative condition, or seizure within 12 months of enrollment
- No active infection
- No history of an allogeneic or autologous stem cell transplantation within 12 weeks of starting LYNOZYFIC
- No prior treatment with BCMA-directed BsAbs, bispecific T-cell–engaging therapies, or BCMA CAR-T therapy (prior treatment with anti-BCMA ADC allowed)

*As assessed by IRC.
†Absolute neutrophil count >1.0 x 10^9/L, platelet count >50 x 10^9/L, hemoglobin level >8 g/dL.
‡CrCl >30 mL/min.
§AST and ALT ≤2.5 x ULN, total bilirubin ≤1.5 x ULN, alkaline phosphatase ≤2.5 x ULN.
ADC, antibody-drug conjugate; anti-CD38 Ab, anti-cluster of differentiation 38 antibody; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BsAb, bispecific antibody; CAR-T, chimeric antigen receptor T cell; CrCl, creatinine clearance; DoR, duration of response; ECOG, Eastern Cooperative Oncology Group; IMiD, immunomodulatory drug; IRC, independent review committee; IV, intravenous; ORR, objective response rate; PI, proteasome inhibitor; PS, performance status; Q2W, every 2 weeks; Q4W, every 4 weeks; QW, every week; ULN, upper limit of normal.

IMPORTANT SAFETY INFORMATION (cont'd)

Warnings and Precautions (cont'd)

Cytokine Release Syndrome (CRS) (cont'd): Clinical signs and symptoms of CRS included, but were not limited to pyrexia, chills, hypoxia, tachycardia, and hypotension. Administer pretreatment medications and initiate therapy according to LYNOZYFIC step-up dosing to reduce the incidence and severity of CRS. Monitor patients for signs and symptoms of CRS after infusion. Counsel patients to seek immediate medical attention should signs or symptoms of CRS occur.

Please see additional IMPORTANT SAFETY INFORMATION throughout and full Prescribing Information, including Boxed WARNING, for LYNOZYFIC.

LINKER-MM1 enrolled patients with late-line R/R multiple myeloma with a broad range of disease characteristics[1,9]

Patient characteristics		Efficacy population (N=80)
Patient demographics	Age, median (range), years	71 (37-83)
	Age ≥75 years	30%
	Male	64%
	White	69%
	Black or African American	14%
	Asian	13%
	Hispanic/Latino	2.5%

Patient characteristics (cont'd)		Efficacy population (N=80)
ECOG PS	0	25%
	1	75%
ISS stage	I	39%
	II	36%
	III	19%
Cytogenetic risk	High risk*	40%

*Presence of del(17p), t(4;14), and t(14;16).[1]
ISS, International Staging System.

IMPORTANT SAFETY INFORMATION (cont'd)

Warnings and Precautions (cont'd)

Cytokine Release Syndrome (CRS) (cont'd): At the first sign of CRS, immediately evaluate patients for hospitalization, manage per current practice guidelines, and administer supportive care; withhold LYNOZYFIC until CRS resolves and modify the next dose or permanently discontinue LYNOZYFIC based on severity.

Infusion Related Reactions

Infusion-related reactions (IRR) may be clinically indistinguishable from manifestations of CRS. In the patients who were treated with the recommended step-up dosing regimen and pretreatment medications, the rate of IRR was 9% [11/117 including Grade 2 IRR (4.3%) and Grade 3 IRR (1.7%)]. For IRR, interrupt or slow the rate of infusion or permanently discontinue LYNOZYFIC based on severity of reaction.

Please see additional IMPORTANT SAFETY INFORMATION throughout and full Prescribing Information, including Boxed WARNING, for LYNOZYFIC.

LINKER-MM1 enrolled patients with late-line R/R multiple myeloma with a broad range of disease characteristics (cont'd)[1,9]

Patient characteristics (cont'd)		**Efficacy population** (N=80)
Plasmacytoma status	Extramedullary disease at baseline	18%
Bone marrow plasma cells (BMPCs)	BMPCs <30%	40%
	BMPCs ≥30% to <60%	20%
	BMPCs ≥60%	16%
Soluble BCMA	Median (range), ng/mL	358.5 (18.7-3,150.0)

Patient characteristics (cont'd)		**Efficacy population** (N=80)
Prior treatment history	Prior lines, median (range)*	5 (4-13)
	Prior SCT	65%
	Prior anti-BCMA ADC	13%
	Triple-class exposed†	100%
	Triple-class refractory†	79%
	Penta-exposed‡	86%
	Penta-refractory‡	33%

*83% were refractory to last line of therapy.
†Triple-class exposed/refractory: ≥1 PI, ≥1 IMiD, and ≥1 anti-CD38 antibody.[7]
‡Penta-exposed/refractory: ≥2 PIs, ≥2 IMiDs, and ≥1 anti-CD38 antibody.[7]
SCT, stem cell transplantation.

IMPORTANT SAFETY INFORMATION (cont'd)

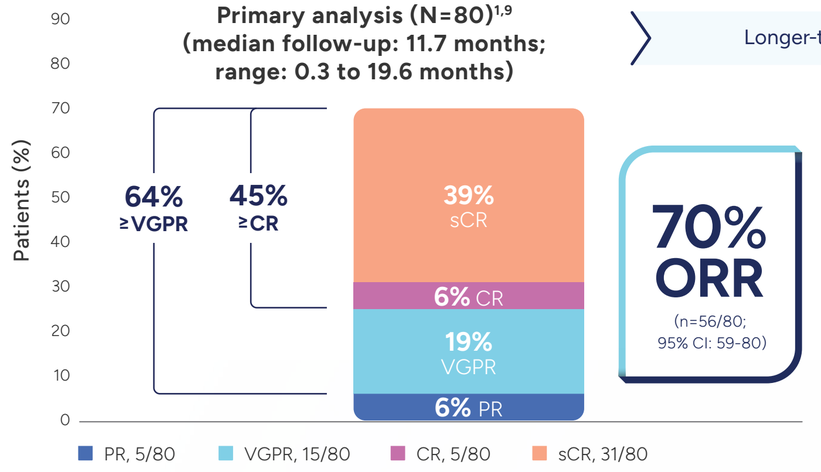
Warnings and Precautions (cont'd)

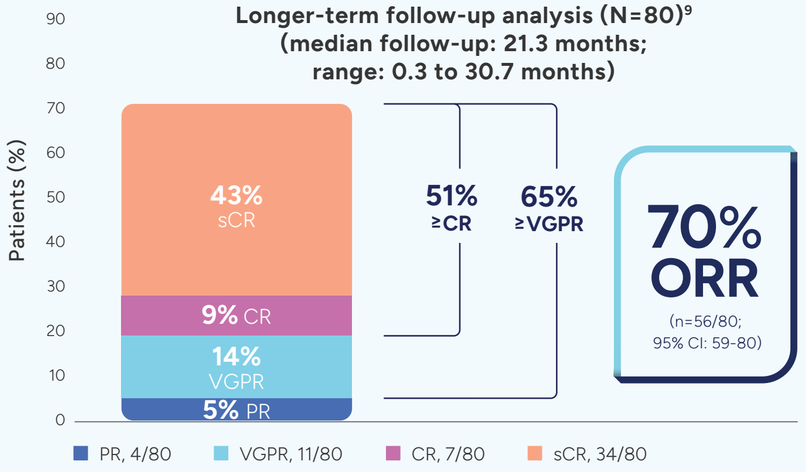
Neurologic Toxicity, including Immune Effector Cell Associated Neurotoxicity Syndrome: LYNOZYFIC can cause serious or life-threatening neurologic toxicity, including ICANS. In LINKER-MM1, neurologic toxicity occurred in 54% of patients, with Grade 3 or 4 neurologic toxicity occurring in 8%, at the recommended dose. Neurologic toxicities included ICANS, depressed level of consciousness, encephalopathy, and toxic encephalopathy. ICANS occurred in 8% of patients who received LYNOZYFIC with the recommended dosing regimen, including Grade 3 events in 2.6%. Most patients experienced ICANS following step-up dose 1 (5%). Two patients (1.8%) experienced initial ICANS following step-up dose 2 and one patient developed the first occurrence of ICANS following a subsequent full dose of LYNOZYFIC. Recurrent ICANS occurred in one patient. The median time to onset of ICANS was 1 (range: 1 to 4) day after the most recent dose with a median duration of 2 (range: 1 to 11) days. The onset of ICANS can be concurrent with CRS, following resolution of CRS, or in the absence of CRS.

Please see additional IMPORTANT SAFETY INFORMATION throughout and full Prescribing Information, including Boxed WARNING, for LYNOZYFIC.

Patients achieved deep* responses with LYNOZYFIC[1]

***Deep response defined as ≥VGPR.**





Post hoc analysis: ≥CR rates increased from 45% to 51% with longer follow-up[1,9]

In the primary analysis, **median time to first response was less than 1 month[1,9]:**

- Median time to first response: 0.95 months (range: 0.5-6.3; n=56)
- Median time to ≥VGPR: 2.5 months (range: 0.7-13.1; n=51)
- Median time to ≥CR: 7.7 months (range: 1.9-13.9; n=36)
- **Limitations: The analyses for median time to ≥VGPR and ≥CR were not prespecified and not powered for statistical significance. Small patient numbers and lack of multiplicity adjustments can be limitations of these analyses**

More than 50% of patients achieved ≥CR in the longer-term follow-up.[9]

CI, confidence interval; CR, complete response; PR, partial response; sCR, stringent complete response; VGPR, very good partial response.

