

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

761400Orig1s000

REMS

Risk Evaluation and Mitigation Strategy (REMS) Document

LYNOZYFIC (linvoseltamab-gcpt) REMS

I. Administrative Information

Risk: Cytokine Release Syndrome (CRS), and neurologic toxicity, including Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS)

Application Number: BLA 761400

Application Holder: Regeneron Pharmaceuticals, Inc.

Initial REMS Approval: 07/2025

II. REMS Goal

The goal of the LYNOZYFIC REMS is to mitigate the risks of Cytokine Release Syndrome (CRS) and neurologic toxicity, including Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS) by:

1. Ensuring prescribers are aware of the importance of monitoring for signs and symptoms of CRS and neurologic toxicity, including ICANS in patients exposed to LYNOZYFIC

III. REMS Requirements

Regeneron Pharmaceuticals, Inc. must ensure that healthcare providers, patients, pharmacies, healthcare settings and wholesalers-distributors comply with the following requirements:

1. Healthcare providers who prescribe LYNOZYFIC must:

To become certified to prescribe	1. Review the drug's Prescribing Information. 2. Review the Prescriber Training Program and Adverse Reaction Management Guide. 3. Successfully complete the Knowledge Assessment and submit it to the REMS. 4. Enroll in the REMS by completing and submitting the Prescriber Enrollment Form to the REMS.
Before treatment initiation (first step-up dose)	5. Counsel the patient on: a. how to recognize and respond to signs and symptoms of CRS and neurologic toxicity, including ICANS, b. the need to report all symptoms suggestive of CRS and neurologic toxicity, including ICANS to their healthcare provider or emergency room provider immediately, c. the need to carry the Patient Wallet Card at all times. 6. Complete the Patient Wallet Card and provide the Patient Wallet Card to the patient.

At all times	7. Report serious adverse events of CRS and neurologic toxicity, including ICANS to the REMS.
2. Patients who are prescribed LYNOZYFIC:	
Before treatment initiation	1. Receive counseling from the prescriber using the Patient Wallet Card .
At all times	2. Have the Patient Wallet Card with you and inform other healthcare providers about treatment with LYNOZYFIC.
3. Pharmacies and healthcare settings that dispense LYNOZYFIC must:	
To become certified to dispense	1. Designate an Authorized Representative to carry out the certification process and oversee implementation and compliance with the REMS requirements on behalf of the pharmacy and/or healthcare setting. 2. Have the Authorized Representative review the Pharmacy and Healthcare Setting Training Program. 3. Have the Authorized Representative enroll in the REMS by completing and submitting the Pharmacy and Healthcare Setting Enrollment Form to the REMS. 4. Train all relevant staff involved in dispensing LYNOZYFIC on the REMS requirements using the Pharmacy and Healthcare Setting Training Program. 5. Establish processes and procedures to verify the prescriber is certified for all dispenses after the first prescription.
Before dispensing, first prescription	6. Obtain authorization to dispense by contacting the REMS to verify the prescriber is certified.
Before dispensing, all subsequent prescriptions	7. Verify the prescriber is certified through the processes and procedures established as a requirement of the REMS.
To maintain certification to dispense	8. Have a new Authorized Representative enroll in the REMS by completing and submitting the Pharmacy and Healthcare Setting Enrollment Form to the REMS if the Authorized Representative changes.
At all times	9. Report serious adverse events of CRS and neurologic toxicity, including ICANS to the REMS. 10. Not distribute, transfer, loan or sell LYNOZYFIC except to certified pharmacies and healthcare settings. 11. Maintain records of staff training. 12. Maintain records that processes and procedures are in place and are being followed. 13. Maintain records of all LYNOZYFIC dispenses and provide data to the REMS, as requested.

14. Comply with audits carried out by Regeneron Pharmaceuticals, Inc. or a third party acting on behalf of Regeneron Pharmaceuticals, Inc. to ensure that all processes and procedures are in place and are being followed.

4. Wholesalers-Distributors that distribute LYNOZYFIC must:

To be able to distribute	1. Establish processes and procedures to ensure that LYNOZYFIC is distributed only to certified pharmacies and healthcare settings. 2. Train all relevant staff involved in distribution on the REMS requirements.
At all times	3. Distribute only to certified pharmacies and healthcare settings. 4. Maintain records that all processes and procedures are in place and are being followed. 5. Maintain and submit records of drug distribution to the REMS at least on a weekly basis. 6. Comply with audits carried out by Regeneron Pharmaceuticals, Inc. or a third party acting on behalf of Regeneron Pharmaceuticals, Inc. to ensure that all processes and procedures are in place and are being followed.

Regeneron Pharmaceuticals, Inc. must provide training to healthcare providers who prescribe LYNOZYFIC. The training includes the following educational materials: [Prescriber Training Program](#), [Adverse Reaction Management Guide](#), and [Knowledge Assessment](#). The training must be available online.

Regeneron Pharmaceuticals, Inc. must provide training to pharmacies and healthcare settings that dispense LYNOZYFIC. The training includes the following educational material: [Pharmacy and Healthcare Setting Training Program](#). The training must be available online.

To inform healthcare providers about the REMS and the risks and safe use of LYNOZYFIC, Regeneron Pharmaceuticals, Inc. must disseminate REMS communication materials according to the table below:

Target Audience	Communication Materials & Dissemination Plan
Healthcare providers, including oncologists, oncology physician assistants, oncology nurse practitioners, hematologists/oncologists, and oncology nurses who are likely to prescribe and care for patients treated with LYNOZYFIC.	REMS Letters: Healthcare Provider REMS Letter, Professional Society REMS Letter with attachment REMS Fact Sheet 1. Email within 30 calendar days of the date LYNOZYFIC is first commercially distributed and again 12 months later. a. Send by mail within 30 calendar days of the date the first email was sent if a healthcare provider's email address is not available, or the email is undeliverable. b. Send a second email within 30 calendar days of the date the first email was sent if the first email is marked unopened. c. Send by mail within 30 calendar days of the date the second email was sent if the second email is marked as unopened.

Target Audience	Communication Materials & Dissemination Plan
	2. Disseminate through field-based sales and medical representatives for 12 months from the date LYNOZYFIC is first commercially distributed. 3. Disseminate within 30 calendar days of the date LYNOZYFIC is first commercially distributed and again 12 months later through the following professional societies and request the letter or content be provided to their members. a. Advanced Practitioner Society for Hematology and Oncology (APSHO); American Geriatrics Society (AGS); American Pharmacists Association (APhA); American Society of Clinical Oncology (ASCO); American Society of Health-System Pharmacists (ASHP); American Society of Hematology (ASH); American Society for Transplantation and Cellular Therapy (ASTCT); Association of VA Hematology/Oncology (AVAHO); Eastern Cooperative Oncology Group and American College of Radiology Imaging Network (ECOG-ACRIN) Cancer Research group; HealthTree Foundation; Hematology Oncology Pharmacy Association (HOPA); International Myeloma Foundation (IMF); International Myeloma Society (IMS); International Society for Experimental Hematology (ISEH); Leukemia and Lymphoma Society (LLS); Michigan Society of Hematology and Oncology (MSHO); Multiple Myeloma Research Foundation (MMRF); National Comprehensive Cancer Network (NCCN); North American Immuno-Hematology Clinical Education and Research Consortium (NICER Consortium); Ohio Hematology Oncology Society (OHOS); Oncology Nursing Society (ONS); Society for Immunotherapy of Cancer (SITC); Society of Hematologic Oncology (SOHO); Southwest Oncology Group Cancer Research Network (SWOG CRN) 4. Disseminate at Professional Meetings where Regeneron Pharmaceuticals, Inc. has a presence for 12 months from the date LYNOZYFIC is first commercially distributed.
	REMS Fact Sheet: 1. Disseminate at Professional Meetings where Regeneron Pharmaceuticals, Inc. has a presence for 12 months from the date LYNOZYFIC is first commercially distributed. 2. Disseminate through field-based sales and medical representatives during the initial and/or follow-up discussion with healthcare providers for 12 months after LYNOZYFIC is first commercially distributed. Field-based sales and/or medical representatives to orally review the key risk messages contained in the REMS Fact Sheet during the visit with the healthcare provider.

To support REMS operations, Regeneron Pharmaceuticals, Inc. must:

1. Authorize dispensing for each patient's first prescription based on verifying the prescriber is certified.
2. Establish and maintain the [REMS Website](#), www.Lynozifycrems.com. The [REMS Website](#) must include the capability to enroll prescribers, pharmacies and healthcare settings, complete training online, maintain records of that training, and an option to print the Prescribing Information (PI),

Medication Guide, and REMS materials. All product websites for consumers and healthcare providers must include prominent REMS-specific links to the [REMS Website](#).

3. Make the [REMS Website](#) fully operational and all REMS materials available through the website and the REMS Coordinating Center at the time LYNOZYFIC first becomes commercially available.
4. Establish and maintain a REMS Coordinating Center for REMS participants at 1-855-212-6391.
5. Establish and maintain a validated, secure database of all REMS participants who are enrolled and/or certified in the REMS.
6. Ensure prescribers, pharmacies and healthcare settings can enroll in the REMS online, by fax and email.
7. Ensure pharmacies and healthcare settings are able to obtain authorization to dispense by phone and online.
8. Notify prescribers, pharmacies and healthcare settings within 1 calendar day after they become certified in the REMS.
9. Provide certified prescribers access to the database of certified pharmacies and healthcare settings.
10. Provide certified pharmacies and healthcare settings access to the database of certified prescribers.
11. Provide authorized wholesalers-distributors access to the database of certified pharmacies and healthcare settings.
12. Report serious adverse events of CRS and neurologic toxicity, including ICANS as soon as possible to the FDA but no later than 15 calendar days from the initial receipt of the information by the applicant. This requirement does not affect the applicant's other reporting and follow-up requirements under applicable FDA regulations.

To ensure REMS participants' compliance with the REMS, Regeneron Pharmaceuticals, Inc. must:

13. Verify annually that the designated Authorized Representative for certified pharmacies and healthcare settings remains the same. If different, the pharmacy and healthcare setting must recertify with a new Authorized Representative.
14. Maintain adequate records to demonstrate that REMS requirements have been met, including, but not limited to records of: LYNOZYFIC distribution and dispensing; certification of prescribers; pharmacies and healthcare settings; authorized wholesalers-distributors; and audits of REMS participants. These records must be readily available for FDA inspections.
15. Monitor prescribers, pharmacies and healthcare settings, and wholesalers-distributors on an ongoing basis to ensure the requirements of the REMS are being met. Take corrective action if noncompliance is identified, including decertification or deauthorization.
16. Establish and maintain a plan for addressing noncompliance with REMS requirements.
17. Audit all certified pharmacies and healthcare settings no later than 180 calendar days after the pharmacy or healthcare setting receives their first shipment of LYNOZYFIC and annually thereafter to ensure that all REMS processes and procedures are in place, functioning, and support the REMS requirements.
18. Audit all wholesalers-distributors that have distributed LYNOZYFIC no later than 180 calendar days of being authorized to distribute LYNOZYFIC and annually thereafter to ensure that all REMS

processes and procedures are in place, functioning, and support the REMS requirements.

19. Take reasonable steps to improve operations of and compliance with the requirements in the LYNOZYFIC REMS based on monitoring and evaluation of the LYNOZYFIC REMS.

IV. REMS Assessment Timetable

Regeneron Pharmaceuticals, Inc. must submit REMS Assessments 12 months from the date of the initial approval of the REMS (MM/DD/YYYY) and annually thereafter. To facilitate inclusion of as much information as possible, while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment should conclude no earlier than 60 calendar days before the submission date for that assessment. Regeneron Pharmaceuticals, Inc. must submit each assessment so that it will be received by the FDA on or before the due date.

V. REMS Materials

The following materials are part of the LYNOZYFIC REMS:

Enrollment Forms

Prescriber:

1. [Prescriber Enrollment Form](#)

Pharmacy and Healthcare Setting:

2. [Pharmacy and Healthcare Setting Enrollment Form](#)

Training and Educational Materials

Prescriber:

3. [Prescriber Training Program](#)
4. [Adverse Reaction Management Guide](#)
5. [Knowledge Assessment](#)

Patient:

6. [Patient Wallet Card](#)

Pharmacy and Healthcare Setting:

7. [Pharmacy and Healthcare Setting Training Program](#)

Communication Materials

8. [Healthcare Provider REMS Letter](#)
9. [Professional Society REMS Letter](#)
10. [REMS Fact Sheet](#)

Other Materials

11. [REMS Website](#)

VI. Statutory Elements

This REMS is required under section 505-1 of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 355-1) and consists of the following elements:

1. Communication Plan
2. Elements to Assure Safe Use (ETASU)
 - Healthcare providers who prescribe LYNOZYFIC are specially certified under 505-1(f)(3)(A)
 - Pharmacies and healthcare settings that dispense LYNOZYFIC are specially certified under 505-1(f)(3)(B)
3. Implementation System
4. Timetable for Submission of Assessments

Prescriber Enrollment Form

Instructions

To become a certified prescriber in the LYNOZYFIC REMS and prescribe LYNOZYFIC:

- Review the Prescribing Information, the **Prescriber Training Program** and **Adverse Reaction Management Guide**.
- Successfully complete and submit the **Knowledge Assessment** and this **Prescriber Enrollment Form**:
 - online at **www.Lynozycicrem.com**, or
 - by email at **LYNOZYFICREMS@ubc.com**, or
 - by fax to 1-866-750-0907

The LYNOZYFIC REMS will verify both the **Knowledge Assessment** and **Prescriber Enrollment Form** are complete and provide confirmation of certification via email.

