

Risk Evaluation and Mitigation Strategy (REMS) Document

PALYNZIQ® (pegvaliase-pqpz) REMS Program

I. Administrative Information

Application Number: BLA 761079
Application Holder: BioMarin Pharmaceutical Inc.
Initial REMS Approval: 05/2018
Most Recent REMS Update: 10/2020

II. REMS Goals

The goal of the PALYNZIQ® (pegvaliase-pqpz) REMS is to mitigate the risk of anaphylaxis associated with PALYNZIQ by:

1. Ensuring that prescribers are educated on the risk of anaphylaxis associated with the use of PALYNZIQ
2. Ensuring that prescribers are educated and adhere to the following:
 - a. Counsel patients on how to recognize and respond to signs and symptoms of anaphylaxis
 - b. Enroll patients in the PALYNZIQ REMS
 - c. Prescribe auto-injectable epinephrine with PALYNZIQ
3. Ensuring that PALYNZIQ is only dispensed to patients with documentation of safe use conditions
 - a. Patient education and enrollment in the PALYNZIQ REMS
 - b. Having auto-injectable epinephrine available at all times
4. Ensuring that patients are educated on the following:
 - a. How to recognize and respond to signs and symptoms of anaphylaxis
 - b. The need to carry auto-injectable epinephrine with them at all times

III. REMS Requirements

BioMarin must ensure that healthcare providers, patients, pharmacies, and wholesalers comply with the following requirements:

1. Healthcare Providers who prescribe PALYNZIQ must:

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- | | |
|--|--|
| To become certified to prescribe | <ol style="list-style-type: none">1. Review the drug's Prescribing Information.2. Review the following: Prescriber Guide and REMS Program Overview.3. Successfully complete the Prescriber Knowledge Assessment and submit it to the REMS program.4. Enroll in the REMS by completing the Prescriber Enrollment Form and submitting it to the REMS Program. |
| Before treatment initiation (first dose) | <ol style="list-style-type: none">5. Assess the patient's need for an adult observer and for premedication as described in the Prescriber Guide. |
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6. Counsel the patient on the risk for anaphylaxis, including how to recognize and respond to signs and symptoms of anaphylaxis and having auto-injectable epinephrine available at all times using the [Patient Guide](#), [Safety Video](#), and [Wallet Card](#).
 7. Provide the patient with the [Patient Guide](#) and [Wallet Card](#), and direct the patient to PALYNZIQREMS.com to view the [Safety Video](#).
 8. Enroll the patient in the REMS Program by completing and submitting the [Patient Enrollment Form](#). Provide a completed copy of the form to the patient and retain a completed copy in the patient's record.
 9. Provide the patient with a prescription for auto-injectable epinephrine to accompany the prescription for PALYNZIQ.

During treatment;
before each
prescription

10. Assess the patient for anaphylaxis episodes.
11. Assess the patient's supply of auto-injectable epinephrine.
12. Provide a prescription for auto-injectable epinephrine, if the patient's supply is inadequate.

At all times

13. Report anaphylaxis episodes to the REMS Program.
14. Report treatment discontinuation or transfer of care to the REMS Program.

2. Patients who are prescribed PALYNZIQ must:

Before treatment
initiation

1. Review the [Patient Guide](#), [Safety Video](#), and [Wallet Card](#).
2. Enroll in the REMS Program by completing the [Patient Enrollment Form](#) with the prescriber. Enrollment information will be provided to the REMS Program.
3. Receive counseling from the prescriber on how to recognize and respond to signs and symptoms of anaphylaxis, and having auto-injectable epinephrine with you at all times using the [Patient Guide](#), [Safety Video](#), and [Wallet Card](#).
4. Adhere to the safe use conditions including obtaining auto-injectable epinephrine.

At all times

5. Inform the prescriber if you have a severe allergic reaction (anaphylaxis).
6. Inform the prescriber if you need more auto-injectable epinephrine.
7. Have auto-injectable epinephrine and the [Wallet Card](#) with you.
8. Inform all doctors about this treatment.
9. Report a change in prescriber or contact information to the REMS Program.
10. Report treatment discontinuation to the REMS Program.