IMPORTANT SAFETY INFORMATION (cont'd)

Warnings and Precautions (cont'd)

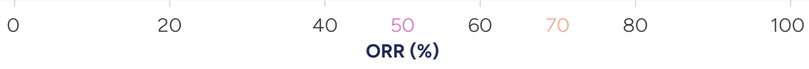
Neurologic Toxicity, including Immune Effector Cell Associated Neurotoxicity Syndrome (cont'd): The most common clinical signs and symptoms of ICANS are confusion, depressed level of consciousness, and lethargy. Monitor patients for signs and symptoms of neurologic toxicity, including ICANS during treatment. At the first sign of neurologic toxicity, including ICANS, immediately evaluate the patient; provide supportive therapy and consider further management per current practice guidelines. Withhold LYNOZYFIC until ICANS resolves and modify the next dose or permanently discontinue LYNOZYFIC based on severity. Counsel patients to seek immediate medical attention should signs or symptoms of neurologic toxicity, including ICANS occur at any time.

Please see additional IMPORTANT SAFETY INFORMATION throughout and full Prescribing Information, including Boxed WARNING, for LYNOZYFIC.

Post hoc analysis: LYNOZYFIC resulted in ≥50% ORR in the majority of subgroups evaluated in LINKER-MM1, including high-risk subgroups[9]

Limitations: Subgroup analyses were not powered for statistical significance. Small patient numbers and lack of multiplicity adjustments can be limitations of these analyses. No firm conclusions can be made.

Subgroup		Responders/Total (n/N)	ORR, % (95% CI)*
Age	<65	15/27	**55.6** (35.3-74.5)
	≥65 to <75	23/29	**79.3** (60.3-92.0)
	≥75	18/24	**75.0** (53.3-90.2)
Race	White	39/55	**70.9** (57.1-82.4)
	Black or African American	9/11	**81.8** (48.2-97.7)
Cytogenetic risk	High	22/32	**68.8** (50.0-83.9)
ISS stage	I	22/31	**71.0** (52.0-85.8)
	II	20/29	**69.0** (49.2-84.7)
	III	10/15	**66.7** (38.4-88.2)
Baseline EMP status	Without EMP	50/66	**75.8** (63.6-85.5)
	With EMP	6/14	**42.9** (17.7-71.1)
Refractory class	Triple-refractory	6/8	**75.0** (34.9-96.8)
	Quadra-refractory	21/29	**72.4** (52.8-87.3)
	Penta-refractory	17/26	**65.4** (44.3-82.8)
BMPCs	>0 to <30%	25/32	**78.1** (60.0-90.7)
	≥30% to <60%	12/16	**75.0** (47.6-92.7)
	≥60%	4/13	**30.8** (9.1-61.4)
Soluble BCMA	<400 ng/mL	35/42	**83.3** (68.6-93.0)
	≥400 ng/mL	17/34	**50.0** (32.4-67.6)



Dotted line at 70% represents ORR of total efficacy population.
*The response rate in prespecified subgroups among the 200 mg-treated patients was determined by an independent review committee (IRC) per IMWG criteria.
BCMA, B-cell maturation antigen; BMPC, bone marrow plasma cell; EMP, extramedullary plasmacytoma; IMWG, International Myeloma Working Group.

IMPORTANT SAFETY INFORMATION (cont'd)

Warnings and Precautions (cont'd)

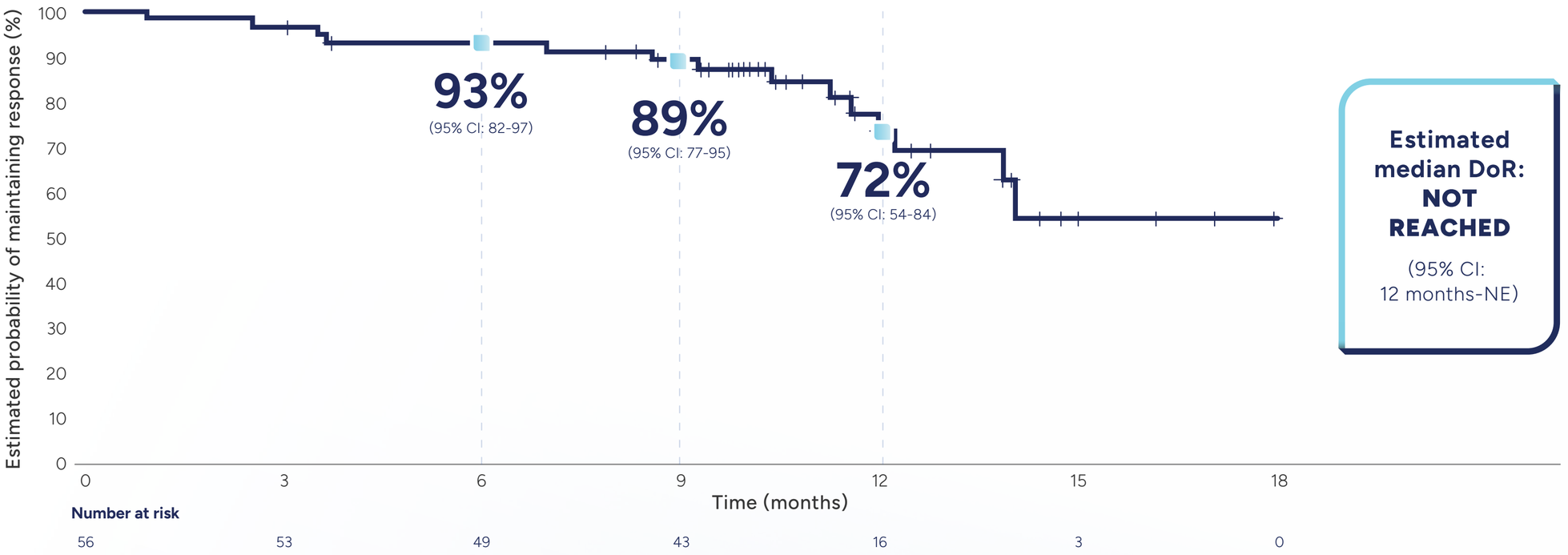
Neurologic Toxicity, including Immune Effector Cell Associated Neurotoxicity Syndrome (cont'd): Due to the potential for neurologic toxicity, including ICANS, patients receiving LYNOZYFIC are at risk of confusion and depressed consciousness. Advise patients to refrain from driving, or operating heavy or potentially dangerous machinery, for 48 hours after completion of each of the step-up doses and in the event of new onset of any neurological symptoms, until symptoms resolve.

Please see additional IMPORTANT SAFETY INFORMATION throughout and full Prescribing Information, including Boxed WARNING, for LYNOZYFIC.

LYNOZYFIC delivered durable responses in patients with R/R multiple myeloma[1,9]

Median DoR was not reached in the primary analysis (median follow-up: 11.3 months among responders; n=56)[1]

- Median duration of treatment was 47 weeks (range: 1-151)[1]



Estimated median DoR: NOT REACHED

(95% CI: 12 months-NE)

Post hoc analysis: At a longer-term median follow-up of 20 months, the estimated median DoR was 21 months (95% CI: 19-NE; n=56).[9]

NE, not evaluable.

IMPORTANT SAFETY INFORMATION (cont'd)

Warnings and Precautions (cont'd)

LYNOZYFIC REMS: LYNOZYFIC is available only through a restricted program under a REMS called the LYNOZYFIC REMS because of the risks of CRS and neurologic toxicity, including ICANS.

Please see additional IMPORTANT SAFETY INFORMATION throughout and full Prescribing Information, including Boxed WARNING, for LYNOZYFIC.

Response data for patients who switched to Q4W dosing (post hoc analysis)

Of 44 patients in the trial who had ≥17 full doses and ≥24 weeks of LYNOZYFIC exposure, **91% (40/44) achieved ≥VGPR and switched to Q4W dosing[9]***

Limitations: The analyses of response data for patients who switched to Q4W dosing were not powered for statistical significance. Small patient numbers and lack of multiplicity adjustments can be limitations. No firm conclusions can be made.

Responses in patients after switching to Q4W dosing

80% **(32/40)** of patients **continued to have a ≥VGPR** at data cutoff after switching to Q4W dosing.[9†]

Of these patients, 7 patients who achieved a VGPR at the time of switching to Q4W dosing subsequently **achieved a ≥CR** by the data cutoff.[9†]

20% **(8/40)** of patients **progressed** by data cutoff after switching to Q4W dosing (including 1 patient with VGPR who achieved ≥CR after switching, and then subsequently progressed).[9†]

Estimated median DoR for patients who switched to Q4W dosing was not reached (95% CI: 14 months-NE; n=41)[‡]

Data cutoff: September 8, 2023.

*Median duration of treatment exposure post-switch: 22.0 weeks (range: 2.0 to 49.4).[‡]
†By IRC assessment.
‡Of the 41 patients used to calculate these values, 1 patient transitioned to Q4W dosing based on an investigator-assessed VGPR. During subsequent IRC evaluation, it was determined that this patient had a PR at the time of the switch.