If LYNOZYFIC will be dispensed and administered in this same location, an Authorized Representative must complete the pharmacy and healthcare setting certification. **Certified LYNOZYFIC prescribers cannot be designated as the Authorized Representative for a pharmacy or healthcare setting.**

Prescriber Information (* indicates required field)

*First Name:		*Last Name:	
*Credentials: ☐ MD ☐ DO ☐ NP ☐ PA ☐ Other (please specify)			
*Specialty (select one): ☐ Oncology ☐ Hematology ☐ Hematology/Oncology ☐ Other (please specify)			
*National Provider Identifier (NPI) #:			
*Practice/Facility Name:			
*Address Line 1:			
Address Line 2:			
*City:		*State:	*ZIP Code:
*Email:	*Phone:	*Fax:	

To become certified to prescribe, I must:

- Review the LYNOZYFIC Prescribing Information.
- Review the **Prescriber Training Program** and **Adverse Reaction Management Guide**.
- Successfully complete the **Knowledge Assessment** and submit it to the REMS.
- Enroll in the REMS by completing and submitting the **Prescriber Enrollment Form** to the REMS.

Before treatment initiation (first step-up dose), I must:

- Counsel the patient on:
 - how to recognize and respond to signs and symptoms of Cytokine Release Syndrome (CRS) and neurologic toxicity, including Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS),
 - the need to report all symptoms suggestive of CRS and neurologic toxicity, including ICANS to their healthcare provider or emergency room provider immediately,
 - the need to carry the **Patient Wallet Card** at all times.
- Complete the **Patient Wallet Card** and provide the **Patient Wallet Card** to the patient.

At all times, I must:

- Report serious adverse events of CRS and neurologic toxicity, including ICANS to the REMS.

By signing this form, I agree to comply with all LYNOZYFIC REMS requirements. Regeneron representatives and its agents, including trusted vendors, may contact me to support the administration and assessment of, and/or education about the REMS.

Healthcare providers must report serious adverse events of CRS and neurologic toxicity, including ICANS to the LYNOZYFIC REMS at 1-855-212-6391.

Healthcare providers should also report all other suspected adverse events associated with LYNOZYFIC to Regeneron Pharmaceuticals, Inc. at 1-844-734-6643 or medical.information@regeneron.com or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Your information (name, location, and contact information) may be listed on a location finder as a location having a LYNOZYFIC REMS certified prescriber. This location finder may be available to healthcare professionals and/or patients seeking LYNOZYFIC REMS certified pharmacy and healthcare settings.

If you do not want your information listed, please call LYNOZYFIC REMS at 1-855-212-6391.

By signing up for the LYNOZYFIC REMS, Regeneron representatives and its agents, including trusted vendors, may contact me to support the administration of and/or education about the REMS, and we will use your information as provided in our Healthcare Provider Privacy Notice which is available here: www.regeneron.com/privacy-notice.

*Prescriber Signature:	*Date (MM/DD/YYYY):
------------------------	---------------------

Phone: 1-855-212-6391

www.Lynozycicrem.com

Fax: 1-866-750-0907

REGENERON
SCIENCE TO MEDICINE™

LYNOZYFICREMS@ubc.com

LYNOZYFIC™
(linvoseltamab-gcpt) injection

Pharmacy and Healthcare Setting Enrollment Form

Instructions

To become certified in the LYNOZYFIC REMS and dispense LYNOZYFIC, a pharmacy and healthcare setting must designate an Authorized Representative to:

- Review the **Pharmacy and Healthcare Setting Training Program**.
- Enroll in the REMS by completing and submitting this **Pharmacy and Healthcare Setting Enrollment Form**:
 - online at **www.Lynozylicrems.com**, or
 - by email at **LYNOZYFICREMS@ubc.com**, or
 - via fax to 1-866-750-0907

The Authorized Representative will receive confirmation of the certification via email. Once certified, the pharmacy and healthcare setting's information will be shared with Regeneron Pharmaceuticals, Inc.'s wholesaler-distributor partners, to allow the pharmacy and healthcare setting to purchase product.

Certified LYNOZYFIC prescribers cannot be designated as the Authorized Representative for a pharmacy and healthcare setting.

Pharmacy and Healthcare Setting Information (*indicates required field)

*Select one ☐ New Certification ☐ Change in Authorized Representative

*Pharmacy/Healthcare Setting Name:

*Stakeholder Type (select one): ☐ Pharmacy ☐ Healthcare Setting

*Pharmacy/Healthcare Setting National Provider Identifier (NPI)#:

DEA# (On file with distributor account):

HIN:

*Pharmacy/Healthcare Setting Type (select one):

- ☐ Inpatient Hospital Pharmacy
 ☐ Outpatient Hospital Pharmacy
 ☐ Oncology Infusion Center
 ☐ Community Oncology Physician Office
☐ Specialty Pharmacy
 ☐ Other (please specify) _____

*Address Line 1:

Address Line 2:

*City:

*State:

*ZIP Code:

*Phone:

*Fax:

Ship To Information (*indicates required field)

Ship To Address: ☐ Same as Above

*Ship To Contact Name:

*Address Line 1:

Address Line 2:

*City:

*State:

*ZIP Code:

Phone:

Fax:

Phone: 1-855-212-6391

REGENERON
SCIENCE TO MEDICINE®

www.Lynozylicrems.com
LYNOZYFICREMS@ubc.com

Fax: 1-866-750-0907

 **LYNOZYFIC™**
(linvoseltamab-gcpt) injection
5mg/1200mg

Authorized Representative Information (all fields required)

*First Name:		*Last Name:
*Credentials (select one): ☐ PharmD ☐ R.Ph ☐ RN ☐ Other (please specify: e.g., MD, DO, Office Administrator, Practice Manager): _____		
*Phone:	*Fax:	*Email:

Authorized Representative Responsibilities
As the Authorized Representative, I must:

- Review the **Pharmacy and Healthcare Setting Training Program**.
- Complete and submit this **Pharmacy and Healthcare Setting Enrollment Form** to the REMS.
- Train all relevant staff involved in dispensing LYNOZYFIC on the LYNOZYFIC REMS requirements using the **Pharmacy and Healthcare Setting Training Program**.
- Establish processes and procedures to verify the prescriber is certified for all dispenses after the first prescription.
- Oversee implementation and compliance with the REMS requirements on behalf of the pharmacy and/or healthcare setting.

Before dispensing, first prescription, staff must:

- Obtain authorization to dispense by contacting the REMS to verify the prescriber is certified.

Before dispensing, all subsequent prescriptions, staff must:

- Verify the prescriber is certified through the processes and procedures established as a requirement of the REMS.

At all times, staff must:

- Report serious adverse events of CRS and neurologic toxicity, including ICANS to the REMS.
- Not distribute, transfer, loan or sell LYNOZYFIC except to certified pharmacies and healthcare settings.
- Maintain records of staff training.
- Maintain records that processes and procedures are in place and are being followed.
- Maintain records of all LYNOZYFIC dispenses and provide data to the REMS, as requested.
- Comply with audits carried out by Regeneron Pharmaceuticals, Inc. or a third party acting on behalf of Regeneron Pharmaceuticals, Inc. to ensure that all training, processes, and procedures are in place and are being followed.

To maintain certification to dispense:

- Have a new Authorized Representative enroll in the REMS by completing and submitting the **Pharmacy and Healthcare Setting Enrollment Form** to the REMS if the Authorized Representative changes.

Your site's information (name, location, and contact information) may be listed on a location finder as a location having a LYNOZYFIC REMS certified pharmacy and healthcare setting. This location finder may be available to healthcare professionals and/or patients seeking LYNOZYFIC REMS certified pharmacy and healthcare settings.

If you do not want your information listed, please call LYNOZYFIC REMS at 1-855-212-6391.

By signing below, you agree that you have read the above responsibilities and understand your requirements as an Authorized Representative, and you agree to oversee the implementation and compliance with the REMS requirements for this pharmacy and healthcare setting.

*Authorized Representative Signature:	*Date (MM/DD/YYYY):
---------------------------------------	---------------------

Phone: 1-855-212-6391
REGENERON
SCIENCE TO MEDICINE®
www.Lynozylicrems.com
LYNOZYFICREMS@ubc.com
Fax: 1-866-750-0907

LYNOZYFIC™
 (linvoseltamab-gcpt) injection
5mg/1200mg

PRESCRIBER TRAINING PROGRAM

Risk Evaluation and Mitigation Strategy (REMS)



© XXXX, Regeneron Pharmaceuticals, Inc. All rights reserved.

Approval: MM/YYYY



LYNOZYFIC REMS Prescriber Training

- This training includes:
 - Information on adverse reactions associated with LYNOZYFIC, including Cytokine Release Syndrome (CRS) and neurologic toxicity, including Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS)
 - Details related to the LYNOZYFIC REMS prescriber requirements

The adverse reactions listed within this training are not all inclusive of adverse reactions associated with LYNOZYFIC. Please refer to the Prescribing Information for additional information.

REGENERON
SCIENCE TO MEDICINE®

 **LYNOZYFIC™**
(linvoseltamab-gcpt) Injection
5mg/1200mg

© XXXX, Regeneron Pharmaceuticals, Inc. All rights reserved.

Approval: MM/YYYY

Training Outline

- Prescriber REMS Requirements
- Risk of Cytokine Release Syndrome
- Risk of Neurologic Toxicity, including ICANS

REGENERON
SCIENCE TO MEDICINE®

 **LYNOZYFIC™**
(linvoseltamab-gcpt) Injection
5mg/1200mg

© XXXX, Regeneron Pharmaceuticals, Inc. All rights reserved.

Approval: MM/YYYY

What is a REMS?

- A Risk Evaluation and Mitigation Strategy (REMS) is a program required by the Food and Drug Administration (FDA) to manage known or potential serious risks associated with a drug product. The FDA has determined that a REMS is necessary to ensure that the benefits of LYNOZYFIC outweigh its risks.
- The goal of the LYNOZYFIC REMS is to mitigate the risks of CRS and neurologic toxicity, including ICANS by:
 - Ensuring prescribers are aware of the importance of monitoring for signs and symptoms of CRS and neurologic toxicity, including ICANS in patients exposed to LYNOZYFIC.

REGENERON
SCIENCE TO MEDICINE®

 **LYNOZYFIC™**
(linvoseltamab-gcpt) Injection
5mg/1200mg

© XXXX, Regeneron Pharmaceuticals, Inc. All rights reserved.

Approval: MM/YYYY

LYNOZYFIC Indication

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.

REGENERON
SCIENCE TO MEDICINE®

 **LYNOZYFIC™**
(linvoseltamab-gcpt) Injection
5mg/1200mg

© XXXX, Regeneron Pharmaceuticals, Inc. All rights reserved.

Approval: MM/YYYY

Prescriber REMS Requirements



© XXXX, Regeneron Pharmaceuticals, Inc. All rights reserved.

Approval: MM/YYYY



Prescriber Certification Requirements

To become certified to prescribe LYNOZYFIC, healthcare providers must:

- Review the drug's Prescribing Information, this **Prescriber Training Program**, and the **Adverse Reaction Management Guide**
- Successfully complete and submit the **Knowledge Assessment** and enroll in the REMS by completing and submitting the **Prescriber Enrollment Form** to the REMS

Before treatment initiation (first step-up dose), certified prescribers must:

- Complete the **Patient Wallet Card** and provide the **Patient Wallet Card** to the patient

At all times, certified prescribers must:

- Report serious adverse events of CRS and neurologic toxicity, including ICANS to the REMS at 1-855-212-6391

Certified LYNOZYFIC prescribers cannot be designated as the Authorized Representative for a certified pharmacy and healthcare setting*.

* If LYNOZYFIC will be dispensed and administered in the same locations, an Authorized Representative who is not the prescriber, must complete the pharmacy and healthcare setting certification.

REGENERON
SCIENCE TO MEDICINE®

 **LYNOZYFIC™**
(linvoseltamab-gcpt) Injection
5mg/1200mg

© XXXX, Regeneron Pharmaceuticals, Inc. All rights reserved.

Approval: MM/YYYY

Patient Counseling

Prescribers must:

- Counsel the patient and their caregiver on how to recognize and respond to signs and symptoms of CRS and neurologic toxicity, including ICANS and report these to their healthcare provider or emergency room provider immediately.
- Counsel the patient and their caregiver using the **Patient Wallet Card** and the need to carry it with them at all times. Complete the **Patient Wallet Card** and provide to the patient.
- Advise patients that they should be hospitalized for 24 hours after administration of the first and second step-up doses of LYNOZYFIC.
- 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.

REGENERON
SCIENCE TO MEDICINE®

 **LYNOZYFIC™**
(linvoseltamab-gcpt) Injection
5mg/1200mg

© XXXX, Regeneron Pharmaceuticals, Inc. All rights reserved.