3. Pharmacies that dispense PALYNZIQ 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 Program on behalf of the pharmacy.
 2. Have the authorized representative review the [REMS Program Overview](#).
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	<ol style="list-style-type: none"> 3. Have the authorized representative enroll in the REMS Program by completing and submitting the Pharmacy Enrollment Form. 4. Establish processes and procedures to verify and document the patient has auto-injectable epinephrine and report anaphylaxis episodes to the REMS Program/manufacturer/prescriber. 5. Train all relevant staff involved in the dispensing of PALYNZIQ on the program requirements using the REMS Program Overview.
Before Dispensing	<ol style="list-style-type: none"> 6. Verify and document that the patient has auto-injectable epinephrine through the processes and procedures established as a requirement of the REMS Program. 7. Obtain authorization to dispense each prescription by contacting the REMS Program to verify prescriber certification and patient enrollment.
To maintain certification to dispense	<ol style="list-style-type: none"> 8. Have the new authorized representative enroll in the REMS Program by completing the Pharmacy Enrollment Form if the authorized representative changes.
At all times	<ol style="list-style-type: none"> 9. Report anaphylaxis episodes to the REMS Program. 10. Not distribute, transfer, loan, or sell PALYNZIQ, except to certified dispensers. 11. Maintain records documenting staff's completion of REMS training. 12. Maintain records that all processes and procedures are in place and are being followed. 13. Comply with audits carried out by BioMarin or a third party acting on behalf of BioMarin to ensure that all processes and procedures are in place and are being followed.

4. Wholesalers that distribute PALYNZIQ must:

To be able to distribute	<ol style="list-style-type: none"> 1. Establish processes and procedures to ensure that the drug is distributed only to certified pharmacies. 2. Train all relevant staff involved in distributing on the REMS Program requirements.
At all times	<ol style="list-style-type: none"> 3. Distribute only to certified pharmacies and maintain records of all distributions. 4. Comply with audits carried out by BioMarin or a third party acting on behalf of BioMarin to ensure that all processes and procedures are in place and are being followed.

BioMarin must provide training to healthcare providers who prescribe PALYNZIQ.

The training includes the following educational materials: [Prescriber Guide](#), [REMS Program Overview](#) and [Prescriber Knowledge Assessment](#). The training must be available online and by hard-copy via fax or mail.

BioMarin must provide training to pharmacies who dispense PALYNZIQ.

The training includes the following educational material: [REMS Program Overview](#). The training must be available online and by hard-copy via fax or mail.

To support REMS Program operations, BioMarin must:

1. Establish and maintain a REMS Program Website, PALYNZIQREMS.com. The REMS Program website must include the capability to complete prescriber certification online, direct pharmacies on how to initiate enrollment inquiry, the capability to enroll patients online, obtain authorization to dispense, report anaphylaxis episodes online, to view the Safety Video, and the option to print the Prescribing Information, Medication Guide, and REMS materials. All product websites for consumers and healthcare providers must include prominent REMS-specific links to the REMS Program website. The REMS Program website must not link back to the promotional product website(s).
2. Make the REMS Program website fully operational and all REMS materials available through the website or call center by the date PALYNZIQ is first commercially distributed.
3. Establish and maintain a REMS Program call center for REMS participants at 1-855-758-REMS (1-855-758-7367).
4. Establish and maintain a validated, secure database of all REMS participants who are enrolled and/or certified in the PALYNZIQ REMS Program.
5. Ensure that prescribers are able to become certified in the REMS by mail, fax, and online.
6. Ensure that prescribers are able to enroll patients in the REMS by fax and online.
7. Ensure that pharmacies are able to become certified in the REMS by fax.
8. Ensure pharmacies are able to verify patient enrollment and prescriber certification and obtain dispensing authorization by phone or online.
9. Ensure prescribers, patients, and pharmacies are able to report anaphylaxis episodes by phone or online.
10. Provide the [Prescriber Guide](#), [Prescriber Enrollment Form](#), [Prescriber Knowledge Assessment](#), [REMS Program Overview](#), [Patient Guide](#), [Patient Enrollment Form](#), [Wallet Card](#), [Safety Video](#), and Prescribing Information to prescribers who (1) attempt to prescribe PALYNZIQ and are not yet certified or (2) inquire about how to become certified.
11. Provide the [Pharmacy Enrollment Form](#) and [REMS Program Overview](#) to pharmacies who (1) attempt to dispense PALYNZIQ and are not yet certified or (2) inquire about how to become certified.
12. Notify prescribers, patients, and pharmacies within two business days after they become certified in the REMS Program.
13. Provide certified prescribers access to the database of certified pharmacies and their enrolled patients.
14. Provide certified pharmacies access to the database of certified prescribers and enrolled patients.