IMPORTANT SAFETY INFORMATION (cont'd)

Warnings and Precautions (cont'd)

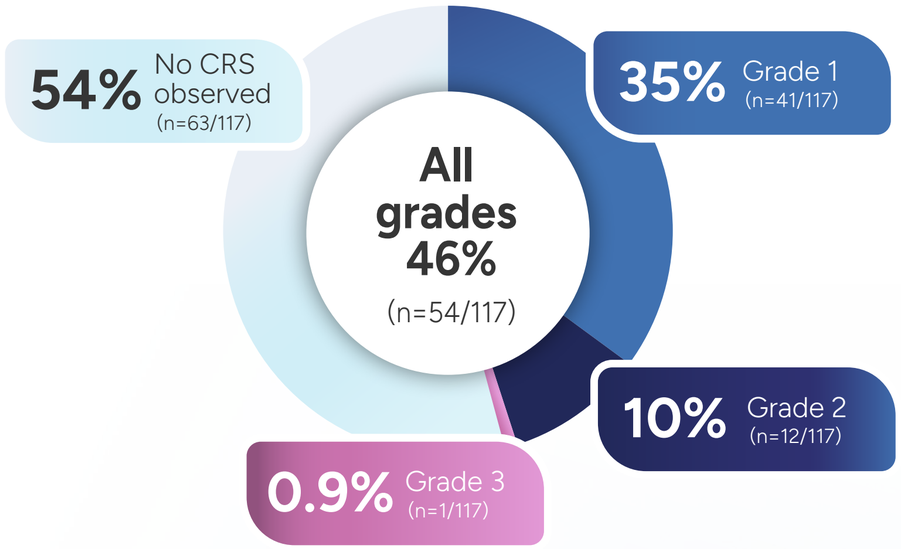
Infections: LYNOZYFIC can cause serious, life-threatening, or fatal infections. In patients who received LYNOZYFIC at the recommended dose in LINKER-MM1, serious infections, including opportunistic infections, occurred in 42% of patients, with Grade 3 or 4 infections in 38% and fatal infections in 4%. The most common serious infection reported (≥10%) were pneumonia and sepsis. Two cases of progressive multifocal leukoencephalopathy (PML) occurred in patients receiving LYNOZYFIC.

Please see additional IMPORTANT SAFETY INFORMATION throughout and full Prescribing Information, including Boxed WARNING, for LYNOZYFIC.

CRS occurred in 46% of patients in LINKER-MM1[1]

CRS events were mostly Grade 1 or 2, with generally early time to onset and short time to resolution in the majority of cases[1]

LYNOZYFIC has a Boxed WARNING for CRS, including serious or life-threatening reactions.[1]



CRS
generally occurred within a day of dosing and resolved within 24 hours[1]

Median time to CRS onset*:	Median duration of CRS:
11 hours (range: -1 to 184)	**15 hours** (range: 1 to 76)

<1% **Grade 3 CRS occurred, with no Grade 4 or Grade 5 events.[1]**

LYNOZYFIC is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called LYNOZYFIC REMS because of the risks of CRS and neurologic toxicity, including ICANS.[1]

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*Negative numbers indicate CRS onset prior to the end of LYNOZYFIC administration.[7]

IMPORTANT SAFETY INFORMATION (cont'd)

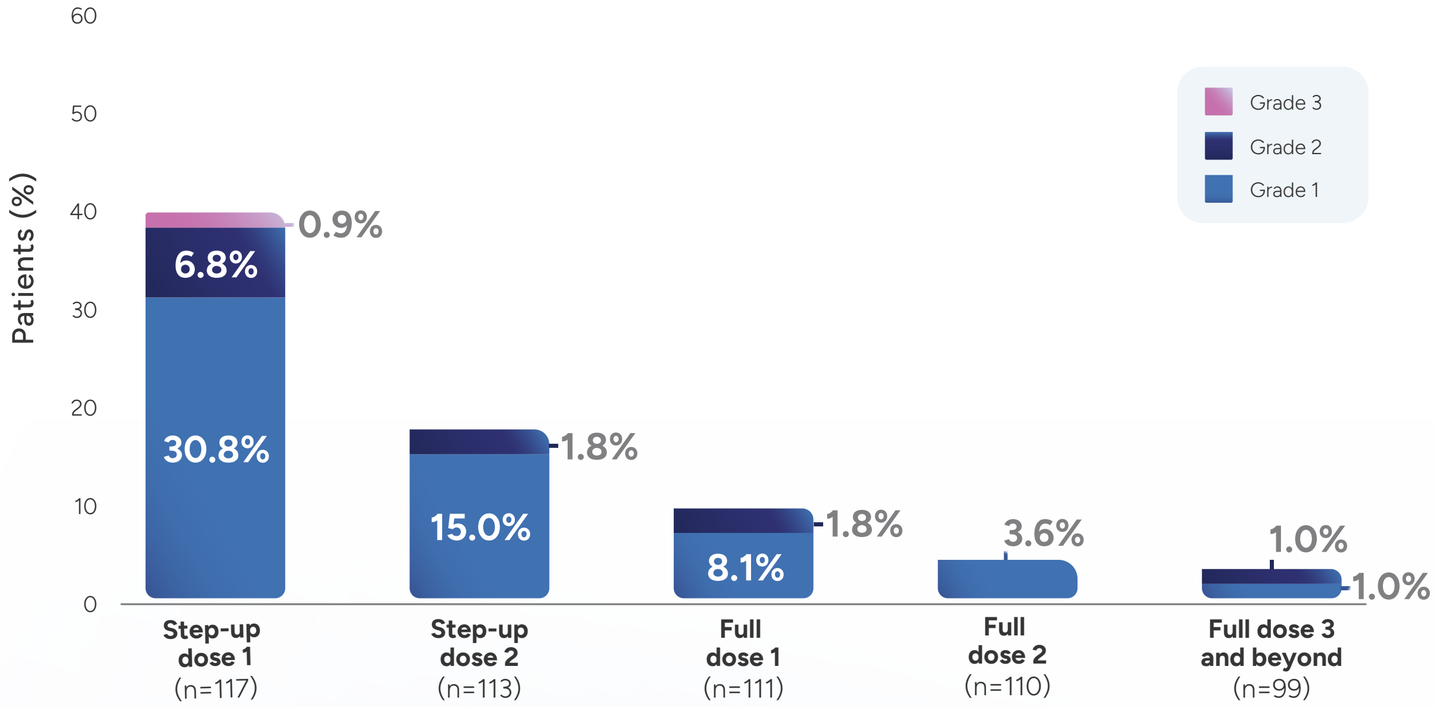
Warnings and Precautions (cont'd)

Infections (cont'd): Monitor patients for signs and symptoms of infection and immunoglobulin levels prior to and during treatment with LYNOZYFIC and treat appropriately. Administer prophylactic antimicrobials, antibiotics, antifungals, antivirals, vaccines, and subcutaneous or intravenous immunoglobulin (IVIG) according to guidelines, including prophylaxis for PJP and herpesviruses. Withhold LYNOZYFIC or consider permanent discontinuation of LYNOZYFIC based on severity of the infection.

Please see additional IMPORTANT SAFETY INFORMATION throughout and full Prescribing Information, including Boxed WARNING, for LYNOZYFIC.

CRS events usually occurred during the step-up dosing period[1]

CRS by dose in LINKER-MM1, 200-mg cohort[7,9]



- 38% (45/117) of patients had a CRS event after step-up dose 1[1]
- 8% (9/117) had an initial CRS event following a subsequent dose[1]
- There was one Grade 3 event, which occurred following step-up dose 1[1]
- Recurrent CRS occurred in 20% (23/117) of patients[1]

IMPORTANT SAFETY INFORMATION (cont'd)

Warnings and Precautions (cont'd)

Neutropenia: LYNOZYFIC can cause neutropenia and febrile neutropenia. In patients who received LYNOZYFIC at the recommended dose in LINKER-MM1, decreased neutrophil count occurred in 62% of patients with Grade 3 or 4 decreased neutrophil count in 47%. Febrile neutropenia occurred in 8% of patients.

Please see additional IMPORTANT SAFETY INFORMATION throughout and full Prescribing Information, including Boxed WARNING, for LYNOZYFIC.

Neurologic toxicity, including ICANS, in LINKER-MM1[1]

Neurologic toxicity occurred in 54% of patients in LINKER-MM1[1]

LYNOZYFIC has a Boxed WARNING for serious or life-threatening neurologic toxicity, including ICANS.[1]

- 8% of patients experienced Grade 3 or 4 neurologic toxicity
- Neurologic toxicities included ICANS, depressed level of consciousness, encephalopathy, and toxic encephalopathy

ICANS events occurred in 8% of patients, which were Grade 3 in 2.6% of patients[1]

ICANS events usually occurred during the step-up dosing period, with generally early time to onset and short time to resolution in the majority of cases[1]

ICANS rates[1,7]	% (n/N)
All grades	8% (9/117)
Grade 1	2.6% (3/117)
Grade 2	2.6% (3/117)
Grade 3	2.6% (3/117)

Median time to ICANS onset[1]:	Median duration of ICANS[1]:
1 day (range: 1 to 4)	**2 days** (range: 1 to 11)

LYNOZYFIC is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called LYNOZYFIC REMS because of the risks of CRS and neurologic toxicity, including ICANS.[1]

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ICANS mostly occurred after the first step-up dose[1]

- No Grade 4 or 5 cases of ICANS occurred with LYNOZYFIC[1,7]
- 5% (6/117) of patients experienced ICANS following the first step-up dose[1,9]
- 1.8% (2/113) experienced initial ICANS after step-up dose 2, and 1 patient developed ICANS following a subsequent full dose[1,9]
- Recurrent ICANS occurred in 1 patient[1]
- The onset of ICANS can be concurrent with CRS, following resolution of CRS, or in the absence of CRS[1]

IMPORTANT SAFETY INFORMATION (cont'd)

Warnings and Precautions (cont'd)

Neutropenia (cont'd): Monitor complete blood cell counts at baseline and periodically during treatment and provide supportive care per local guidelines. Monitor patients with neutropenia for signs of infection. Withhold LYNOZYFIC based on severity.