Approval: MM/YYYY

LYNOZYFIC Boxed Warning

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.

REGENERON
SCIENCE TO MEDICINE®

 **LYNOZYFIC™**
(linvoseltamab-gcpt) Injection
5mg/1200mg

© XXXX, Regeneron Pharmaceuticals, Inc. All rights reserved.

Approval: MM/YYYY

Cytokine Release Syndrome (CRS)

Cytokine Release Syndrome

- LYNZOZYFIC can cause CRS, which can be serious or life-threatening
- In the clinical trial (n=117), CRS occurred in 46% (54/117) of patients who received LYNZOZYFIC at the recommended dose:
 - Grade 1: 35% (41/117)
 - Grade 2: 10% (12/117)
 - Grade 3: 0.9% (1/117)
- Most cases of CRS occurred following step-up dose 1 or step-up dose 2
 - 38% (45/117) of patients had CRS following step-up dose 1; 8% (9/117) had an initial CRS event following a subsequent dose
 - 17% (19/113) of patients developed CRS after step-up dose 2
 - 10% (11/111) of patients developed CRS after the first full 200 mg dose of LYNZOZYFIC
 - 3.6% (4/110) of patients developed CRS after the second full dose
 - There was one Grade 3 case of CRS after the first step-up 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 of LYNZOZYFIC
- Median duration of CRS was 15 (range: 1 to 76) hours

REGENERON
SCIENCE TO MEDICINE®

 **LYNZOZYFIC™**
(linvoseltamab-gcpt) Injection
5mg/1200mg

© XXXX, Regeneron Pharmaceuticals, Inc. All rights reserved.

Approval: MM/YYYY

Clinical Signs and Symptoms of CRS

- Patients should be closely monitored for signs or symptoms of CRS
- Clinical signs and symptoms include, but are not limited to:
 - pyrexia
 - chills
 - hypoxia
 - tachycardia
 - hypotension

REGENERON
SCIENCE TO MEDICINE®

 **LYNOZYFIC™**
(linvoseltamab-gcpt) Injection
5mg/1200mg

© XXXX, Regeneron Pharmaceuticals, Inc. All rights reserved.

Approval: MM/YYYY

LYNOZYFIC Step-up Dosing Schedule

To reduce the risk of CRS, initiate therapy according to step-up dosing.

Table 1: LYNOZYFIC Dosing Schedule				
Dosing Schedule	Day ^a	LYNOZYFIC Dose		Duration of Infusion
Step-up Dosing Schedule	Day 1	Step-up dose 1	5 mg	4 hours
	Day 8	Step-up dose 2	25 mg	
	Day 15	First treatment dose	200 mg	
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	1 hour for the second treatment dose, and 30 minutes for subsequent doses ^b
Biweekly (Every 2 Weeks) Dosing Schedule	Week 14 and every 2 weeks thereafter	Subsequent treatment doses	200 mg	30 minutes
Patients who have achieved and maintained VGPR or better at or after Week 24 <u>and</u> received at least 17 doses of 200 mg				
Every 4 Weeks Dosing Schedule	At Week 24 or after and every 4 weeks thereafter		200 mg	30 minutes
^a 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. ^b 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 (e.g., 4 hours, 1 hour, then 30 minutes).				

LYNOZYFIC Premedications

To reduce the risk of CRS, administer pretreatment medications.

Recommended Pretreatment Medications

Administer the following pre-treatment medications before each dose of the LYNOZYFIC step-up dosing schedule, which includes step-up dose 1, step-up dose 2, and the first treatment dose, the second treatment dose, and if indicated, subsequent treatment doses (see [Tables 1, 2, and 3](#) of the Prescribing Information), to reduce the risk of CRS and/or infusion-related reactions (IRR).

- acetaminophen (or equivalent) 650 mg to 1,000 mg orally 30 to 60 minutes prior to infusion
- diphenhydramine (or equivalent) 25 mg orally or intravenously 30 to 60 minutes prior to infusion
- dexamethasone (or equivalent) intravenously 1 to 3 hours prior to infusion
 - 40 mg dexamethasone (or equivalent) before step-up dose 1, step-up dose 2, and the first full treatment dose
 - Once a 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

Pre-treatment medications may be discontinued once a treatment dose of LYNOZYFIC is tolerated without CRS and/or IRR following pre-treatment with 10 mg dexamethasone (or equivalent), acetaminophen (or equivalent), and diphenhydramine (or equivalent) as described.

CRS Management

- Monitor patients for signs and symptoms of CRS after infusion.
- Counsel patients and their caregivers to seek immediate medical attention should the patient have signs or symptoms of CRS.
- At the first sign of CRS:
 - immediately evaluate patients for hospitalization.
 - manage according to the recommendations below in [Table 2](#) and per current practice guidelines.
 - administer supportive therapy, which may include intensive care for severe or life-threatening CRS.
 - withhold LYNOSYFIC until CRS resolves and modify the next dose or permanently discontinue LYNOSYFIC based on severity.

REGENERON
SCIENCE TO MEDICINE®

 **LYNOSYFIC™**
(linvoseltamab-gcpt) Injection
5mg/1200mg

© XXXX, Regeneron Pharmaceuticals, Inc. All rights reserved.

Approval: MM/YYYY

Recommendations for Management of CRS

Table 2: Recommendations for Management of CRS

Grade ^a	Presenting Symptoms	Recommendations
Grade 1	Fever ≥ 100.4°F (38°C) ^b	- Withhold LYNOZYFIC until CRS resolves. - Provide supportive care, which may include intensive care. - When CRS resolves, resume LYNOZYFIC.^{c, d}
Grade 2	Fever ≥ 100.4°F (38°C) ^b with: Hypotension responsive to fluids and not requiring vasopressors and/or hypoxia requiring low-flow oxygen ^e by nasal cannula or blow-by	- Withhold LYNOZYFIC until CRS resolves. - Provide supportive care, which may include intensive care. - When CRS resolves, resume treatment with LYNOZYFIC.^{c, d} - Consider a decrease in infusion rate up to 50% (no more than 6 hours total) when resuming treatment. Increase rate on subsequent infusions if tolerated. - Monitor patients within proximity of a healthcare facility for 24 hours following this dose, and consider hospitalization.
Grade 3	Fever ≥ 100.4°F (38°C) ^b with: Hypotension requiring a vasopressor (with or without vasopressin) and/or hypoxia requiring high-flow oxygen ^e by nasal cannula, face mask, non-rebreather mask, or Venturi mask.	- Withhold LYNOZYFIC until CRS resolves. - Provide supportive care, which may include intensive care. - When CRS resolves, resume treatment with LYNOZYFIC at reduced dose:^{c, f} - Decrease infusion rate up to 50% (no more than 6 hours total). - Hospitalize for 24 hours after the administration for this dose. - After resuming treatment, if the administered dose is tolerated: - Continue with the next dose of the recommended dosing regimen per Table 1. - If the full dose is tolerated, infusion rate can be increased to the rate prior to the adverse reaction. - Permanently discontinue LYNOZYFIC if Grade 3 CRS recurs with subsequent infusions.

Table 2: Recommendations for Management of CRS (continued)

Grade ^a	Presenting Symptoms	Recommendations
Grade 4	Fever $\geq 100.4^{\circ}\text{F}$ (38°C) ^b with: Hypotension requiring multiple vasopressors (excluding vasopressin) and/or hypoxia requiring oxygen by positive pressure (e.g., continuous positive airway pressure (CPAP), bilevel positive airway pressure (BiPAP), intubation, and mechanical ventilation).	- Discontinue LYNOZYFIC permanently. - CRS should be managed per Grade 3 recommendations.
Other	AST/ALT greater than 5 times ULN associated with CRS Grade 3 or less	- Withhold LYNOZYFIC until CRS resolves and AST/ALT are less than 3 times ULN if baseline was normal or 1.5 to 3 times baseline if baseline was abnormal. - Provide supportive care, which may include intensive care, and monitor. - No change in dose is needed in patients without CRS symptoms with transaminase levels that are trending towards baseline within 7 days. - If values do not trend towards baseline in 7 days, decrease the dose.^f - See infusion rate information by CRS grade.

^a Based on American Society for Transplantation and Cellular Therapy (ASTCT) criteria for grading CRS (2019).

^b Attributed to CRS. Fever may not always be present concurrently with hypotension or hypoxia as it may be masked by interventions such as steroids, antipyretics or anticytokine therapy.

^c Administer pretreatment medications prior to next dose [see Dosage and Administration (2.3) of the Prescribing Information].

^d Follow the recommendations in Table 2 of the Prescribing Information for restarting dosing.

^e Low-flow oxygen defined as oxygen delivered at less than 6 L/minute; high-flow oxygen defined as oxygen delivered at greater than or equal to 6 L/minute.

^f If the last dose administered was 5 mg, administer 2.5 mg. If the last dose administered was 25 mg, restart step-up dosing from 5 mg. If the last dose administered was 200 mg, refer to Table 2 of the Prescribing Information for recommendations regarding restarting therapy based on time since the last dose.

Neurologic Toxicity, Including ICANS



© XXXX, Regeneron Pharmaceuticals, Inc. All rights reserved.

Approval: MM/YYYY



Neurologic Toxicity, Including ICANS

- 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.
- ICANS occurred in 8% of patients who received LYNOZYFIC with the recommended dosing regimen
 - Grade 3: 2.6%
- Most patients experienced ICANS following step-up dose 1 (5%)
 - 2 patients (1.8%) experienced initial ICANS following step-up dose 2
 - 1 patient developed the first occurrence of ICANS following a subsequent full dose of LYNOZYFIC
- Recurrent ICANS occurred in 1 patient
- The median time to onset of ICANS was 1 (range: 1 to 4) days 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

REGENERON
SCIENCE TO MEDICINE®

 **LYNOZYFIC™**
(linvoseltamab-gcpt) Injection
5mg/1200mg

© XXXX, Regeneron Pharmaceuticals, Inc. All rights reserved.

Approval: MM/YYYY

Clinical Signs and Symptoms of Neurologic Toxicity, including ICANS

- Monitor patients for signs and symptoms of ICANS during treatment
- Clinical signs and symptoms may include but are not limited to:
 - confusion
 - depressed level of consciousness
 - lethargy

REGENERON
SCIENCE TO MEDICINE®

 **LYNOZYFIC™**
(linvoseltamab-gcpt) Injection
5mg/1200mg

© XXXX, Regeneron Pharmaceuticals, Inc. All rights reserved.

Approval: MM/YYYY

Management of Neurologic Toxicity, including ICANS

- Monitor patients for signs and symptoms of neurologic toxicity, including ICANS during treatment.
- Counsel patients to seek immediate medical attention should signs or symptoms of neurologic toxicity occur at any time.
- 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.

REGENERON
SCIENCE TO MEDICINE®

 **LYNOZYFIC™**
(linvoseltamab-gcpt) Injection
5mg/1200mg

© XXXX, Regeneron Pharmaceuticals, Inc. All rights reserved.

Approval: MM/YYYY

Recommendations for Management of ICANS

Table 3: Recommendations for Management of ICANS

Grade ^a	Presenting Symptoms ^b	Recommendations
Grade 1	ICE ^c score 7-9, or depressed level of consciousness ^d : awakens spontaneously.	• Withhold until neurologic symptoms resolve or return to baseline.^e • Provide supportive therapy. Manage per current practice guidelines. • Consider non-sedating, anti-seizure medications for seizure prophylaxis.
Grade 2	ICE ^c score 3-6, or depressed level of consciousness ^d : awakens to voice.	• Withhold until neurologic symptoms resolve or return to baseline.^e • Provide supportive therapy. Manage per current practice guidelines. • Administer dexamethasone^f 10 mg intravenously every 6 hours. Continue dexamethasone use until resolution to Grade 1 or less, then taper. • Consider non-sedating, anti-seizure medications for seizure prophylaxis. • Monitor patients within proximity of a healthcare facility for 24 hours following the next dose of LYNOZYFIC and consider hospitalization.
Grade 3	ICE ^c score 0-2, or depressed level of consciousness ^d : awakens only to tactile stimulus, or seizures, either: • any clinical seizure, focal or generalized, that resolves rapidly, or • non-convulsive seizures on electroencephalogram (EEG) that resolve with intervention, or raised intracranial pressure: focal/local edema on neuroimaging.	• Withhold until neurologic symptoms resolve or return to baseline. • Provide supportive therapy, which may include intensive care. Manage per current practice guidelines. • Consider neurology evaluation. • Administer dexamethasone^f 10 mg intravenously every 6 hours. Continue dexamethasone use until resolution to Grade 1 or less, then taper. • Consider non-sedating, anti-seizure medications for seizure prophylaxis. • Permanently discontinue LYNOZYFIC for recurrent Grade 3 ICANS. • Resume treatment with LYNOZYFIC at a reduced dose^g and hospitalize for 24 hours after the administration of the dose. After resuming treatment, if the administered dose is tolerated, continue with the next dose of the recommended dosing regimen per Table 1.