To ensure REMS participants' compliance with the REMS Program, BioMarin must:

15. Verify annually that the designated authorized representative for the certified pharmacy remains the same. If different, the pharmacy must recertify with a new authorized representative.
16. Maintain adequate records to demonstrate that REMS requirements have been met, including, but not limited to records of: PALYNZIQ distribution and dispensing; certification of prescribers and pharmacies; enrolled patients; and audits of REMS participants. These records must be readily available for FDA inspections.
17. Establish a plan for addressing noncompliance with REMS Program requirements.

18. Monitor prescribers and pharmacies on an ongoing basis to ensure the requirements of the REMS are being met. Take corrective action if noncompliance is identified, including decertification.
19. Audit pharmacies no later than 90 calendar days after they become certified to ensure that all REMS processes and procedures are in place, functioning, and support the REMS Program requirements.
20. Take reasonable steps to improve implementation of and compliance with the requirements in the PALYNZIQ REMS Program based on monitoring and evaluation of the PALYNZIQ REMS.

IV. REMS Assessment Timetable

BioMarin must submit REMS Assessments at 6 months, 12 months, and annually thereafter from the date of the initial approval of the REMS (05/2018). 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. BioMarin 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 PALYNZIQ REMS:

Enrollment Forms:

Prescriber:

1. [Prescriber Enrollment Form](#)

Patient:

2. [Patient Enrollment Form](#)

Pharmacy:

3. [Pharmacy Enrollment Form](#)

Training and Educational Materials

Prescriber:

4. [Prescriber Guide](#)
5. [Prescriber Knowledge Assessment](#)

Patient:

6. [Patient Guide](#)
7. [Safety Video](#)
8. [Wallet Card](#)

Pharmacy:

9. [REMS Program Overview](#)

Other Materials

10. [REMS Program website](#)



PALYNZIQ® REMS Prescriber Enrollment Form

PALYNZIQ® (pegvaliase-pqpz) is available only through the PALYNZIQ REMS, a restricted distribution program. Only prescribers, patients, and a limited network of certified pharmacies enrolled in the program are able to prescribe, receive, and dispense PALYNZIQ.

Instructions:

1. Review the PALYNZIQ Prescribing Information (PI), the REMS Program Overview, and Prescriber Guide
2. Complete the Prescriber Knowledge Assessment and this enrollment form
3. Submit the completed form:
 - Online at PALYNZIQREMS.com
 - Fax: 1-866-713-8421
 - Mail: PALYNZIQ REMS, 200 Pinecrest Plaza, Morgantown, WV 26505-8065

PLEASE COMPLETE ALL MANDATORY FIELDS ON THIS FORM TO AVOID A DELAY IN THE ENROLLMENT PROCESS.

PRESCRIBER AGREEMENT

By completing, signing, and submitting this form, I acknowledge and agree that:

- PALYNZIQ is only available through the PALYNZIQ REMS, and I must comply with the REMS requirements to prescribe PALYNZIQ
- I have reviewed the Prescribing Information, *Prescriber Guide*, and *REMS Program Overview*
- I understand the risk of anaphylaxis associated with PALYNZIQ
- I have successfully completed the *Prescriber Knowledge Assessment*
- To prescribe PALYNZIQ to a patient, I must enroll each patient in the PALYNZIQ REMS by:
 - Counseling the patient about the risks of PALYNZIQ, including anaphylaxis, and the need to carry auto-injectable epinephrine with them at all times
 - Reviewing the *Patient Guide*, *Safety Video*, and *Wallet Card* with the patient
 - Providing the *Patient Guide* and *Wallet Card* to the patient and **directing the patient to PALYNZIQREMS.com to view the Safety Video**
- Completing and submitting the *Patient Enrollment Form* to the PALYNZIQ REMS, retaining a copy in the patient's records, and providing a copy to the patient
- I will assess the patient's need for an adult observer and for premedication as described in the *Prescriber Guide*
- I will provide prescriptions for auto-injectable epinephrine to each patient
- I will report anaphylaxis episodes to the PALYNZIQ REMS
- I will report discontinuation of treatment or transfer of care to the PALYNZIQ REMS
- I understand that if I do not maintain compliance with the requirements of the PALYNZIQ REMS, I will no longer be able to prescribe PALYNZIQ
- PALYNZIQ REMS, its agents, or contractors may contact me to support the PALYNZIQ REMS

For additional information, visit PALYNZIQREMS.com or call the PALYNZIQ REMS at 1-855-758-REMS (1-855-758-7367).