Please see additional IMPORTANT SAFETY INFORMATION throughout and full Prescribing Information, including Boxed WARNING, for LYNOZYFIC.

Rate of infections with LYNOZYFIC in LINKER-MM1[1]

LYNOZYFIC can cause serious, life-threatening, or fatal infections.[1]

Most common infections (≥10%; N=117)[1]

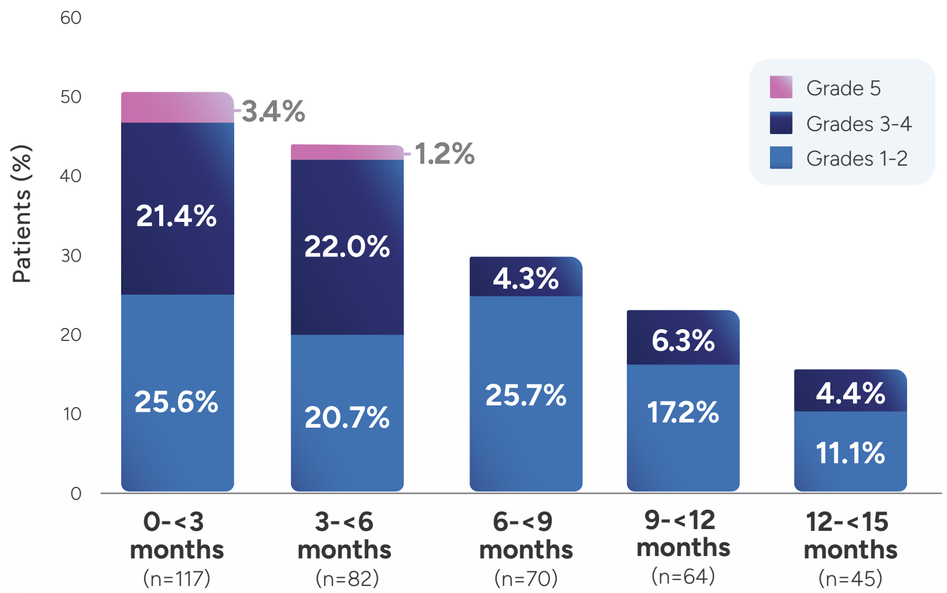
Adverse reaction	All grades (%)	Grades 3-4 (%)
Infections and infestations		
Upper respiratory tract infection*	35	6‖
Pneumonia†‡	28	21
COVID-19§	17	5
Urinary tract infections*	16	8‖
Sepsis	10	6

- Serious infections, including opportunistic infections, occurred in 42% of patients[1]
  - The most common serious infections reported (≥10%) were pneumonia and sepsis[1]
- Grade 3 or 4 infections occurred in 38% of patients[1]
- Fatal infections occurred in 4% of patients[1]
- 2 cases of PML occurred in patients receiving LYNOZYFIC[1]

*Includes other related terms.
†Includes fatal outcome.
‡Pneumonia includes atypical pneumonia, COVID-19 pneumonia, PJP, pneumonia, pneumonia cytomegaloviral, pneumonia fungal, pneumonia influenzal, and pneumonia viral.
§The LINKER-MM1 trial was initiated in 2019, prior to the development of the COVID-19 vaccines and management protocols.[9]
‖Only Grade 3 adverse reactions occurred.

PJP, *Pneumocystis jirovecii* pneumonia; PML, progressive multifocal leukoencephalopathy.

Observed rate of infections over time with LYNOZYFIC (median follow-up: 11.1 months)[9]



Time period of onset of infections and infestations

Limitations: There is a suggestion of a decrease in infection incidence with ≥9 months on treatment, but no firm conclusions can be made.[9] This analysis was not powered for statistical significance. Small patient numbers and lack of multiplicity adjustments can be limitations.

IMPORTANT SAFETY INFORMATION (cont'd)

Warnings and Precautions (cont'd)

Hepatotoxicity: LYNOZYFIC can cause hepatotoxicity. In LINKER-MM1, elevated ALT occurred in 46% of patients, with Grade 3 or 4 ALT elevation occurring in 6%; elevated AST occurred in 61% of patients, with Grade 3 or 4 AST elevation occurring in 10% of patients who received the recommended dose. Grade 3 or 4 total bilirubin elevations occurred in 1.7% of patients. Liver enzyme elevation can occur with or without concurrent CRS.

Please see additional IMPORTANT SAFETY INFORMATION throughout and full Prescribing Information, including Boxed WARNING, for LYNOZYFIC.

LYNOZYFIC safety profile in LINKER-MM1[1]

Safety data from LINKER-MM1[1]

- Serious adverse reactions occurred in 74% of patients. Serious adverse reactions that occurred in >5% of patients included CRS (27%), pneumonia (13%), COVID-19 (7%), and acute kidney injury (5%)
- Fatal adverse reactions occurred in 7% of patients and included sepsis (3.4%), chronic kidney disease (0.9%), pneumonia (0.9%), tumor lysis syndrome (0.9%), and encephalopathy (0.9%)
- Permanent discontinuation of LYNOZYFIC due to adverse reactions occurred in 16% of patients. Adverse reactions leading to discontinuation that occurred in at least 2 patients included sepsis, pneumonia, and encephalopathy
- Dose interruptions or delays of LYNOZYFIC due to adverse reactions occurred in 74% of patients. Adverse reactions that required a dosage interruption or delay in >10% of patients included neutropenia (29%), upper respiratory tract infection (18%), pneumonia (15%), and COVID-19 infection (11%)
- The most common adverse reactions (≥20%) were musculoskeletal pain, CRS, cough, upper respiratory tract infection, diarrhea, fatigue, pneumonia, nausea, headache, and dyspnea
- The most common Grade 3 or 4 laboratory abnormalities (≥30%) were decreased lymphocyte count, decreased neutrophil count, decreased hemoglobin, and decreased white blood cell count

Please see additional warnings and precautions on neutropenia, hepatotoxicity, and embryo-fetal toxicity in the LYNOZYFIC Prescribing Information.

IMPORTANT SAFETY INFORMATION (cont'd)

Warnings and Precautions (cont'd)

Hepatotoxicity (cont'd): Monitor liver enzymes and bilirubin at baseline and during treatment as clinically indicated. Withhold LYNOZYFIC or consider permanent discontinuation of LYNOZYFIC based on severity.

Embryo-Fetal Toxicity: Based on its mechanism of action, LYNOZYFIC may cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to the fetus. Advise females of reproductive potential to use effective contraception during treatment with LYNOZYFIC and for 3 months after the last dose.

Please see additional IMPORTANT SAFETY INFORMATION throughout and full Prescribing Information, including Boxed WARNING, for LYNOZYFIC.

LYNOZYFIC safety profile in LINKER-MM1 (cont'd)[1]

Adverse reactions occurring in ≥10% of patients receiving LYNOZYFIC (N=117)[1]

Adverse reaction	All grades (%)	Grades 3-4 (%)
Musculoskeletal and connective tissue disorders		
Musculoskeletal pain*	53	3.4†
Immune system disorders		
Cytokine release syndrome	46	0.9†
Hypogammaglobulinemia	13	0.9†
Respiratory, thoracic, and mediastinal disorders		
Cough*	39	0
Dyspnea*	21	0.9†
Nasal congestion	16	0

Adverse reaction (cont'd)	All grades (%)	Grades 3-4 (%)
Infections and infestations		
Upper respiratory tract infection*	35	6†
Pneumonia‡[a]	28	21
COVID-19	17	5
Urinary tract infections*	16	8†
Sepsis	10	6
Gastrointestinal disorders		
Diarrhea	35	1.7†
Nausea	23	0
Vomiting	19	0
Constipation	17	0

*Includes other related terms.
†Only Grade 3 adverse reactions occurred.
‡Includes fatal outcome.
[a]Pneumonia includes atypical pneumonia, COVID-19 pneumonia, PJP, pneumonia, pneumonia cytomegaloviral, pneumonia fungal, pneumonia influenzal, and pneumonia viral.

IMPORTANT SAFETY INFORMATION (cont'd)

Adverse Reactions

The most common adverse reactions (≥20%) are musculoskeletal pain, cytokine release syndrome, cough, upper respiratory tract infection, diarrhea, fatigue, pneumonia, nausea, headache, and dyspnea. The most common Grade 3 or 4 laboratory abnormalities (≥30%) are decreased lymphocyte count, decreased neutrophil count, decreased hemoglobin, and decreased white blood cell count.

Use in Specific Populations

Lactation: Advise not to breastfeed.

Please see additional IMPORTANT SAFETY INFORMATION throughout and full Prescribing Information, including Boxed WARNING, for LYNOZYFIC.