Table 3: Recommendations for Management of ICANS (continued)

Grade ^a	Presenting Symptoms ^b	Recommendations
Grade 4	ICE^c score 0, or depressed level of consciousness^d: either: • patient is unarousable or requires vigorous or repetitive tactile stimuli to arouse, or • stupor or coma, or seizures, either: • life-threatening prolonged seizure (> 5 minutes), or • repetitive clinical or electrical seizures without return to baseline in between, or motor findings: • deep focal motor weakness such as hemiparesis or paraparesis, or raised intracranial pressure/cerebral edema, with signs/symptoms such as: • diffuse cerebral edema on neuroimaging, or • decerebrate or decorticate posturing, or • cranial nerve VI palsy, or • papilledema, or • Cushing's triad.	• Permanently discontinue LYNOZYFIC. • Provide supportive therapy, which may include intensive care. Manage per current practice guidelines. • Consider neurology evaluation. • Administer dexamethasone^f 10 mg intravenously every 6 hours. Continue dexamethasone use until resolution to Grade 1 or less, then taper. • Consider non-sedating, anti-seizure medications for seizure prophylaxis.

^a Based on American Society for Transplantation and Cellular Therapy (ASTCT) 2019 grading for ICANS.

^b Management is determined by the most severe event, not attributable to any other cause.

^c If patient is arousable and able to perform Immune Effector Cell-Associated Encephalopathy (ICE) Assessment, assess: Orientation (oriented to year, month, city, hospital = 4 points); Naming (name 3 objects, e.g., point to clock, pen, button = 3 points); Following Commands (e.g., "show me 2 fingers" or "close your eyes and stick out your tongue" = 1 point); Writing (ability to write a standard sentence = 1 point); and Attention (count backwards from 100 by ten = 1 point). If patient is unarousable and unable to perform ICE Assessment (Grade 4 ICANS) = 0 points.

^d Not attributable to any other cause.

^e Follow the recommendations in Table 2 of the Prescribing Information for restarting dosing.

^f All references to dexamethasone administration are dexamethasone or equivalent.

^g If the last dose administered was 5 mg, administer 2.5 mg. If the last dose administered was 25 mg, restart step-up dosing from 5 mg. If the last dose administered was 200 mg, refer to Table 2 of the Prescribing Information for recommendations regarding restarting therapy based on time since the last dose.

Adverse Event Reporting

Healthcare providers must report serious adverse events of CRS and neurologic toxicity, including ICANS to the LYNOZYFIC REMS at 1-855-212-6391.

Healthcare providers should also report all other suspected adverse events associated with LYNOZYFIC to Regeneron Pharmaceuticals, Inc. at 1-844-734-6643 or medical.information@regeneron.com or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.



© XXXX, Regeneron Pharmaceuticals, Inc. All rights reserved.

Approval: MM/YYYY

Additional LYNOZYFIC REMS Information

For further information, please visit www.Lynozifycrems.com or call 1-855-212-6391.



© XXXX, Regeneron Pharmaceuticals, Inc. All rights reserved.

Approval: MM/YYYY





LYNOZYFIC Adverse Reaction Management Guide

This is supplemental to the LYNZOZYFIC US Prescribing Information (USPI).

REGENERON
SCIENCE TO MEDICINE®

Management of Cytokine Release Syndrome (CRS)

Identify CRS based on clinical presentation. Clinical signs and symptoms of CRS included, but were not limited to pyrexia, chills, hypoxia, tachycardia, and hypotension.

- Other causes of fever, hypoxia, and hypotension should be evaluated and treated. At the first sign of CRS, immediately evaluate patients for hospitalization.
- If CRS is suspected, withhold LYNZOZYFIC until CRS resolves and modify the next dose or permanently discontinue LYNZOZYFIC based on severity.
- Manage CRS per current practice guidelines and administer supportive care, which may include intensive care for severe or life-threatening CRS.
- Manage according to the recommendations for management of CRS in [Table 1](#).

Recommended Pretreatment Medications

Administer the following pre-treatment medications before each dose of the LYNZOZYFIC step-up dosing schedule, which includes step-up dose 1, step-up dose 2, and the first treatment dose, the second treatment dose, and if indicated, subsequent treatment doses (see [Tables 1, 2, and 3](#) of the Prescribing Information), to reduce the risk of CRS and/or infusion-related reactions (IRR).

- acetaminophen (or equivalent) 650 mg to 1,000 mg orally 30 to 60 minutes prior to infusion
- diphenhydramine (or equivalent) 25 mg orally or intravenously 30 to 60 minutes prior to infusion
- dexamethasone (or equivalent) intravenously 1 to 3 hours prior to infusion
 - 40 mg dexamethasone (or equivalent) before step-up dose 1, step-up dose 2, and the first full treatment dose
 - Once a treatment dose of LYNZOZYFIC is tolerated without CRS and/or IRR with 40 mg dexamethasone (or equivalent), administer 10 mg dexamethasone (or equivalent) prior to the subsequent LYNZOZYFIC treatment dose

Pre-treatment medications may be discontinued once a treatment dose of LYNZOZYFIC is tolerated without CRS and/or IRR following pre-treatment with 10 mg dexamethasone (or equivalent), acetaminophen (or equivalent), and diphenhydramine (or equivalent) as described.

Table 1: Recommendations for Management of CRS

Grade ^a	Presenting Symptoms	Recommendations
Grade 1	Fever $\geq 100.4^{\circ}\text{F}$ (38°C) ^b	- Withhold LYNOZYFIC until CRS resolves. - Provide supportive care, which may include intensive care. - When CRS resolves, resume LYNOZYFIC.^{c, d}
Grade 2	Fever $\geq 100.4^{\circ}\text{F}$ (38°C) ^b with: Hypotension responsive to fluids and not requiring vasopressors and/or hypoxia requiring low-flow oxygen ^e by nasal cannula or blow-by	- Withhold LYNOZYFIC until CRS resolves. - Provide supportive care, which may include intensive care. - When CRS resolves, resume treatment with LYNOZYFIC.^{c, d} - Consider a decrease in infusion rate up to 50% (no more than 6 hours total) when resuming treatment. Increase rate on subsequent infusions if tolerated. - Monitor patients within proximity of a healthcare facility for 24 hours following this dose, and consider hospitalization.
Grade 3	Fever $\geq 100.4^{\circ}\text{F}$ (38°C) ^b with: Hypotension requiring a vasopressor (with or without vasopressin) and/or hypoxia requiring high-flow oxygen ^e by nasal cannula, face mask, non-rebreather mask, or Venturi mask.	- Withhold LYNOZYFIC until CRS resolves. - Provide supportive care, which may include intensive care. - When CRS resolves, resume treatment with LYNOZYFIC at reduced dose:^{c, f} - Decrease infusion rate up to 50% (no more than 6 hours total). - Hospitalize for 24 hours after the administration for this dose. - After resuming treatment, if the administered dose is tolerated: - Continue with the next dose of the recommended dosing regimen per Table 1 of the Prescribing Information. - If the full dose is tolerated, infusion rate can be increased to the rate prior to the adverse reaction. - Permanently discontinue LYNOZYFIC if Grade 3 CRS recurs with subsequent infusions.

Grade ^a	Presenting Symptoms	Recommendations
Grade 4	Fever $\geq 100.4^{\circ}\text{F}$ (38°C)^b with: Hypotension requiring multiple vasopressors (excluding vasopressin) and/or hypoxia requiring oxygen by positive pressure (e.g., continuous positive airway pressure (CPAP), bilevel positive airway pressure (BiPAP), intubation, and mechanical ventilation).	- Discontinue LYNOZYFIC permanently. - CRS should be managed per Grade 3 recommendations.
Other	AST/ALT greater than 5 times ULN associated with CRS Grade 3 or less	- Withhold LYNOZYFIC until CRS resolves and AST/ALT are less than 3 times ULN if baseline was normal or 1.5 to 3 times baseline if baseline was abnormal. - Provide supportive care, which may include intensive care, and monitor. - No change in dose is needed in patients without CRS symptoms with transaminase levels that are trending towards baseline within 7 days. - If values do not trend towards baseline in 7 days, decrease the dose.^f - See infusion rate information by CRS grade.

^a Based on American Society for Transplantation and Cellular Therapy (ASTCT) criteria for grading CRS (2019).

^b Attributed to CRS. Fever may not always be present concurrently with hypotension or hypoxia as it may be masked by interventions such as steroids, antipyretics or anticytokine therapy.

^c Administer pretreatment medications prior to next dose [see Dosage and Administration (2.3) of the Prescribing Information].

^d Follow the recommendations in Table 2 of the Prescribing Information for restarting dosing.

^e Low-flow oxygen defined as oxygen delivered at less than 6 L/minute; high-flow oxygen defined as oxygen delivered at greater than or equal to 6 L/minute.

^f If the last dose administered was 5 mg, administer 2.5 mg. If the last dose administered was 25 mg, restart step-up dosing from 5 mg. If the last dose administered was 200 mg, refer to Table 2 of the Prescribing Information for recommendations regarding restarting therapy based on time since the last dose.

Neurologic Toxicity, Including Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS)

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.

At the first sign of neurologic toxicity, including ICANS, immediately evaluate the patient.

- Rule out other causes of neurologic symptoms.
- Provide supportive therapy, which may include intensive care for severe or life-threatening ICANS.
- Withhold LYNZOZYFIC until ICANS resolves and modify the next dose or permanently discontinue LYNZOZYFIC based on severity.
- General management for ICANS is summarized in [Table 2](#) below.

Table 2: Recommendations for Management of ICANS

Grade ^a	Presenting Symptoms ^b	Recommendations
Grade 1	ICE ^c score 7-9, or depressed level of consciousness ^d : awakens spontaneously.	• Withhold until neurologic symptoms resolve or return to baseline.^e • Provide supportive therapy. Manage per current practice guidelines. • Consider non-sedating, anti-seizure medications for seizure prophylaxis.
Grade 2	ICE ^c score 3-6, or depressed level of consciousness ^d : awakens to voice.	• Withhold until neurologic symptoms resolve or return to baseline.^e • Provide supportive therapy. Manage per current practice guidelines. • Administer dexamethasone^f 10 mg intravenously every 6 hours. Continue dexamethasone use until resolution to Grade 1 or less, then taper. • Consider non-sedating, anti-seizure medications for seizure prophylaxis. • Monitor patients within proximity of a healthcare facility for 24 hours following the next dose of LYNZOZYFIC and consider hospitalization.
Grade 3	ICE ^c score 0-2, or depressed level of consciousness ^d : awakens only to tactile stimulus, or seizures, either: • any clinical seizure, focal or generalized, that resolves rapidly, or • non-convulsive seizures on electroencephalogram (EEG) that resolve with intervention, or raised intracranial pressure: focal/local edema on neuroimaging.	• Withhold until neurologic symptoms resolve or return to baseline. • Provide supportive therapy, which may include intensive care. Manage per current practice guidelines. • Consider neurology evaluation. • Administer dexamethasone^f 10 mg intravenously every 6 hours. Continue dexamethasone use until resolution to Grade 1 or less, then taper. • Consider non-sedating, anti-seizure medications for seizure prophylaxis. • Permanently discontinue LYNZOZYFIC for recurrent Grade 3 ICANS. • Resume treatment with LYNZOZYFIC at a reduced dose^g and hospitalize for 24 hours after the administration of the dose. After resuming treatment, if the administered dose is tolerated, continue with the next dose of the recommended dosing regimen per Table 1 of the Prescribing Information.

Grade ^a	Presenting Symptoms ^b	Recommendations
Grade 4	ICE^c score 0, or depressed level of consciousness^d: either: • patient is unarousable or requires vigorous or repetitive tactile stimuli to arouse, or • stupor or coma, or seizures, either: • life-threatening prolonged seizure (>5 minutes), or • repetitive clinical or electrical seizures without return to baseline in between, or motor findings: • deep focal motor weakness such as hemiparesis or paraparesis, or raised intracranial pressure/cerebral edema, with signs/symptoms such as: • diffuse cerebral edema on neuroimaging, or • decerebrate or decorticate posturing, or • cranial nerve VI palsy, or • papilledema, or • Cushing's triad.	• Permanently discontinue LYNZOZYFIC. • Provide supportive therapy, which may include intensive care. Manage per current practice guidelines. • Consider neurology evaluation. • Administer dexamethasone^f 10 mg intravenously every 6 hours. Continue dexamethasone use until resolution to Grade 1 or less, then taper. • Consider non-sedating, anti-seizure medications for seizure prophylaxis

^aBased on American Society for Transplantation and Cellular Therapy (ASTCT) 2019 grading for ICANS.

^bManagement is determined by the most severe event, not attributable to any other cause.

^cIf patient is arousable and able to perform Immune Effector Cell-Associated Encephalopathy (ICE) Assessment, assess: Orientation (oriented to year, month, city, hospital = 4 points); Naming (name 3 objects, e.g., point to clock, pen, button = 3 points); Following Commands (e.g., "show me 2 fingers" or "close your eyes and stick out your tongue" = 1 point); Writing (ability to write a standard sentence = 1 point); and Attention (count backwards from 100 by ten = 1 point). If patient is unarousable and unable to perform ICE Assessment (Grade 4 ICANS) = 0 points.

^dNot attributable to any other cause.

^eFollow the recommendations in Table 2 of the Prescribing Information for restarting dosing.

^fAll references to dexamethasone administration are dexamethasone or equivalent.

^gIf the last dose administered was 5 mg, administer 2.5 mg. If the last dose administered was 25 mg, restart step-up dosing from 5 mg. If the last dose administered was 200 mg, refer to Table 2 of the Prescribing Information for recommendations regarding restarting therapy based on time since the last dose.

Table 3: Recommendations for Management of Neurologic Adverse Reactions (excluding ICANS)

Adverse Reactions	Grade ^a	Recommendations
Neurologic Adverse Reactions (excluding ICANS)	Grade 2	• Withhold LYNOZYFIC until symptoms resolve to Grade 1 or baseline. ^b
	Grade 3 (First occurrence)	• Withhold LYNOZYFIC until Grade 1 or baseline. ^b
	Grade 3 (Recurrent) or	• Permanently discontinue LYNOZYFIC.
	Grade 4	

^a Based on National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE), Version 5.0

^b Follow the recommendations in Table 2 of the Prescribing Information for restarting dosing.

Please visit www.Lynozyficrems.com for further information and resources.

Knowledge Assessment

Prescriber Information (all fields required)

First Name:		Last Name:	
NPI #:			
Address:			
City:		State:	ZIP Code:
Credentials: ☐ MD ☐ DO ☐ NP ☐ PA ☐ Other (please specify):			
Specialty (select one): ☐ Oncology ☐ Hematology ☐ Hematology/Oncology ☐ Other (please specify)			
Phone:		Fax:	Email:

As a condition of certification, the prescriber must complete this **Knowledge Assessment**. All 8 questions must be answered correctly.

The **Knowledge Assessment** can be completed online at www.Lynozylicrems.com or a completed hard copy can be submitted via fax to 1-866-750-0907 or email at LYNOZYFICREMS@ubc.com. You must also complete the **Prescriber Enrollment Form** at www.Lynozylicrems.com for your certification to be complete.

The LYNOZYFIC REMS will verify that both the **Knowledge Assessment** and **Prescriber Enrollment Form** are complete and will provide confirmation of certification via email.

*Signature:

*Date (MM/DD/YYYY):

- LYNOZYFIC is indicated for the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least 4 prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody:
 - True
 - False
- Patients with CRS may present with the following signs and symptoms:
 - Pyrexia
 - Hypotension
 - Hypoxia
 - Tachycardia
 - All of the above
- Which one of the following is true regarding the median time to onset of CRS from the end of infusion of LYNOZYFIC? It typically occurs (select the one best response):
 - 2 hours after the most recent dose, with a median duration of 4 hours
 - 11 hours after the most recent dose, with a median duration of 15 hours
 - 24 hours after the most recent dose with a median duration of 30 hours
 - Rarely starts during the first week following LYNOZYFIC dosing
- Which of the following regarding Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS) are correct:
 - ICANS can be concurrent with CRS, following resolution of CRS, or in the absence of CRS
 - Withhold LYNOZYFIC until ICANS resolves and modify the next dose or permanently discontinue LYNOZYFIC based on severity
 - Provide supportive therapy, which may include intensive care for severe or life-threatening ICANS
 - Most patients experienced ICANS following step-up dose 1
 - All of the above
- As a part of patient/caregiver counseling, which of the following are correct regarding LYNOZYFIC
 - Before treatment initiation (first dose), the **Patient Wallet Card** must be provided
 - Patients should carry the **Patient Wallet Card** with them and inform other healthcare providers about treatment with LYNOZYFIC
 - Patients should seek immediate medical attention should signs or symptoms of CRS or neurologic toxicity, including ICANS occur at any time
 - All of the above
- Clinical signs and symptoms of ICANS may include:
 - Depressed level of consciousness
 - Confusion
 - Lethargy
 - All of the above
- Administer diphenhydramine and acetaminophen 30 to 60 minutes prior to each step-up dose, the first two full doses, and subsequent doses until dose is tolerated to reduce the risk of CRS:
 - True
 - False
- If Grade 2 CRS is suspected during treatment with LYNOZYFIC, which of the following supportive measures should be considered:
 - Provide supportive therapy, which may include intensive care
 - Withhold LYNOZYFIC until CRS resolves
 - Once CRS resolves, administer pretreatment medications prior to the next dose
 - All of the above

Phone: 1-855-212-6391

www.Lynozylicrems.com

Fax: 1-866-750-0907

REGENERON
SCIENCE TO MEDICINE™

LYNOZYFICREMS@ubc.com

LYNOZYFIC™
(linvoseltamab-gcpt) Injection
5mg/120mg

First Infusion Date

Healthcare Setting Name

Office Phone Number

After Hours Phone Number

Name of LYNOZYFIC Prescriber

This patient has received LYNOZYFIC

LYNOZYFIC therapy can cause Cytokine Release Syndrome (CRS) or Neurologic Toxicity, including Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS), which can be serious or life-threatening.



FOR HEALTHCARE PROFESSIONALS
IMPORTANT SAFETY INFORMATION
YOU SHOULD KNOW:

LYNOZYFIC REMS PATIENT WALLET CARD

Carry this card with you at all times. **SHOW THIS CARD** to any healthcare provider involved in your care and if you go to the emergency room.

**IMPORTANT SAFETY INFORMATION FOR PATIENTS
 RECEIVING TREATMENT WITH LYNOZYFIC**

FOR THE PATIENT

Call your healthcare provider or get medical help right away if you develop any of these symptoms:

Symptoms of CRS:

- Fever of 100.4°F (38°C) or higher
- Chills or shaking
- Trouble breathing
- Fast heartbeat
- Dizziness or light-headedness

Symptoms of ICANS:

- Headache
- Agitation, trouble staying awake, confusion or disorientation, seeing or hearing things that are not real (hallucinations)
- Trouble speaking, writing, thinking, remembering things, paying attention, or understanding things
- Problems walking, muscle weakness, shaking (tremors), loss of balance, or muscle spasms
- Numbness and tingling (feeling like “pins and needles”)
- Burning, throbbing, or stabbing pain
- Changes in your handwriting
- Seizures

You should always ask your doctor about taking other medications while taking LYNOZYFIC

IMPORTANT TO REMEMBER: Due to the risk of CRS and neurologic problems, you will receive LYNOZYFIC on a “step-up dosing schedule” and should be hospitalized for 24 hours after the first and second “step-up” doses. Your doctor will tell you if you need further monitoring for any other dose administration. If you have any of these symptoms, CALL YOUR DOCTOR at _____ or seek emergency medical attention right away! You should also tell your doctor if you have any other symptoms that bother you or do not go away.

Phone: 1-855-212-6391

REGENERON
SCIENCE TO MEDICINE®

www.Lynozylicrems.com
LYNOZYFICREMS@ubc.com

Fax: 1-866-750-0907

 **LYNOZYFIC**
(linvoseltamab-gcpt) injection 5mg/1200mg

LYNOZYFIC
(Linvoseltamab-gcpt)

PHARMACY AND HEALTHCARE SETTING TRAINING PROGRAM

Risk Evaluation and Mitigation Strategy (REMS)



© XXXX, Regeneron Pharmaceuticals, Inc. All rights reserved.

Approval: MM/YYYY



LYNOZYFIC Pharmacy and Healthcare Setting Training Program

This training includes details related to pharmacy and healthcare setting requirements of the LYNOZYFIC REMS.

Please refer to the Prescribing Information for additional information on LYNOZYFIC.

REGENERON
SCIENCE TO MEDICINE®

 **LYNOZYFIC™**
(linvoseltamab-gcpt) Injection
5mg/1200mg

© XXXX, Regeneron Pharmaceuticals, Inc. All rights reserved.

Approval: MM/YYYY

What is a REMS?

- A Risk Evaluation and Mitigation Strategy (REMS) is a program required by the Food and Drug Administration (FDA) to manage known or potential serious risks associated with a drug product. The FDA has determined that a REMS is necessary to ensure that the benefits of LYNOZYFIC outweigh its risks
- The goal of the LYNOZYFIC REMS is to mitigate the risks of Cytokine Release Syndrome (CRS) and neurologic toxicity, including Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS) by:
 - Ensuring prescribers are aware of the importance of monitoring for signs and symptoms of CRS and neurologic toxicity, including ICANS in patients exposed to LYNOZYFIC

REGENERON
SCIENCE TO MEDICINE®

 **LYNOZYFIC™**
(linvoseltamab-gcpt) Injection
5mg/1200mg

© XXXX, Regeneron Pharmaceuticals, Inc. All rights reserved.

Approval: MM/YYYY

LYNOZYFIC Indication

- 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.

REGENERON
SCIENCE TO MEDICINE®

 **LYNOZYFIC™**
(linvoseltamab-gcpt) Injection
5mg/1200mg

© XXXX, Regeneron Pharmaceuticals, Inc. All rights reserved.

Approval: MM/YYYY

Pharmacy and Healthcare Setting Certification Requirements

Requirements to become certified to dispense LYNOZYFIC are as follows:

- Designate an Authorized Representative to carry out the certification process and oversee implementation and compliance with the REMS requirements on behalf of the pharmacy and/or healthcare setting
- Have the Authorized Representative review this **Pharmacy and Healthcare Setting Training Program**
- Have the Authorized Representative enroll in the REMS by completing and submitting the **Pharmacy and Healthcare Setting Enrollment Form** to the REMS:
 - Online at www.Lynozifycrems.com, or
 - By downloading the document at www.Lynozifycrems.com and faxing to 1-866-750-0907 or sending by email to LYNOZYFICREMS@ubc.com
- Train all relevant staff involved in the dispensing of LYNOZYFIC on the REMS requirements using this **Pharmacy and Healthcare Setting Training Program**
- Establish processes and procedures to verify the prescriber is certified for all dispenses after the first prescription

Before dispensing the first prescription:

- Obtain authorization to dispense by contacting the REMS to verify the prescriber is certified
 - Obtaining authorization to dispense (REMS Dispense Authorization [RDA]) is required for the first prescription written by each prescriber, for each patient, which verifies the prescriber is certified
 - Pharmacies and healthcare settings can obtain authorization to dispense on www.Lynozifycrems.com using their login credentials or by calling the REMS Coordinating Center at 1-855-212-6391

Before dispensing, for all subsequent prescriptions:

- Verify the prescriber is certified through the processes and procedures established as a requirement of the REMS
 - Subsequent prescriptions from the same prescriber, for the same patient, do not require obtaining an RDA, but pharmacies and healthcare settings can check the database of certified prescribers thereafter

REGENERON
SCIENCE TO MEDICINE®

 **LYNOZYFIC**
(linvoseltamab-gcpt) Injection
5mg/1200mg

© XXXX, Regeneron Pharmaceuticals, Inc. All rights reserved.

Approval: MM/YYYY

Pharmacy and Healthcare Setting Requirements

At all times:

- Report serious adverse events of CRS and neurologic toxicity, including ICANS to the REMS at 1-855-212-6391
- Not distribute, transfer, loan or sell LYNOZYFIC except to certified pharmacies and healthcare settings
- Maintain records of staff training
- Maintain records that processes and procedures are in place and are being followed
- Maintain records of all LYNOZYFIC dispenses and provide data to the REMS, as requested
- Comply with audits carried out by Regeneron Pharmaceuticals, Inc. or a third party acting on behalf of Regeneron Pharmaceuticals, Inc. to ensure that all processes and procedures are in place and are being followed

To maintain certification to dispense:

- Have a new Authorized Representative enroll in the REMS by completing and submitting the **Pharmacy and Healthcare Setting Enrollment Form** to the REMS if the Authorized Representative changes



© XXXX, Regeneron Pharmaceuticals, Inc. All rights reserved.

Approval: MM/YYYY

Who Can Be an Authorized Representative?

An Authorized Representative at the pharmacy can be a:

- Licensed Pharmacist
- Pharmacy Technician
- Any responsible individual assigned by the pharmacy

An Authorized Representative at the healthcare setting can be a:

- Pharmacist
- Registered Nurse
- Any responsible individual assigned by the healthcare setting (e.g., Office administrator, Practice manager)

Certified LYNOZYFIC prescribers cannot be designated as an Authorized Representative for a certified pharmacy and healthcare setting.

One Authorized Representative must enroll for each pharmacy and healthcare setting and be responsible for compliance with the REMS requirements as stated on the Pharmacy and Healthcare Setting Enrollment Form.

REGENERON
SCIENCE TO MEDICINE®

 **LYNOZYFIC™**
(linvoseltamab-gcpt) Injection
5mg/1200mg

© XXXX, Regeneron Pharmaceuticals, Inc. All rights reserved.

Approval: MM/YYYY

Managing Pharmacy and Healthcare Setting Staff

- Upon certification of the pharmacy and healthcare setting, the Authorized Representative will receive access to the REMS Portal
- The Authorized Representative may grant pharmacy and healthcare setting staff access via the staff management tab on the LYNOZYFIC REMS Portal
- Once the Authorized Representative has added the staff member through this page, the staff member will receive an automated email
- The staff member will then have the ability to access the portal to confirm prescriber certification prior to dispensing LYNOZYFIC

The Authorized Representative is responsible for ensuring staff access is only available to individuals actively supporting the LYNOZYFIC REMS.



© XXXX, Regeneron Pharmaceuticals, Inc. All rights reserved.