LYNOZYFIC safety profile in LINKER-MM1 (cont'd)[1]

Adverse reactions occurring in ≥10% of patients receiving LYNOZYFIC (N=117)[1]

Adverse reaction (cont'd)	All grades (%)	Grades 3-4 (%)
General disorders and administration site conditions		
Fatigue*	34	0
Edema*	19	0.9†
Pyrexia	17	0
Nervous system disorders		
Headache*	22	0.9†
Encephalopathy‡[a]	18	3.4
Sensory neuropathy*	13	0.9

Adverse reaction (cont'd)	All grades (%)	Grades 3-4 (%)
Metabolism and nutrition disorders		
Decreased appetite	15	0.9†
Skin and subcutaneous tissue disorders		
Rash[b]	15	1.7†
Psychiatric disorders		
Insomnia	13	0
Vascular disorders		
Hypertension	10	4.3†

- Clinically significant adverse reactions that occurred in <10% of patients treated with LYNOZYFIC included **IRR, motor dysfunction, febrile neutropenia, ICANS, CMV infection, and PML**

*Includes other related terms.
†Only Grade 3 adverse reactions occurred.
‡Includes fatal outcome.
[a]Encephalopathy includes agitation, amnesia, cognitive disorder, confusional state, delirium, depressed level of consciousness, encephalopathy (including hyperammonemic and toxic encephalopathy), irritability, lethargy, memory impairment, mental status changes, somnolence, and excludes ICANS.
[b]Rash includes dermatitis acneiform, dermatitis contact, drug eruption, erythema, rash, rash erythematous, rash maculopapular, rash pruritic, and stasis dermatitis.

CMV, cytomegalovirus.

IMPORTANT SAFETY INFORMATION (cont'd)

Warnings and Precautions

Cytokine Release Syndrome (CRS): LYNOZYFIC can cause CRS, which can be serious or life-threatening. In LINKER-MM1, CRS occurred in 46% (54/117) of patients who received LYNOZYFIC at the recommended dose, with Grade 1 CRS occurring in 35% (41/117) of patients, Grade 2 in 10% (12/117), and Grade 3 in 0.9% (1/117). Thirty-eight percent (45/117) of patients had CRS following step-up dose 1, including 1 patient who experienced Grade 3 CRS; 8% (9/117) had an initial CRS event following a subsequent dose. Seventeen percent (19/113) of patients developed CRS after step-up dose 2, 10% (11/111) developed CRS after the first full 200-mg dose of LYNOZYFIC, and 3.6% (4/110) developed CRS after the second full dose. Recurrent CRS occurred in 20% (23/117) of patients. The median time to onset of CRS from the end of infusion was 11 (range: -1 to 184) hours after the most recent dose, with a median duration of 15 (range: 1 to 76) hours.

Please see additional IMPORTANT SAFETY INFORMATION throughout and full Prescribing Information, including Boxed WARNING, for LYNOZYFIC.

LYNOZYFIC safety profile in LINKER-MM1 (cont'd)[1]

Select laboratory abnormalities (≥5% for Grade 3 or 4; worsened from baseline) in patients with R/R multiple myeloma receiving LYNOZYFIC (N=117)[1]*

Laboratory abnormality†	All grades (%)	Grades 3-4 (%)
Hematology		
Lymphocyte count decreased	97	92
Hemoglobin decreased	72	42
Platelet count decreased	64	19
White blood cell count decreased	63	31
Neutrophil count decreased	62	47
Chemistry		
Aspartate aminotransferase increased	61	10
Phosphorus decreased	55	24
Creatinine increased	47	7
Alanine aminotransferase increased	46	6

*The denominator used to calculate the rate varied from 106 to 117, based on the number of patients with a baseline value and at least 1 posttreatment value.
†Laboratory tests were graded according to NCI CTCAE version 5.0.
NCI CTCAE, National Cancer Institute Common Terminology Criteria for Adverse Events.

IMPORTANT SAFETY INFORMATION (cont'd)

Warnings and Precautions (cont'd)

Cytokine Release Syndrome (CRS) (cont'd): Clinical signs and symptoms of CRS included, but were not limited to pyrexia, chills, hypoxia, tachycardia, and hypotension. Administer pretreatment medications and initiate therapy according to LYNOZYFIC step-up dosing to reduce the incidence and severity of CRS. Monitor patients for signs and symptoms of CRS after infusion. Counsel patients to seek immediate medical attention should signs or symptoms of CRS occur.

Please see additional IMPORTANT SAFETY INFORMATION throughout and full Prescribing Information, including Boxed WARNING, for LYNOZYFIC.

LYNOZYFIC safety profile in LINKER-MM1 (cont'd)[10]

Longer-term safety data (median follow-up: 21.3 months)[10]

Adverse reactions in ≥20% of patients (N=117)[10]

AR	All grades (%)	Grades 3-4 (%)
Hematologic ARs		
Neutropenia*	43.6	42.7
Anemia*	40.2	30.8
Non-hematologic ARs		
CRS	46.2	0.9
Diarrhea	40.2	1.7
Cough	40.2	0
Fatigue	34.2	0.9
Arthralgia	32.5	1.7
Hypokalemia*	24.8	3.4
Headache*	24.8	0.9
Nausea	23.9	0
Dyspnea	23.1	0.9
COVID-19*	22.2	9.4
Back pain	21.4	2.6
Upper respiratory tract infection	21.4	1.7
Vomiting	21.4	0

*Composite terms.
AR, adverse reaction.

- Infections occurred in 76.1% of patients, with Grades 3-4 in 37.6%; fatal infections occurred in 5.1% of patients[9,10]
- ARs that led to death within 30 days of the last treatment dose were reported in 9 patients (7.7%), 6 of which were due to infection, 1 due to tumor lysis syndrome, 1 due to encephalopathy, and 1 due to chronic kidney disease[9]
- Median exposure to treatment was 53.0 weeks (range: 1.0-194.0)[10]
- There were no additional CRS or ICANS events reported between the primary analysis and longer-term follow-up[10]

IMPORTANT SAFETY INFORMATION (cont'd)

Warnings and Precautions (cont'd)

Cytokine Release Syndrome (CRS) (cont'd): At the first sign of CRS, immediately evaluate patients for hospitalization, manage per current practice guidelines, and administer supportive care; withhold LYNOZYFIC until CRS resolves and modify the next dose or permanently discontinue LYNOZYFIC based on severity.

Please see additional IMPORTANT SAFETY INFORMATION throughout and full Prescribing Information, including Boxed WARNING, for LYNOZYFIC.

LYNOZYFIC is the only BsAb in R/R multiple myeloma that offers the potential for Q4W dosing with 30-minute IV infusions as early as 24 weeks[1]

Off-the-shelf LYNOZYFIC offers the potential for on-label Q4W dosing with ≥VGPR at or after Week 24 and ≥17 full doses[1,7]

- Treatment with LYNOZYFIC may be continued until disease progression or unacceptable toxicity[1]

QW dosing					Q2W dosing for all patients	Q4W dosing if ≥VGPR at or after Week 24 and ≥17 full doses
Step-up dose 1 (Day 1)	Step-up dose 2 (Day 8)	Full dose 1 (Day 15)	Full dose 2 (Week 4)	Weeks 5-13*	At Week 14 and every 2 weeks thereafter†	At Week 24 or after and every 4 weeks thereafter‡
5 mg	25 mg	200 mg	200 mg	200 mg	200 mg	200 mg
4-hr infusion			**1-hr** infusion if tolerated§		**30-min** infusion if tolerated§	

LYNOZYFIC dosing aims to reduce the logistical burden for patients and their caregivers with fewer visits over the course of LYNOZYFIC treatment.[1]

Please see additional important administration information on the next page and full dosing information in the LYNOZYFIC Prescribing Information.

*Weekly doses should be at least 5 days apart.
†Biweekly doses should be at least 10 days apart.
‡Every-4-week doses should be at least 24 days apart.
§For patients who experienced CRS with the previous dose of LYNOZYFIC, the duration of infusion should be maintained at the duration of the previous infusion; reduce the duration of infusion sequentially in subsequent doses in patients who do not experience CRS (eg, 4 hours, 1 hour, then 30 minutes).

IMPORTANT SAFETY INFORMATION (cont'd)

Warnings and Precautions (cont'd)

Cytokine Release Syndrome (CRS) (cont'd): *Infusion Related Reactions*

Infusion-related reactions (IRR) may be clinically indistinguishable from manifestations of CRS. In the patients who were treated with the recommended step-up dosing regimen and pretreatment medications, the rate of IRR was 9% [11/117 including Grade 2 IRR (4.3%) and Grade 3 IRR (1.7%)]. For IRR, interrupt or slow the rate of infusion or permanently discontinue LYNOZYFIC based on severity of reaction.

Please see additional IMPORTANT SAFETY INFORMATION throughout and full Prescribing Information, including Boxed WARNING, for LYNOZYFIC.