Approval: MM/YYYY

How to Confirm Prescriber Certification

- When an order for LYNOZYFIC is received, the Authorized Representative or designated staff must verify the prescriber is certified in the LYNOZYFIC REMS
- For the first prescription written by each prescriber, for each patient, the AR or designated staff must generate an RDA and obtain authorization to dispense LYNOZYFIC
- AR or designated pharmacy staff will log into the LYNOZYFIC REMS portal at **www.lynozyficREMS.com**
- Select **REMS Dispense Authorization (RDA)**
- After entering either the ordering Prescriber's NPI# or name, and clicking on the Generate Authorization Code, one of the following messages will appear:
 - DO NOT DISPENSE
 - OK TO DISPENSE
 - The RDA code will display for documentation purposes
 - Obtaining authorization to dispense is required for the first prescription written by each prescriber, for each patient, only. After the first prescription, healthcare setting staff can check the REMS portal to verify prescriber certification prior to dispense
- The Authorized Representative or designated staff may also contact the LYNOZYFIC REMS Coordinating Center via phone at 1-855-212-6391 to obtain an RDA

REGENERON
SCIENCE TO MEDICINE®

 **LYNOZYFIC™**
(linvoseltamab-gcpt) Injection
5mg/1200mg

© XXXX, Regeneron Pharmaceuticals, Inc. All rights reserved.

Approval: MM/YYYY

Adverse Event Reporting

Pharmacy and healthcare setting staff must report serious adverse events of CRS and neurologic toxicity, including ICANS to the LYNOZYFIC REMS at 1-855-212-6391.

Pharmacy and healthcare setting staff should also report all other suspected adverse events associated with LYNOZYFIC to Regeneron Pharmaceuticals, Inc. at 1-844-734-6643 or medical.information@regeneron.com or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.



© XXXX, Regeneron Pharmaceuticals, Inc. All rights reserved.

Approval: MM/YYYY

Additional LYNOZYFIC REMS Information

For further information, please visit www.Lynozylicrems.com or call 1-855-212-6391.



© XXXX, Regeneron Pharmaceuticals, Inc. All rights reserved.

Approval: MM/YYYY



FDA-Required REMS Safety Information

- Risk of Cytokine Release Syndrome (CRS) and neurologic toxicity, including Immune Effector-Cell Associated Neurotoxicity Syndrome (ICANS) with LYNOZYFIC
- Required REMS certification to prescribe LYNOZYFIC

Dear Healthcare Provider,

The purpose of this letter is to inform you of important safety information for LYNOZYFIC based on current Prescribing Information. FDA has required this safety notice as part of the LYNOZYFIC REMS (**R**isk **E**valuation and **M**itigation **S**trategy) to inform you about the serious risks of CRS and neurologic toxicity, including ICANS.

Serious Risks of LYNOZYFIC

- **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 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.

Enclosed for your review and awareness of these serious risks is the LYNOZYFIC **REMS Fact Sheet**, a non-promotional Fact Sheet reviewed by the FDA, which will provide you with more information about these risks and the LYNOZYFIC REMS requirements.

REMS Requirements

- LYNOZYFIC can only be prescribed and/or dispensed by certified prescribers and certified pharmacies and healthcare settings.
- Those who prescribe and/or dispense LYNOZYFIC must be aware of how to manage the risks of CRS and neurologic toxicity, including ICANS.
- Prescribers must counsel patients and their caregivers on how to recognize and respond to signs and symptoms of CRS and neurologic toxicity, including ICANS, the need to report all symptoms suggestive of CRS and neurologic toxicity, including ICANS to their healthcare

provider or emergency room provider immediately, and the need to carry the **Patient Wallet Card** at all times.

- Prescribers must complete the **Patient Wallet Card** and provide the **Patient Wallet Card** to the patient or caregiver before treatment initiation (first step-up dose).

Indication

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.

Adverse Event Reporting

Healthcare providers must report serious adverse events of CRS and neurologic toxicity, including ICANS to the LYNOZYFIC REMS at 1-855-212-6391.

Healthcare providers should also report all other suspected adverse events associated with LYNOZYFIC to Regeneron Pharmaceuticals, Inc. at 1-844-734-6643 or medical.information@regeneron.com or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

For a complete safety profile of LYNOZYFIC, please see the Prescribing Information included. For additional details about the REMS, please visit **www.Lynozyficrems.com** or contact the LYNOZYFIC REMS Coordinating Center at 1-855-212-6391.

Sincerely,

Regeneron Pharmaceuticals, Inc.

FDA-Required REMS Safety Information

- Risk of Cytokine Release Syndrome (CRS) and neurologic toxicity, including Immune Effector-Cell Associated Neurotoxicity Syndrome (ICANS) with LYNOZYFIC
- Required REMS certification to prescribe LYNOZYFIC

Dear Professional Society,

We request that you share this safety information with your members.

The purpose of this letter is to inform you of important safety information for LYNOZYFIC based on current Prescribing Information. FDA has required this safety notice as part of the LYNOZYFIC REMS (Risk Evaluation and Mitigation Strategy) to inform you about the serious risks of CRS and neurologic toxicity, including ICANS.

Serious Risks of LYNOZYFIC

- **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 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.

Enclosed for your review and awareness of these serious risks is the LYNOZYFIC **REMS Fact Sheet**, a non-promotional Fact Sheet reviewed by the FDA which will provide you with more information about these risks and the LYNOZYFIC REMS requirements..

REMS Requirements

- LYNOZYFIC can only be prescribed and/or dispensed by certified prescribers and certified pharmacies and healthcare settings.
- Those who prescribe and/or dispense LYNOZYFIC must be aware of how to manage the risks of CRS and neurologic toxicity, including ICANS.
- Prescribers must counsel patients and their caregivers on how to recognize and respond to signs and symptoms of CRS and neurologic toxicity, including ICANS, the need to report all symptoms suggestive of CRS and neurologic toxicity, including ICANS to their healthcare provider or emergency room provider immediately, and the need to carry the **Patient Wallet Card** at all times.
- Prescribers must complete the **Patient Wallet Card** and provide the **Patient Wallet Card** to the patient or caregiver before treatment initiation (first step-up dose).

Indication

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.

For a complete safety profile of LYNOZYFIC, please see the Prescribing Information included. For additional details about the REMS, please visit **www.Lynozyficrems.com** or contact the LYNOZYFIC REMS Coordinating Center at 1-855-212-6391.

Sincerely,

Regeneron Pharmaceuticals, Inc.

LYNOZYFIC REMS FACT SHEET

FDA – REQUIRED REMS SAFETY INFORMATION

LYNOZYFIC REMS Overview

- The LYNOZYFIC Risk Evaluation and Mitigation Strategy (REMS) is a safety program that manages the risks of Cytokine Release Syndrome (CRS) and neurologic toxicity, including Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS). The LYNOZYFIC REMS is required by the Food and Drug Administration (FDA) to ensure that the benefits of the drug outweigh its risks.
- Healthcare providers and pharmacies and healthcare settings that prescribe and/or dispense LYNOZYFIC must be specially certified and trained on how to manage the risks of CRS and neurologic toxicity, including ICANS.
- Patients or their caregivers must receive the **Patient Wallet Card** before treatment initiation (first step-up dose).
- Wholesalers and distributors must only distribute LYNOZYFIC to certified pharmacies and healthcare settings.

What Are the Risks?

- 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, modify the next dose or permanently discontinue based on severity.
- Neurologic toxicity, including 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.



How Can Healthcare Providers Manage the Risks?

- Follow the LYNOZYFIC step-up dosing schedule as outlined in the **Prescriber Training Program**.
- Administer pretreatment medications and initiate therapy according to LYNOZYFIC step-up dosing to reduce the risk of CRS as outlined in the **Prescriber Training Program**.
- Counsel patients and their caregivers to seek immediate medical attention should the patient have signs or symptoms of CRS or neurologic toxicity, including ICANS.
- Complete the **Patient Wallet Card** and provide patients or their caregivers with the **Patient Wallet Card** prior to treatment initiation (first step-up dose).
- Advise patients that they should be hospitalized for 24 hours after administration of the first and second step-up doses of LYNOZYFIC.
 - Pretreatment medications as described in Section 2.3 of the Prescribing Information should be administered until two full doses are tolerated without CRS.
- 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.
- Monitor patients for signs and symptoms of CRS after infusion. 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.
- Monitor patients for signs or 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.
- For further details on recommended actions to be taken and treatment guidance for CRS and neurologic toxicity, including ICANS refer to the **Prescriber Training Program** and **Adverse Reaction Management Guide**.

Key Requirements of the LYNOZYFIC REMS



Healthcare providers who prescribe LYNOZYFIC

- Receive training on the REMS requirements at www.Lynozylicrems.com using the **Prescribing Training Program** and the **Adverse Reaction Management Guide**.
- Successfully complete and submit the **Knowledge Assessment** and enroll in the REMS by completing and submitting the **Prescriber Enrollment Form**.
- If LYNOZYFIC will be dispensed and administered in the same location, an Authorized Representative must complete the pharmacy and healthcare setting certification.
- Instruct patients that they 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. Monitor patients for signs and symptoms of CRS and neurologic toxicity, including ICANS during treatment.



Pharmacies and Healthcare Settings that dispense LYNOZYFIC

- Designate an Authorized Representative to carry out the certification process and oversee implementation and compliance with the REMS requirements on behalf of the pharmacy and healthcare setting.
Note: Certified LYNOZYFIC prescribers cannot be designated as an Authorized Representative for a certified pharmacy and healthcare setting.
- Have the Authorized Representative review the **Pharmacy and Healthcare Setting Training Program**.
- Have the Authorized Representative enroll in the REMS by completing and submitting the **Pharmacy and Healthcare Setting Enrollment Form**.
- Train all relevant staff involved in dispensing LYNOZYFIC on the REMS requirements using the **Pharmacy and Healthcare Setting Training Program**.
- Pharmacies and healthcare settings must verify prescriber certification in the LYNOZYFIC REMS before dispensing LYNOZYFIC.
 - Pharmacies and healthcare settings must obtain authorization to dispense (REMS Dispense Authorization [RDA]) for the first prescription written by each prescriber, for each patient, which verifies the prescriber is certified.
 - Subsequent prescriptions from the same prescriber, for the same patient, do not require obtaining an RDA, but pharmacies and healthcare settings can check the database of certified prescribers thereafter.



Patients who are prescribed LYNOZYFIC

- Receive counseling from the prescriber using the **Patient Wallet Card** before treatment initiation.
- Receive the **Patient Wallet Card** from the prescriber.
- Have the **Patient Wallet Card** with them at all times and inform other healthcare providers about treatment with LYNOZYFIC.

Adverse Event Reporting

Healthcare providers must report serious adverse events of CRS and neurologic toxicity, including ICANS to the LYNOZYFIC REMS at 1-855-212-6391.

Healthcare providers should also report all other suspected adverse events associated with LYNOZYFIC to Regeneron Pharmaceuticals, Inc. at 1-844-734-6643 or medical.information@regeneron.com or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

For further information, to enroll in the LYNOZYFIC REMS, and for all REMS materials please visit www.Lynozylicrems.com or call 1-855-212-6391.

Phone: 1-855-212-6391



www.Lynozylicrems.com
LYNOZYFICREMS@ubc.com

Fax: 1-866-750-0907



LYNOZYFIC Risk Evaluation and Mitigation Strategy (REMS)

LYNOZYFIC REMS

The goal of the LYNOZYFIC REMS is to mitigate the risks of Cytokine Release Syndrome (CRS) and neurologic toxicity, including Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS) by:

1. Ensuring prescribers are aware of the importance of monitoring for signs and symptoms of CRS and neurologic toxicity, including ICANS in patients receiving LYNOZYFIC.

Prescribers

Prescribers must be certified in the LYNOZYFIC REMS to treat patients with LYNOZYFIC.

[Learn More >](#)

Pharmacies and Healthcare Settings

Pharmacies and healthcare settings must be certified in the LYNOZYFIC REMS to dispense LYNOZYFIC to patients.

[Learn More >](#)



Resources for Prescribers

- [Prescriber Enrollment Form](#)
- [Prescriber Training Program](#)
- [Adverse Reaction Management Guide](#)
- [Knowledge Assessment](#)
- [Patient Wallet Card - English](#)
- [Patient Wallet Card - Arabic](#)
- [Patient Wallet Card - Spanish](#)
- [Patient Wallet Card - Mandarin](#)
- [Healthcare Provider Letter](#)
- [Professional Society Letter](#)
- [REMS Fact Sheet](#)

[REGISTER](#)

[LOGIN >](#)

Indication

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.

Reporting Adverse Events

Report serious adverse events of CRS and neurologic toxicity, including ICANS to the LYNOZYFIC REMS at 1-855-212-6391.

Report all other suspected adverse events associated with LYNOZYFIC to Regeneron Pharmaceuticals, at 1-844-734-6643 or medical.information@regeneron.com or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

[Pharmacy and Healthcare Setting Enrollment Form](#)

[Pharmacy and Healthcare Setting Training Program](#)

[REMS Fact Sheet](#)

[Download All Pharmacy and Healthcare Settings](#)

Resources for Patients

All patients treated with LYNOZYFIC will receive a **Patient Wallet Card**. Patients should carry the **Patient Wallet Card** to remind them of the signs and symptoms of CRS and neurologic toxicity, including ICANS, and when to seek immediate medical attention. Patients should show this card to all of their healthcare providers to inform them of the LYNOZYFIC treatment and when to contact their prescriber.