Patients treated with LYNOZYFIC should be hospitalized for 24 hours after the first and second step-up dose[1]

Monitoring and hospitalization instructions[1]

- Administer pretreatment medications and initiate therapy according to LYNOZYFIC step-up dosing to reduce the incidence and severity of CRS
- Due to the risk of CRS and neurologic toxicity, including ICANS, patients should be **hospitalized for 24 hours after administration of the first step-up dose,** and for **24 hours after administration of the second step-up dose**
  - This helps ensure your patients will receive prompt care for CRS and ICANS events, given that the median time to onset of CRS from the end of infusion was 11 hours (range: -1 to 184) and the median time to onset of ICANS was 1 day (range: 1 to 4) after the most recent dose

Additional important administration instructions[1]

- Administer LYNOZYFIC intravenously according to the step-up schedule to reduce the incidence and severity of cytokine release syndrome (CRS)
- Administer only as an IV infusion after dilution in 0.9% Sodium Chloride Injection
- LYNOZYFIC should be administered by an HCP with immediate access to emergency equipment and appropriate medical support to manage severe reactions such as CRS, IRR, and neurologic toxicity, including ICANS
- Administer pretreatment medications as described on page 22 to reduce the risk of CRS and/or IRR
- Refer to the Prescribing Information or the LYNOZYFIC Treatment Management Guide for recommendations for management of CRS, neurologic toxicity, including ICANS, and other adverse reactions

IMPORTANT SAFETY INFORMATION (cont'd)

Warnings and Precautions (cont'd)

Neurologic Toxicity, including Immune Effector Cell Associated Neurotoxicity Syndrome: LYNOZYFIC can cause serious or life-threatening neurologic toxicity, including ICANS. In LINKER-MM1, neurologic toxicity occurred in 54% of patients, with Grade 3 or 4 neurologic toxicity occurring in 8%, at the recommended dose. Neurologic toxicities included ICANS, depressed level of consciousness, encephalopathy, and toxic encephalopathy. ICANS occurred in 8% of patients who received LYNOZYFIC with the recommended dosing regimen, including Grade 3 events in 2.6%. Most patients experienced ICANS following step-up dose 1 (5%). Two patients (1.8%) experienced initial ICANS following step-up dose 2 and one patient developed the first occurrence of ICANS following a subsequent full dose of LYNOZYFIC. Recurrent ICANS occurred in one patient. The median time to onset of ICANS was 1 (range: 1 to 4) day after the most recent dose with a median duration of 2 (range: 1 to 11) days. The onset of ICANS can be concurrent with CRS, following resolution of CRS, or in the absence of CRS.

Please see additional IMPORTANT SAFETY INFORMATION throughout and full Prescribing Information, including Boxed WARNING, for LYNOZYFIC.

Recommendations for pretreatment medications to help reduce the risk of CRS and/or IRR[1]

Dose	Pretreatment medications	Administration relative to LYNOZYFIC infusion
Step-up dose 1, step-up dose 2, the first full treatment dose, the second full treatment dose	Acetaminophen (or equivalent) 650 mg to 1,000 mg orally	30 to 60 minutes prior to infusion
	Diphenhydramine (or equivalent) 25 mg orally or IV	30 to 60 minutes prior to infusion
	Dexamethasone (or equivalent) intravenously • 40 mg dexamethasone (or equivalent) before step-up dose 1, step-up dose 2, and the first full treatment dose • Once a full treatment dose of LYNOZYFIC is tolerated without CRS and/or IRR with 40 mg dexamethasone (or equivalent), administer 10 mg dexamethasone (or equivalent) prior to the subsequent LYNOZYFIC treatment dose	1 to 3 hours prior to infusion
Subsequent doses	Pretreatment medications may be discontinued once a treatment dose of LYNOZYFIC is tolerated without CRS and/or IRR following pretreatment with 10 mg dexamethasone (or equivalent), acetaminophen (or equivalent), and diphenhydramine (or equivalent) as described.	

IMPORTANT SAFETY INFORMATION (cont'd)

Warnings and Precautions (cont'd)

Neurologic Toxicity, including Immune Effector Cell Associated Neurotoxicity Syndrome (cont'd): The most common clinical signs and symptoms of ICANS are confusion, depressed level of consciousness, and lethargy. Monitor patients for signs and symptoms of neurologic toxicity, including ICANS during treatment. At the first sign of neurologic toxicity, including ICANS, immediately evaluate the patient; provide supportive therapy and consider further management per current practice guidelines. Withhold LYNOZYFIC until ICANS resolves and modify the next dose or permanently discontinue LYNOZYFIC based on severity. Counsel patients to seek immediate medical attention should signs or symptoms of neurologic toxicity, including ICANS occur at any time.

Please see additional IMPORTANT SAFETY INFORMATION throughout and full Prescribing Information, including Boxed WARNING, for LYNOZYFIC.

Nurse Educators are available to help

The Regeneron Nurse Educator team is available to provide educational support to healthcare providers as they integrate LYNOZYFIC into their practice. A locally designated Nurse Educator can:

Deliver in-service education on product dosing, administration, and adverse reaction management

Support the incorporation of LYNOZYFIC into your practice

Provide print and digital educational resources for healthcare providers and their patients

Prior to your first administration of LYNOZYFIC, you may reach out to your local Nurse Educator to discuss the educational support available for your practice.

IMPORTANT SAFETY INFORMATION (cont'd)

Warnings and Precautions (cont'd)

Neurologic Toxicity, including Immune Effector Cell Associated Neurotoxicity Syndrome (cont'd): Due to the potential for neurologic toxicity, including ICANS, patients receiving LYNOZYFIC are at risk of confusion and depressed consciousness. Advise patients to refrain from driving, or operating heavy or potentially dangerous machinery, for 48 hours after completion of each of the step-up doses and in the event of new onset of any neurological symptoms, until symptoms resolve.

Please see additional IMPORTANT SAFETY INFORMATION throughout and full Prescribing Information, including Boxed WARNING, for LYNOZYFIC.

About LYNOZYFIC Surround™

LYNOZYFIC SURROUND™

LYNOZYFIC Surround may help eligible patients access LYNOZYFIC and navigate the health insurance process

You are your patient's most trusted source for information about their condition and treatment. Along with your guidance, LYNOZYFIC Surround is here to help.

Financial support

Support that facilitates access to medication when eligible patients need assistance with out-of-pocket costs. LYNOZYFIC Surround will help investigate your patients' eligibility for the following programs:

- Commercial Copay Program
- Patient Assistance Program

Access and reimbursement support

Support to help your patients get access to their prescribed LYNOZYFIC as quickly as possible, including:

- Benefits investigation
- Prior authorization and appeal assistance
- Claims assistance for billing and reimbursement
- Product support

Additional LYNOZYFIC Surround support

Support from our dedicated Patient Navigators, who are available to educate and assist patients once they are prescribed LYNOZYFIC

For more information, call 1.844.RGN.HEME (1.844.746.4363), Option 1, Monday–Friday, 8 AM–8 PM Eastern time, or visit LYNOZYFIChcp.com.

Please see IMPORTANT SAFETY INFORMATION throughout and full Prescribing Information, including Boxed WARNING, for LYNOZYFIC.

IMPORTANT SAFETY INFORMATION (cont'd)

Warnings and Precautions (cont'd)

LYNOZYFIC REMS: LYNOZYFIC is available only through a restricted program under a REMS called the LYNOZYFIC REMS because of the risks of CRS and neurologic toxicity, including ICANS.

Infections: LYNOZYFIC can cause serious, life-threatening, or fatal infections. In patients who received LYNOZYFIC at the recommended dose in LINKER-MM1, serious infections, including opportunistic infections, occurred in 42% of patients, with Grade 3 or 4 infections in 38% and fatal infections in 4%. The most common serious infection reported (≥10%) were pneumonia and sepsis. Two cases of progressive multifocal leukoencephalopathy (PML) occurred in patients receiving LYNOZYFIC.

Monitor patients for signs and symptoms of infection and immunoglobulin levels prior to and during treatment with LYNOZYFIC and treat appropriately. Administer prophylactic antimicrobials, antibiotics, antifungals, antivirals, vaccines, and subcutaneous or intravenous immunoglobulin (IVIG) according to guidelines, including prophylaxis for PJP and herpesviruses. Withhold LYNOZYFIC or consider permanent discontinuation of LYNOZYFIC based on severity of the infection.

Neutropenia: LYNOZYFIC can cause neutropenia and febrile neutropenia. In patients who received LYNOZYFIC at the recommended dose in LINKER-MM1, decreased neutrophil count occurred in 62% of patients with Grade 3 or 4 decreased neutrophil count in 47%. Febrile neutropenia occurred in 8% of patients.

Monitor complete blood cell counts at baseline and periodically during treatment and provide supportive care per local guidelines. Monitor patients with neutropenia for signs of infection. Withhold LYNOZYFIC based on severity.

Hepatotoxicity: LYNOZYFIC can cause hepatotoxicity. In LINKER-MM1, elevated ALT occurred in 46% of patients, with Grade 3 or 4 ALT elevation occurring in 6%; elevated AST occurred in 61% of patients, with Grade 3 or 4 AST elevation occurring in 10% of patients who received the recommended dose. Grade 3 or 4 total bilirubin elevations occurred in 1.7% of patients. Liver enzyme elevation can occur with or without concurrent CRS.

Monitor liver enzymes and bilirubin at baseline and during treatment as clinically indicated. Withhold LYNOZYFIC or consider permanent discontinuation of LYNOZYFIC based on severity.

Embryo-Fetal Toxicity: Based on its mechanism of action, LYNOZYFIC may cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to the fetus. Advise females of reproductive potential to use effective contraception during treatment with LYNOZYFIC and for 3 months after the last dose.

Adverse Reactions

The most common adverse reactions (≥20%) are musculoskeletal pain, cytokine release syndrome, cough, upper respiratory tract infection, diarrhea, fatigue, pneumonia, nausea, headache, and dyspnea. The most common Grade 3 or 4 laboratory abnormalities (≥30%) are decreased lymphocyte count, decreased neutrophil count, decreased hemoglobin, and decreased white blood cell count.

Use in Specific Populations

Lactation: Advise not to breastfeed..

Please see full Prescribing Information, including Boxed WARNING, for LYNOZYFIC.

IMPORTANT SAFETY INFORMATION

INDICATION AND USAGE

LYNOZYFIC is a bispecific B-cell maturation antigen (BCMA)-directed CD3 T-cell engager indicated for the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least four prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody.

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 confirmatory trial(s).

IMPORTANT SAFETY INFORMATION

WARNING: CYTOKINE RELEASE SYNDROME and NEUROLOGIC TOXICITY, including IMMUNE EFFECTOR CELL-ASSOCIATED NEUROTOXICITY SYNDROME

- **Cytokine release syndrome (CRS), including serious or life-threatening reactions, can occur in patients receiving LYNOZYFIC. Initiate treatment with LYNOZYFIC step-up dosing to reduce the risk of CRS. Manage CRS, withhold LYNOZYFIC until CRS resolves, and modify the next dose or permanently discontinue based on severity.**
- **Neurologic toxicity, including immune effector cell-associated neurotoxicity syndrome (ICANS), including serious or life-threatening reactions, can occur in patients receiving LYNOZYFIC. Monitor patients for signs or symptoms of neurologic toxicity, including ICANS during treatment. Manage neurologic toxicity, including ICANS, withhold LYNOZYFIC until neurologic toxicity, including ICANS resolves, and modify the next dose or permanently discontinue based on severity.**
- **Because of the risk of CRS and neurologic toxicity, including ICANS, LYNOZYFIC is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the LYNOZYFIC REMS.**

Warnings and Precautions

Cytokine Release Syndrome (CRS): LYNOZYFIC can cause CRS, which can be serious or life-threatening. In LINKER-MM1, CRS occurred in 46% (54/117) of patients who received LYNOZYFIC at the recommended dose, with Grade 1 CRS occurring in 35% (41/117) of patients, Grade 2 in 10% (12/117), and Grade 3 in 0.9% (1/117). Thirty-eight percent (45/117) of patients had CRS following step-up dose 1, including 1 patient who experienced Grade 3 CRS; 8% (9/117) had an initial CRS event following a subsequent dose. Seventeen percent (19/113) of patients developed CRS after step-up dose 2, 10% (11/111) developed CRS after the first full 200-mg dose of LYNOZYFIC, and 3.6% (4/110) developed CRS after the second full dose. Recurrent CRS occurred in 20% (23/117) of patients. The median time to onset of CRS from the end of infusion was 11 (range: -1 to 184) hours after the most recent dose, with a median duration of 15 (range: 1 to 76) hours.

Clinical signs and symptoms of CRS included, but were not limited to pyrexia, chills, hypoxia, tachycardia, and hypotension. Administer pretreatment medications and initiate therapy according to LYNOZYFIC step-up dosing to reduce the incidence and severity of CRS. Monitor patients for signs and symptoms of CRS after infusion. Counsel patients to seek immediate medical attention should signs or symptoms of CRS occur.

At the first sign of CRS, immediately evaluate patients for hospitalization, manage per current practice guidelines, and administer supportive care; withhold LYNOZYFIC until CRS resolves and modify the next dose or permanently discontinue LYNOZYFIC based on severity.

Infusion Related Reactions

Infusion-related reactions (IRR) may be clinically indistinguishable from manifestations of CRS. In the patients who were treated with the recommended step-up dosing regimen and pretreatment medications, the rate of IRR was 9% [11/117 including Grade 2 IRR (4.3%) and Grade 3 IRR (1.7%)]. For IRR, interrupt or slow the rate of infusion or permanently discontinue LYNOZYFIC based on severity of reaction.

Please see additional IMPORTANT SAFETY INFORMATION throughout and full Prescribing Information, including Boxed WARNING, for LYNOZYFIC.

IMPORTANT SAFETY INFORMATION (cont'd)

Warnings and Precautions (cont'd)

Neurologic Toxicity, including Immune Effector Cell Associated Neurotoxicity Syndrome: LYNOZYFIC can cause serious or life-threatening neurologic toxicity, including ICANS. In LINKER-MM1, neurologic toxicity occurred in 54% of patients, with Grade 3 or 4 neurologic toxicity occurring in 8%, at the recommended dose. Neurologic toxicities included ICANS, depressed level of consciousness, encephalopathy, and toxic encephalopathy. ICANS occurred in 8% of patients who received LYNOZYFIC with the recommended dosing regimen, including Grade 3 events in 2.6%. Most patients experienced ICANS following step-up dose 1 (5%). Two patients (1.8%) experienced initial ICANS following step-up dose 2 and one patient developed the first occurrence of ICANS following a subsequent full dose of LYNOZYFIC. Recurrent ICANS occurred in one patient. The median time to onset of ICANS was 1 (range: 1 to 4) day after the most recent dose with a median duration of 2 (range: 1 to 11) days. The onset of ICANS can be concurrent with CRS, following resolution of CRS, or in the absence of CRS.

The most common clinical signs and symptoms of ICANS are confusion, depressed level of consciousness, and lethargy. Monitor patients for signs and symptoms of neurologic toxicity, including ICANS during treatment. At the first sign of neurologic toxicity, including ICANS, immediately evaluate the patient; provide supportive therapy and consider further management per current practice guidelines. Withhold LYNOZYFIC until ICANS resolves and modify the next dose or permanently discontinue LYNOZYFIC based on severity. Counsel patients to seek immediate medical attention should signs or symptoms of neurologic toxicity, including ICANS occur at any time.

Due to the potential for neurologic toxicity, including ICANS, patients receiving LYNOZYFIC are at risk of confusion and depressed consciousness. Advise patients to refrain from driving, or operating heavy or potentially dangerous machinery, for 48 hours after completion of each of the step-up doses and in the event of new onset of any neurological symptoms, until symptoms resolve.

LYNOZYFIC REMS: LYNOZYFIC is available only through a restricted program under a REMS called the LYNOZYFIC REMS because of the risks of CRS and neurologic toxicity, including ICANS.

Infections: LYNOZYFIC can cause serious, life-threatening, or fatal infections. In patients who received LYNOZYFIC at the recommended dose in LINKER-MM1, serious infections, including opportunistic infections, occurred in 42% of patients, with Grade 3 or 4 infections in 38% and fatal infections in 4%. The most common serious infection reported (≥10%) were pneumonia and sepsis. Two cases of progressive multifocal leukoencephalopathy (PML) occurred in patients receiving LYNOZYFIC.

Monitor patients for signs and symptoms of infection and immunoglobulin levels prior to and during treatment with LYNOZYFIC and treat appropriately. Administer prophylactic antimicrobials, antibiotics, antifungals, antivirals, vaccines, and subcutaneous or intravenous immunoglobulin (IVIG) according to guidelines, including prophylaxis for PJP and herpesviruses. Withhold LYNOZYFIC or consider permanent discontinuation of LYNOZYFIC based on severity of the infection.

Neutropenia: LYNOZYFIC can cause neutropenia and febrile neutropenia. In patients who received LYNOZYFIC at the recommended dose in LINKER-MM1, decreased neutrophil count occurred in 62% of patients with Grade 3 or 4 decreased neutrophil count in 47%. Febrile neutropenia occurred in 8% of patients.

Monitor complete blood cell counts at baseline and periodically during treatment and provide supportive care per local guidelines. Monitor patients with neutropenia for signs of infection. Withhold LYNOZYFIC based on severity.

Hepatotoxicity: LYNOZYFIC can cause hepatotoxicity. In LINKER-MM1, elevated ALT occurred in 46% of patients, with Grade 3 or 4 ALT elevation occurring in 6%; elevated AST occurred in 61% of patients, with Grade 3 or 4 AST elevation occurring in 10% of patients who received the recommended dose. Grade 3 or 4 total bilirubin elevations occurred in 1.7% of patients. Liver enzyme elevation can occur with or without concurrent CRS.

Monitor liver enzymes and bilirubin at baseline and during treatment as clinically indicated. Withhold LYNOZYFIC or consider permanent discontinuation of LYNOZYFIC based on severity.

Please see additional IMPORTANT SAFETY INFORMATION throughout and full Prescribing Information, including Boxed WARNING, for LYNOZYFIC.

IMPORTANT SAFETY INFORMATION (cont'd)

Warnings and Precautions (cont'd)

Embryo-Fetal Toxicity: Based on its mechanism of action, LYNOZYFIC may cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to the fetus. Advise females of reproductive potential to use effective contraception during treatment with LYNOZYFIC and for 3 months after the last dose.

Adverse Reactions

The most common adverse reactions (≥20%) are musculoskeletal pain, cytokine release syndrome, cough, upper respiratory tract infection, diarrhea, fatigue, pneumonia, nausea, headache, and dyspnea. The most common Grade 3 or 4 laboratory abnormalities (≥30%) are decreased lymphocyte count, decreased neutrophil count, decreased hemoglobin, and decreased white blood cell count.

Use in Specific Populations

Lactation: Advise not to breastfeed.

Please see full Prescribing Information, including Boxed WARNING, for LYNOZYFIC.