[Patient Wallet Card - English](#)

[Patient Wallet Card - Arabic](#)

[Patient Wallet Card - Spanish](#)

[Patient Wallet Card - Mandarin](#)

Have Questions?

Contact the LYNOZYFIC REMS by calling 1-855-212-6391.



Prescribers

LYNOZYFIC REMS Requirements

In order to prescribe LYNOZYFIC, healthcare providers must be trained on the LYNOZYFIC REMS requirements, must successfully complete the **Knowledge Assessment**, and must enroll in the LYNOZYFIC REMS by completing the **Prescriber Enrollment Form**.

How do I become certified in the LYNOZYFIC REMS?

1 Step 1: Review the **following materials**

Prescribing Information	Prescriber Training Program	Adverse Reaction Management Guide
-------------------------	-----------------------------	-----------------------------------

2 Step 2: Successfully complete the **Knowledge Assessment** and submit it to the REMS

Online	By email at LynozyticREMS@ubc.com	By fax at 1-866-750-0907
--	--	--

3 Step 3: Enroll in the REMS by completing and submitting the **Prescriber Enrollment Form** to the REMS

Online	By email at LynozyticREMS@ubc.com	By fax at 1-866-750-0907
--	--	--

Resources for Prescribers

[Prescriber Enrollment Form](#)

[Prescriber Training Program](#)

[Adverse Reaction Management Guide](#)

[Knowledge Assessment](#)

[Patient Wallet Card](#)

[Patient Wallet Card - English](#)

[Patient Wallet Card - Arabic](#)

[Patient Wallet Card - Spanish](#)

[Patient Wallet Card - Mandarin](#)

[Healthcare Provider Letter](#)

[Professional Society Letter](#)

[REMS Fact Sheet](#)

[Download All Prescriber Resources](#)

What do I need to do prior to LYNOZYFIC initiation (first step-up dose)?

Counsel the patient and caregivers on:

- the need to be hospitalized for 24 hours after administration of the first and second step-up doses,
- how to recognize and respond to signs and symptoms of CRS and neurologic toxicity, including ICANS,
- the need to report all symptoms suggestive of CRS and neurologic toxicity, including ICANS to their healthcare provider or emergency room provider immediately, and
- the need to carry the **Patient Wallet Card** at all times.

Complete the **Patient Wallet Card** and provide the **Patient Wallet Card** to the patient or caregiver

A detailed description of prescriber REMS requirements are included in the Prescriber Training Program.



Review Materials



As a condition of certification, the prescriber must complete this **Knowledge Assessment**. You will have 3 attempts to answer all 8 questions correctly.

- The **Knowledge Assessment** can be completed [online](#) or a completed hard copy can be submitted via fax to 1-866-750-0907 or via email at LYNOZYFICREMS@ubc.com. You must also complete the **Prescriber Enrollment Form** at LYNOZYFICREMS@ubc.com for your certification to be complete.
- The LYNOZYFIC REMS will verify that both the **Knowledge Assessment** and **Prescriber Enrollment Form** are complete and will provide confirmation of certification via email.

Please review the materials now by clicking on each link. Please note that you will not be able to continue to the **Knowledge Assessment** page until all 3 links have been opened and reviewed. Each document will open up in a new window for you to review.

LYNOZYFIC REMS Materials for Prescribers

- [Prescribing Information](#)
- [Prescriber Training Program](#)
- [Adverse Reaction Management Guide](#)

[Next](#)

Knowledge Assessment

Please complete the following assessment and click "Submit".



LYNOZYFIC REMS Knowledge Assessment

You have **3** attempt(s) to correctly answer all questions. You will be given the opportunity to retake any questions you answer incorrectly.

Question 1:

LYNOZYFIC is indicated for the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least 4 prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody.

- ☐ True
☐ False

Question 2:

Patients with CRS may present with the following signs and symptoms:

- ☐ Pyrexia
☐ Hypotension
☐ Hypoxia
☐ Tachycardia
☐ All of the above

Question 3:

Which one of the following is true regarding the median time to onset of CRS from the end of infusion of LYNOZYFIC? It typically occurs (select the one best response):

- ☐ 2 hours after the most recent dose, with a median duration of 4 hours
☐ 11 hours after the most recent dose, with a median duration of 15 hours
☐ 24 hours after the most recent dose with a median duration of 30 hours
☐ Rarely starts during the first week following LYNOZYFIC dosing

Question 4:

Which of the following regarding Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS) are correct:

- ☐ ICANS can be concurrent with CRS, following resolution of CRS, or in the absence of CRS
☐ Withhold LYNOZYFIC until ICANS resolves and modify the next dose or permanently discontinue LYNOZYFIC based on severity
☐ Provide supportive therapy, which may include intensive care for severe or life-threatening ICANS
☐ Most patients experienced ICANS following step-up dose 1
☐ All of the above

Question 5:

As a part of patient/caregiver counseling, which of the following are correct regarding LYNOZYFIC:

- ☐ Before treatment initiation (first dose), the **Patient Wallet Card** must be provided
☐ Patients should carry the **Patient Wallet Card** with them and inform other healthcare providers about treatment with LYNOZYFIC
☐ Patients should seek immediate medical attention should signs or symptoms of CRS or neurologic toxicity, including ICANS occur at any time
☐ All of the above

Question 6:

Clinical signs and symptoms of ICANS may include:

- ☐ Depressed level of consciousness
☐ Confusion
☐ Lethargy
☐ All of the above

Question 7:

Administer diphenhydramine and acetaminophen 30 to 60 minutes prior to each step-up dose, the first two full doses, and subsequent doses until dose is tolerated to reduce the risk of CRS:

- ☐ True
☐ False

Question 8:

If Grade 2 CRS is suspected during treatment with LYNOZYFIC, which of the following supportive measures should be considered:

- ☐ Provide supportive therapy, which may include intensive care
☐ Withhold LYNOZYFIC until CRS resolves
☐ Once CRS resolves, administer pretreatment medications prior to the next dose
☐ All of the above

Submit



Online Enrollment



LYNOZYFIC™ REMS
Prescriber Enrollment Form

Instructions

- To become a certified prescriber in the LYNOZYFIC REMS and prescribe LYNOZYFIC:
- Review the Prescribing Information, the **Prescriber Training Program**, and **Adverse Reaction Management Guide**.
 - Successfully complete and submit the **Knowledge Assessment** and this **Prescriber Enrollment Form**:
 - online below, or
 - by email at LynozyticREMS@ubc.com or
 - via fax to 1-866-750-0907

The LYNOZYFIC REMS will verify both the **Knowledge Assessment** and **Prescriber Enrollment Form** are complete and provide confirmation of certification via e-mail.

If LYNOZYFIC will be dispensed and administered in the same location, an Authorized Representative must complete the pharmacy and healthcare setting certification.

Certified LYNOZYFIC prescribers cannot be designated as the Authorized Representative for a pharmacy or healthcare setting.

*indicates required field

Prescriber Information

* National Provider Identifier (NPI)#

1234567890

* First Name

Steve

* Last Name

Meru

* Credentials (select one)

☒ MD ☐ DO ☐ NP ☐ PA ☐ Other (please specify)

* Specialty (select one)

☐ Oncology ☒ Hematology ☐ Oncology/Hematology ☐ Other (please specify)

* Practice/Facility Name

ABC pharmacy

* Address Line 1

123 Main Street

Address Line 2

* City

Philadelphia

* State

PA

* ZIP Code

99999

* Email

smeru@abc.com

* Phone

555-333-2121

* Fax

555-333-2222

Prescriber Responsibilities

- To become certified to prescribe, I must:
- Review the LYNOZYFIC Prescribing Information.
 - Review the **Prescriber Training Program** and **Adverse Reaction Management Guide**.
 - Successfully complete the **Knowledge Assessment** and submit it to the REMS.
 - Enroll in the REMS by completing and submitting the **Prescriber Enrollment Form** to the REMS.

- Before treatment initiation (first step-up dose), I must:
- Counsel the patient on:
 - how to recognize and respond to signs and symptoms of Cytokine Release Syndrome (CRS) and neurologic toxicity, including Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS),
 - the need to report all symptoms suggestive of CRS and neurologic toxicity, including ICANS to their healthcare provider or emergency room provider immediately
 - the need to carry the **Patient Wallet Card** at all times.
 - Complete the **Patient Wallet Card** and provide the **Patient Wallet Card** to the patient.

- At all times, I must:
- Report serious adverse events of CRS and neurologic toxicity, including ICANS to the REMS.

By signing this form, I agree to comply with all LYNOZYFIC REMS requirements. Regeneron representatives and its agents, including trusted vendors, may contact me to support the administration and assessment of, and/or education about the REMS.

Healthcare providers must report serious adverse events of CRS and neurologic toxicity, including ICANS to the LYNOZYFIC REMS at 1-855-212-6391.

Healthcare providers should also report all other suspected adverse events associated with LYNOZYFIC to Regeneron Pharmaceuticals, Inc. at 1-844-734-6643 or medical.information@regeneron.com or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Your information (name, location, and contact information) may be listed on a location finder as a location having a LYNOZYFIC REMS certified prescriber. This location finder may be available to healthcare professionals and/or patients seeking LYNOZYFIC REMS certified prescribers.

If you do not want your information listed, please call LYNOZYFIC REMS at 1-855-212-6391.

By signing up for the LYNOZYFIC REMS, Regeneron representatives and its agents, including trusted vendors, may contact me to support the administration of and/or education about the REMS, and we will use your information as provided in our Healthcare Provider Privacy Notice which is available here: www.regeneron.com/privacy-notice.

* Prescriber Signature:

Clear Signature

Please use your mouse or stylus to sign below

I authorize the above signature to be legally binding equivalent of my handwritten signature.

Cancel

Clear

Submit



REGISTER

LOGIN >

Home

Prescribers

Pharmacies and Healthcare Settings

Certified Participant Locator

Pharmacies and Healthcare Settings

LYNOZYFIC REMS Requirements

All pharmacies and healthcare settings involved in the dispensing of LYNOZYFIC must become certified in the LYNOZYFIC REMS

How does a Pharmacy and Healthcare Setting become certified in the LYNOZYFIC REMS?

- Step 1:** Designate an Authorized Representative for the pharmacy and healthcare setting
- Step 2:** Authorized Representative must review the [Pharmacy and Healthcare Setting Training Program](#)
- Step 3:** Authorized Representative must enroll in the REMS by completing and submitting the **Pharmacy and Healthcare Setting Enrollment Form** to the REMS

Online

By email
at LynozyticREMS@ubc.com

By fax
at 1-866-750-0907
- Step 4:** Train all relevant staff involved in dispensing LYNOZYFIC on the REMS requirements using the [Pharmacy and Healthcare Setting Training Program](#)
- Step 5:** Establish processes and procedures to verify the prescriber is certified for all dispenses after the first prescription

Resources for Pharmacies and Healthcare Settings

[Pharmacy and Healthcare Setting Enrollment Form](#)
[Pharmacy and Healthcare Setting Training Program](#)
[REMS Fact Sheet](#)
[Download All Pharmacy and Healthcare Settings](#)

What does a pharmacy and healthcare setting need to do prior to dispensing LYNOZYFIC?

Before dispensing the first prescription: Obtain authorization to dispense by contacting the REMS to verify the prescriber is certified.

Before dispensing, all subsequent prescriptions: Verify the prescriber is certified through the processes and procedures established as a requirement of the REMS.

A detailed description of pharmacy and healthcare setting REMS requirements are included in the [Pharmacy and Healthcare Setting Training Program](#).



REGISTER

LOGIN >

Home

Prescribers

Pharmacies and Healthcare Settings

Certified Participant Locator

Pharmacies and Healthcare Settings

LYNOZYFIC RISK EVALUATION MITIGATION STRATEGY (REMS) Pharmacy and Healthcare Setting Enrollment Form

Instructions

To become certified in the LYNOZYFIC REMS and dispense LYNOZYFIC, a pharmacy and healthcare setting must designate an Authorized Representative to:

- Review the **Pharmacy and Healthcare Setting Training Program**.
- Enroll in the REMS by completing and submitting this **Pharmacy and Healthcare Setting Enrollment Form**:
 - online below, or
 - by email at LynozyticREMS@ubc.com, or
 - via fax to 1-866-750-0907

The Authorized Representative will receive confirmation of the certification via email. Once certified, the pharmacy and healthcare setting's information will be shared with Regeneron Pharmaceuticals, Inc.'s wholesaler-distributor partners, to allow the pharmacy and healthcare setting to purchase product.

Certified LYNOZYFIC prescribers cannot be designated as the Authorized Representative for a pharmacy and healthcare setting.

*indicates required field

Pharmacy and Healthcare Setting Information

*Pharmacy/Healthcare Setting National Provider Identifier (NPI)#

Continue >



REGISTER

LOGIN >

Home

Prescribers

Pharmacies and Healthcare Settings

Certified Participant Locator

Pharmacies and Healthcare Settings

LYNOZYFIC RISK EVALUATION MITIGATION STRATEGY (REMS) Pharmacy and Healthcare Setting Enrollment Form

Instructions

To become certified in the LYNOZYFIC REMS and dispense LYNOZYFIC, a pharmacy and healthcare setting must designate an Authorized Representative to:

- Review the **Pharmacy and Healthcare Setting Training Program**.
- Enroll in the REMS by completing and submitting this **Pharmacy and Healthcare Setting Enrollment Form**:
 - online below, or
 - by email at LynozyficREMS@ubc.com, or
 - via fax to 1-866-750-0907

The Authorized Representative will receive confirmation of the certification via email. Once certified, the pharmacy and healthcare setting's information will be shared with Regeneron Pharmaceuticals, Inc.'s wholesaler-distributor partners, to allow the pharmacy and healthcare setting to purchase product.

Certified LYNOZYFIC prescribers cannot be designated as the Authorized Representative for a pharmacy and healthcare setting.

*indicates required field

Pharmacy and Healthcare Setting Information

*Pharmacy/Healthcare Setting National Provider Identifier (NPI)#

1234567890

*Select one

- ☐ New Certification ☐ Change in Authorized Representative

*Pharmacy/Healthcare Setting Name

University Hospital

*Stakeholder Type (select one)

- ☐ Pharmacy ☐ Healthcare Setting

*Pharmacy/Healthcare Setting Type (select one)

- ☐ Inpatient Hospital Pharmacy ☐ Outpatient Hospital Pharmacy ☐ Specialty Pharmacy
☐ Oncology Infusion Center ☐ Community Oncology Physician Office ☐ Other (please specify)

DEA#

HIN#

*Address Line 1

Address Line 2

*City

*State

-- Please Select --

*ZIP Code

*Phone

*Fax

Ship To Information

☐ Ship To Address - Same as above

*Ship To Contact Name

*Address Line 1

Address Line 2

*City

*State

-- Please Select --

*ZIP Code

Phone

Fax

Authorized Representative Information

*First Name

*Last Name

*Credentials (select one)

- ☐ PharmD ☐ R.Ph ☐ RN
☐ Other (please specify: e.g., MD, DO, Office Administrator, Practice Manager)

*Phone

*Fax

*Email

Authorized Representative Responsibilities

As the Authorized Representative, I must:

- Review the **Pharmacy and Healthcare Setting Training Program**.
- Complete and submit this **Pharmacy and Healthcare Setting Enrollment Form** to the REMS.
- Train all relevant staff involved in dispensing LYNOZYFIC on the LYNOZYFIC REMS requirements using the **Pharmacy and Healthcare Setting Training Program**.
- Establish processes and procedures to verify the prescriber is certified for all dispenses after the first prescription.
- Oversee implementation and compliance with the REMS requirements on behalf of the pharmacy and/or healthcare setting.

Before dispensing, first prescription, staff must:

- Obtain authorization to dispense by contacting the REMS to verify the prescriber is certified.

Before dispensing, all subsequent prescriptions, staff must:

- Verify the prescriber is certified through the processes and procedures established as a requirement of the REMS.

At all times, staff must:

- Report serious adverse events of CRS and neurologic toxicity including ICANS to the REMS.
- Not distribute, transfer, loan or sell LYNOZYFIC except to certified pharmacies and healthcare settings.
- Maintain records of staff training.
- Maintain records that processes and procedures are in place and are being followed.
- Maintain records of all LYNOZYFIC dispenses and provide data to the REMS, as requested.
- Comply with audits carried out by Regeneron Pharmaceuticals Inc. or a third party acting on behalf of Regeneron Pharmaceuticals, Inc. to ensure that all training, processes, and procedures are in place and are being followed.

To maintain certification to dispense:

- Have a new Authorized Representative enroll in the REMS by completing and submitting the **Pharmacy and Healthcare Setting Enrollment Form** to the REMS if the Authorized Representative changes.

By signing below, you agree that you have read the above responsibilities and understand your requirements as an Authorized Representative, and you agree to oversee the implementation and compliance with the REMS requirements for this pharmacy and healthcare setting.

Your site's information (name, location, and contact information) may be listed on a location finder as a location having a LYNOZYFIC REMS certified pharmacy and healthcare setting. This location finder may be available to healthcare professionals and/or patients seeking LYNOZYFIC REMS certified pharmacy and healthcare settings.

If you do not want your information listed, please call LYNOZYFIC REMS at 1-855-212-6391.

*Authorized Representative Signature:

Clear Signature

Please use your mouse or stylus to sign below

I authorize the above signature to be legally binding equivalent of my handwritten signature.

Cancel

Submit >



REGISTER

LOGIN >

Home

Prescribers

Pharmacies and Healthcare Settings

Certified Participant Locator

Pharmacies and Healthcare Settings

LYNOZYFIC RISK EVALUATION MITIGATION STRATEGY (REMS) Pharmacy and Healthcare Setting Enrollment Form

Instructions

To become certified in the LYNOZYFIC REMS and dispense LYNOZYFIC, a pharmacy and healthcare setting must designate an Authorized Representative to:

- Review the **Pharmacy and Healthcare Setting Training Program**.
- Enroll in the REMS by completing and submitting this **Pharmacy and Healthcare Setting Enrollment Form**:
 - online below, or
 - by email at LynozyficREMS@ubc.com, or
 - via fax to 1-866-750-0907

The Authorized Representative will receive confirmation of the certification via email. Once certified, the pharmacy and healthcare setting's information will be shared with Regeneron Pharmaceuticals, Inc.'s wholesaler-distributor partners, to allow the pharmacy and healthcare setting to purchase product.

Certified LYNOZYFIC prescribers cannot be designated as the Authorized Representative for a pharmacy and healthcare setting.

*indicates required field

Pharmacy and Healthcare Setting Information

*Pharmacy/Healthcare Setting National Provider Identifier (NPI)#

1234567890

*Select one

- ☐ New Certification ☐ Change in Authorized Representative

*Pharmacy/Healthcare Setting Name

University Hospital

*Stakeholder Type (select one)

- ☐ Pharmacy ☐ Healthcare Setting

*Pharmacy/Healthcare Setting Type (select one)

- ☐ Inpatient Hospital Pharmacy ☐ Outpatient Hospital Pharmacy ☐ Specialty Pharmacy
☐ Oncology Infusion Center ☐ Community Oncology Physician Office ☒ Other (please specify)

*Other Pharmacy/Healthcare Setting Type

Other

DEA#

HIN#

*Address Line 1

Address Line 2

*City

*State

-- Please Select --

*ZIP Code

*Phone

*Fax

Ship To Information

☐ Ship To Address - Same as above

*Ship To Contact Name

*Address Line 1

Address Line 2

*City

*State

-- Please Select --

*ZIP Code

Phone

Fax

Authorized Representative Information

*First Name

*Last Name

*Credentials (select one)

- ☐ PharmD ☐ R.Ph ☐ RN
☒ Other (please specify: e.g., MD, DO, Office Administrator, Practice Manager)

*Other Credentials

Please Specify

*Phone

*Fax

*Email

Authorized Representative Responsibilities

As the Authorized Representative, I must:

- Review the **Pharmacy and Healthcare Setting Training Program**.
- Complete and submit this **Pharmacy and Healthcare Setting Enrollment Form** to the REMS.
- Train all relevant staff involved in dispensing LYNOZYFIC on the LYNOZYFIC REMS requirements using the **Pharmacy and Healthcare Setting Training Program**.
- Establish processes and procedures to verify the prescriber is certified for all dispenses after the first prescription.
- Oversee implementation and compliance with the REMS requirements on behalf of the pharmacy and/or healthcare setting.

Before dispensing, first prescription, staff must:

- Obtain authorization to dispense by contacting the REMS to verify the prescriber is certified.

Before dispensing, all subsequent prescriptions, staff must:

- Verify the prescriber is certified through the processes and procedures established as a requirement of the REMS.

At all times, staff must:

- Report serious adverse events of CRS and neurologic toxicity including ICANS to the REMS.
- Not distribute, transfer, loan or sell LYNOZYFIC except to certified pharmacies and healthcare settings.
- Maintain records of staff training.
- Maintain records that processes and procedures are in place and are being followed.
- Maintain records of all LYNOZYFIC dispenses and provide data to the REMS, as requested.
- Comply with audits carried out by Regeneron Pharmaceuticals Inc. or a third party acting on behalf of Regeneron Pharmaceuticals, Inc. to ensure that all training, processes, and procedures are in place and are being followed.

To maintain certification to dispense:

- Have a new Authorized Representative enroll in the REMS by completing and submitting the **Pharmacy and Healthcare Setting Enrollment Form** to the REMS if the Authorized Representative changes.

By signing below, you agree that you have read the above responsibilities and understand your requirements as an Authorized Representative, and you agree to oversee the implementation and compliance with the REMS requirements for this pharmacy and healthcare setting.

Your site's information (name, location, and contact information) may be listed on a location finder as a location having a LYNOZYFIC REMS certified pharmacy and healthcare setting. This location finder may be available to healthcare professionals and/or patients seeking LYNOZYFIC REMS certified pharmacy and healthcare settings.

If you do not want your information listed, please call LYNOZYFIC REMS at 1-855-212-6391.

*Authorized Representative Signature:

Clear Signature

Please use your mouse or stylus to sign below

I authorize the above signature to be legally binding equivalent of my handwritten signature.

Cancel

Submit >



[REGISTER](#)

[LOGIN >](#)

[Home](#)

[Prescribers](#)

[Pharmacies and Healthcare Settings](#)

[Certified Participant Locator](#)

Pharmacies and Healthcare Settings

Thank you for submitting your information to enroll in the LYNZYFIC REMS.

Confirmation of this submission has been sent to the email address provided. You can expect to receive an email with a link to create your online web account.

If you do not receive the email within the next few hours or would like to update your enrollment information at any time, please contact the LYNZYFIC REMS at 1-855-212-6391.



[REGISTER](#)

[LOGIN >](#)

[Home](#)

[Prescribers](#)

[Pharmacies and Healthcare Settings](#)

[Certified Participant Locator](#)

Certified Participant Locator

Enter your location below to find your nearest LYNZYFIC REMS certified prescriber and pharmacy/healthcare setting.

* Zip Code

* Search Radius

Within 25 miles

▼

Search >

Regeneron is providing this feature to help patients find prescribers and healthcare facilities that have been certified in the LYNZYFIC REMS. Regeneron does not receive payment for providing this feature, and does not endorse, recommend, have jurisdiction over, or accept responsibility for the actions of any of the prescribers or healthcare facilities listed herein.

This site is provided as a resource and is not intended as medical advice. Information on the site is updated periodically.

If you have questions about the LYNZYFIC REMS or need help enrolling, please call the LYNZYFIC REMS at 1-855-212-6391. Monday through Friday 8am-8pm ET, excluding observed US holidays.

© XXXX, Regeneron Pharmaceuticals, Inc. All rights reserved.

[Terms and Conditions](#) [Privacy Policy](#) [Contact Us](#)

Reference ID: 5618212



REGISTER

LOGIN >

Certified Participant Locator

Enter your location below to find your nearest LYNOZYFIC REMS certified prescriber and pharmacy/healthcare setting.

Certified Pharmacies and Healthcare Settings

Certified Prescribers

*Zip Code

12345

*Search Radius

Within 25 miles

Search >

MapSatellite

Map data ©2018 Google 5 km Terms of Use Report a map error

PREScriBER NAME

24.1 miles

100 Main St
Blue Bell, PA 19422
555 555-1212

Directions

PREScriBER NAME

24.6 miles

100 Main St
Blue Bell, PA 19422
555 555-1212

Directions

PREScriBER NAME

24.6 miles

100 Main St
Blue Bell, PA 19422
555 555-1212

Directions

PREScriBER NAME

24.6 miles

100 Main St
Blue Bell, PA 19422
555 555-1212

Directions

PREScriBER NAME

24.2 miles

100 Main St
Blue Bell, PA 19422
555 555-1212

Directions

Regeneron is providing this feature to help patients find prescribers and healthcare facilities that have been certified in the LYNOZYFIC REMS. Regeneron does not receive payment for providing this feature, and does not endorse, recommend, have jurisdiction over, or accept responsibility for the actions of any of the prescribers or healthcare facilities listed herein.

This site is provided as a resource and is not intended as medical advice. Information on the site is updated periodically.

If you have questions about the LYNOZYFIC REMS or need help enrolling, please call the LYNOZYFIC REMS at 1-855-212-6391. Monday through Friday 8am-8pm ET, excluding observed US holidays.

© XXXX, Regeneron Pharmaceuticals, Inc. All rights reserved. Terms and Conditions Privacy Policy Contact Us

Reference ID: 5618212



[REGISTER](#)

[LOGIN >](#)

[Home](#)

[Prescribers](#)

[Pharmacies and Healthcare Settings](#)

[Certified Participant Locator](#)

Contact Us

Phone

1-855-212-6391

Fax

1-866-750-0907

Hours of Operation

Monday - Friday
08:00 AM – 08:00 PM Eastern

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

ROMEO A DE CLARO
07/02/2025 09:31:28 AM