References: 1. LYNOZYFIC (linvoseltamab-gcpt) full U.S. prescribing information. Regeneron Pharmaceuticals, Inc.; 2025. **2.** Bumma N, Richter J, Jagannath S, et al. *J Clin Oncol*. 2024;16:JCO2401008. doi:10.1200/JCO.24.01008 **3.** Dima D, Jiang D, Singh DJ, et al. *Cancers (Basel)*. 2022;14(17):4082. doi:10.3390/cancers14174082 **4.** Parsons JA, Greenspan NR, Baker NA, McKillop C, Hicks LK, Chan O. *BMC Cancer*. 2019;19(1):264. doi:10.1186/s12885-019-5467-x **5.** Zhang SC, Ballas LK. *Semin Radiat Oncol*. 2025;35(1):87-98. doi:10.1016/j.semradonc.2024.10.004 **6.** Dhakal B, Einsele H, Schecter JM, et al. *Blood Adv*. 2024;8(19):5062-5071. doi:10.1182/bloodadvances.2024012640 **7.** Jagannath S, Richter J, Dhodapkar MV, et al. Linvoseltamab, a B-cell maturation antigen-targeted T-cell-engaging bispecific antibody in patients with relapsed or refractory multiple myeloma, including difficult-to-treat subgroups. Presented at: American Association for Cancer Research 2024 Annual Meeting; April 5-10, 2024; San Diego, California. **8.** Grywalska E, Zaborek M, Łyczba J, et al. *Cells*. 2020;9(11):2398. doi:10.3390/cells9112398 **9.** Data on file. Regeneron Pharmaceuticals, Inc. **10.** Shah MR, Richter J, Lee HC, et al. Linvoseltamab in patients with relapsed/refractory multiple myeloma: Longer follow-up and selected high-risk subgroup analyses of the LINKER-MM1 study. Presented at: American Society of Hematology (ASH) Congress; December 7-10, 2024; San Diego, California. **11.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Multiple Myeloma V.2.026. © National Comprehensive Cancer Network, Inc. 2025. All rights reserved. Accessed July 16, 2025. To view the most recent and complete version of the guideline, go online to NCCN.org.

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use LYNOZYFIC safely and effectively. See full prescribing information for LYNOZYFIC.

LYNOZYFIC™ (linvoseltamab-gcpt) injection, for intravenous use
Initial U.S. Approval: 2025

WARNING: CYTOKINE RELEASE SYNDROME and NEUROLOGIC TOXICITY, including IMMUNE EFFECTOR CELL-ASSOCIATED NEUROTOXICITY SYNDROME
See full prescribing information for complete boxed warning.

- **Cytokine release syndrome (CRS), including serious or life-threatening reactions, can occur in patients receiving LYNOZYFIC. Initiate treatment with LYNOZYFIC step-up dosing to reduce the risk of CRS. Manage CRS, withhold LYNOZYFIC until CRS resolves and modify the next dose or permanently discontinue based on severity. (2.2, 2.4, 2.5, 5.1)**
- **Neurologic Toxicity, including immune effector cell-associated neurotoxicity syndrome (ICANS), including serious or life-threatening reactions, can occur in patients receiving LYNOZYFIC. Monitor patients for signs or symptoms of neurologic toxicity, including ICANS during treatment. Manage neurologic toxicity, including ICANS, withhold LYNOZYFIC until neurologic toxicity, including ICANS resolves and modify the next dose or permanently discontinue based on severity. (2.2, 2.4, 2.5, 5.2)**
- **LYNOZYFIC is available only through a restricted program called the LYNOZYFIC Risk Evaluation and Mitigation Strategy (REMS). (5.3)**

INDICATIONS AND USAGE

LYNOZYFIC is a bispecific B-cell maturation antigen (BCMA)-directed CD3 T-cell engager indicated for the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least four prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody.

Dosing Schedule	Day	Dose of LYNOZYFIC	
Weekly Dosing Schedule	One week after Day 15 treatment dose and once weekly from Week 4 to Week 13 for 10 treatment doses	Second and subsequent treatment doses	200 mg
Biweekly (Every 2 Weeks) Dosing Schedule	Week 14 and every 2 weeks thereafter	Subsequent treatment doses	200 mg
Patients who have achieved and maintained VGPR or better at or after Week 24 and received at least 17 doses of 200 mg			
Every 4 Weeks Dosing Schedule	At Week 24 or after and every 4 weeks thereafter	Subsequent treatment doses	200 mg

- Patients should be hospitalized for 24 hours after administration of the first step-up dose and for 24 hours after administration of the second step-up dose. (2.1)
- See Full Prescribing Information for instructions on preparation and administration. (2.6)

DOSAGE FORMS AND STRENGTHS

Injection:

- 5 mg/2.5 mL (2 mg/mL) single-dose vial (3)
- 200 mg/10 mL (20 mg/mL) single-dose vial (3)

CONTRAINDICATIONS

None. (4)

WARNINGS AND PRECAUTIONS

- Infections: Can cause serious or fatal infections. Monitor patients for signs or symptoms of infection and treat accordingly. (5.4)
- Neutropenia: Monitor complete blood cell counts at baseline and periodically during treatment. (5.5)
- Hepatotoxicity: Can cause hepatotoxicity. Monitor liver enzymes and bilirubin at baseline and during treatment as clinically indicated. (5.6)
- Embryo-Fetal Toxicity: May cause fetal harm. Advise females of reproductive potential of the potential risk to the fetus and to use effective contraception. (5.7, 8.1, 8.3)

NCCN recommends linvoseltamab-gcpt (LYNOZYFIC) in R/R multiple myeloma[11]

NCCN
CATEGORY 2A
PREFERRED

Linvoseltamab-gcpt (LYNOZYFIC) is a Preferred, Category 2A therapy for relapsed/refractory multiple myeloma patients after at least four prior therapies, including an anti-CD38 monoclonal antibody, a proteasome inhibitor, and an immunomodulatory agent, recommended by the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®).[11]*

NCCN makes no warranties of any kind whatsoever regarding their content, use, or application, and disclaims any responsibility for their application or use in any way. See the NCCN Guidelines® for detailed recommendations.

*See NCCN Guidelines for the NCCN definitions of Categories of Preference and Categories of Evidence and Consensus.

SELECT IMPORTANT SAFETY INFORMATION

Warnings and Precautions

Cytokine Release Syndrome (CRS): LYNOZYFIC can cause CRS, which can be serious or life-threatening. In LINKER-MM1, CRS occurred in 46% (54/117) of patients who received LYNOZYFIC at the recommended dose, with Grade 1 CRS occurring in 35% (41/117) of patients, Grade 2 in 10% (12/117), and Grade 3 in 0.9% (1/117). Thirty-eight percent (45/117) of patients had CRS following step-up dose 1, including 1 patient who experienced Grade 3 CRS; 8% (9/117) had an initial CRS event following a subsequent dose. Seventeen percent (19/113) of patients developed CRS after step-up dose 2, 10% (11/111) developed CRS after the first full 200-mg dose of LYNOZYFIC, and 3.6% (4/110) developed CRS after the second full dose. Recurrent CRS occurred in 20% (23/117) of patients. The median time to onset of CRS from the end of infusion was 11 (range: -1 to 184) hours after the most recent dose, with a median duration of 15 (range: 1 to 76) hours.

Please see additional IMPORTANT SAFETY INFORMATION throughout and full Prescribing Information, including Boxed WARNING, for LYNOZYFIC.

LYNOZYFIC showed deep* and durable responses and is an FDA-approved bispecific antibody offering the potential for Q4W dosing in R/R multiple myeloma[1]

70% ORR (95% CI: 59-80)
≥CR in 45% of patients
(95% CI: 34-57)[1]

- Median time to first response: 0.95 months (range: 0.5-6.3)[1,9]
- Estimated DoR: median not reached (95% CI: 12-NE); 89% (95% CI: 77-95) still responding at 9 months[1]

Explore the deep* and durable responses on page 7 >

CRS occurred in 46% of patients, and neurologic toxicity occurred in 54% of patients[1]

- CRS: 45% Grade 1 or 2, 0.9% Grade 3; median time to onset: 11 hours (range: -1 to 184)[1]
- ICANS occurred in 8% of patients, 2.6% Grade 3; median time to onset: 1 day (range: 1 to 4)[1]

Learn more about safety on page 11 >

24-hour hospitalization after both step-up doses[1]

- Due to the risk of CRS and neurologic toxicity, including ICANS, patients should be hospitalized for 24 hours after the first and second step-up dose[1]

Q4W dosing option included in the clinical trial and FDA-approved label[1]

- Patients who achieve and maintain ≥VGPR at or after Week 24 and receive ≥17 full doses can switch to every-4-week dosing[1]

See the full dosing schedule on page 20 >

***Deep response defined as ≥VGPR.**

INDICATION AND USAGE

LYNOZYFIC is a bispecific B-cell maturation antigen (BCMA)-directed CD3 T-cell engager indicated for the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least four prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody.

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 confirmatory trial(s).

Please see additional IMPORTANT SAFETY INFORMATION throughout and full Prescribing Information, including Boxed WARNING, for LYNOZYFIC.

IMPORTANT SAFETY INFORMATION

WARNING: CYTOKINE RELEASE SYNDROME and NEUROLOGIC TOXICITY, including IMMUNE EFFECTOR CELL-ASSOCIATED NEUROTOXICITY SYNDROME

- **Cytokine release syndrome (CRS), including serious or life-threatening reactions, can occur in patients receiving LYNOZYFIC. Initiate treatment with LYNOZYFIC step-up dosing to reduce the risk of CRS. Manage CRS, withhold LYNOZYFIC until CRS resolves, and modify the next dose or permanently discontinue based on severity.**
- **Neurologic toxicity, including immune effector cell-associated neurotoxicity syndrome (ICANS), including serious or life-threatening reactions, can occur in patients receiving LYNOZYFIC. Monitor patients for signs or symptoms of neurologic toxicity, including ICANS during treatment. Manage neurologic toxicity, including ICANS, withhold LYNOZYFIC until neurologic toxicity, including ICANS resolves, and modify the next dose or permanently discontinue based on severity.**
- **Because of the risk of CRS and neurologic toxicity, including ICANS, LYNOZYFIC is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the LYNOZYFIC REMS.**

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