PRESCRIBER INFORMATION (please print)

* indicates a REQUIRED field

First Name:*		Middle Initial:	Last Name:*	
Institution Name (if applicable):			Prescriber NPI#:*	State License Number:
Prescriber Address:*		City:*	State:*	ZIP Code:*
Office Phone Number:*	Mobile Phone Number:	Office Fax Number:*	Email:*	
Prescriber Degree: * <input type="checkbox"/> MD <input type="checkbox"/> DO <input type="checkbox"/> Other (please specify): _____				
Specialty: * <input type="checkbox"/> Genetics <input type="checkbox"/> Internal Medicine <input type="checkbox"/> Other (please specify): _____				
Office Contact First Name:		Last Name:	Phone Number:	
Second Contact First Name:		Last Name:	Phone Number:	
Prescriber Signature:*			Date:*	

Access this form and enroll online at PALYNZIQREMS.com.
To submit this form via fax, please complete all required fields and fax to PALYNZIQ REMS at 1-866-713-8421.

PALYNZIQREMS.com
Phone: 1-855-758-REMS (1-855-758-7367)
Fax: 1-866-713-8421

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Palynziq®
(pegvaliase-pqpz) Injection



PALYNZIQ REMS Patient Enrollment Form

PALYNZIQ® (pegvaliase-pqpz) is available only through the PALYNZIQ REMS, a restricted distribution program. Only prescribers, patients, and a limited network of certified pharmacies enrolled in the program are able to prescribe, receive, and dispense PALYNZIQ. Your certified healthcare provider will help you complete this form and provide you with a copy.

Access this form and enroll online at PALYNZIQREMS.com. To submit this form via fax, please complete all required fields below and fax to the PALYNZIQ REMS at 1-866-713-8421.

PATIENT INFORMATION (please print)				* indicates a REQUIRED field	
First Name:*	Last Name:*	Date of Birth:*	Gender: <input type="checkbox"/> M <input type="checkbox"/> F <input type="checkbox"/> Other		
Address:*	City:*	State:*	ZIP Code:*		
Email:*	Primary Phone Number:*	Secondary Phone Number:			
Preferred method(s) of contact: * <input type="checkbox"/> Primary Phone <input type="checkbox"/> Email					
In addition, I give permission and allow for the sharing of my health information to the designated individual named below. BioMarin may contact the individual designated below to discuss my enrollment in the PALYNZIQ REMS. (* indicates required if designated individual is provided)					
Designated Individual:	Relationship:*	Email:*	Phone Number:*		
PRESCRIBER INFORMATION (please print)				* indicates a REQUIRED field	
First Name:*	Last Name:*	Phone Number:*	Prescriber NPI #:*		
PATIENT AGREEMENT					
By signing this form, I understand and acknowledge that:					
<ul style="list-style-type: none"> I have received, read, and understand the <i>Patient Guide</i> I have watched and understand the <i>Safety Video</i> To receive PALYNZIQ, I am required to enroll in the PALYNZIQ REMS, and my information will be stored in a secure database of all patients who receive PALYNZIQ in the United States. After enrolling, my doctor will provide me with a signed copy of this enrollment form PALYNZIQ can cause severe allergic reactions (anaphylaxis) that may be life-threatening. My doctor has reviewed with me the risks of treatment with PALYNZIQ and answered all of my questions I must receive and fill a prescription for auto-injectable epinephrine and carry auto-injectable epinephrine with me at all times I will tell my doctor if I have any signs or symptoms of a severe allergic reaction (anaphylaxis) 		<ul style="list-style-type: none"> My doctor has given me the <i>Wallet Card</i>, which I will carry with me at all times. I will show this card to all my doctors involved in my medical treatment, even if it is not for my phenylketonuria (PKU) I will tell all of my doctors that I have been treated with PALYNZIQ I will tell my doctor if I need more auto-injectable epinephrine I will tell the PALYNZIQ REMS right away if I change my PALYNZIQ doctor, if my contact information changes, or if I discontinue PALYNZIQ I give permission to BioMarin and its agents to use and share my personal health information for the purposes of enrolling me into and administering the PALYNZIQ REMS, and coordinating the dispensing of PALYNZIQ BioMarin and its agents may contact me via phone, mail, or email to support the PALYNZIQ REMS 			
PATIENT ACKNOWLEDGMENT					
Patient/Patient Representative Signature:*		Date:*			
Print Name:*		Relationship to Patient* (if signing on behalf of patient):			
PRESCRIBER ACKNOWLEDGMENT					
I have reviewed and discussed the risks of PALYNZIQ and the requirements of the PALYNZIQ REMS with this patient and prescribed auto-injectable epinephrine for this patient.					
Prescriber Signature:*		Date:*			

**Access this form and enroll online at PALYNZIQREMS.com.
To submit this form via fax, please complete all required fields
and fax to the PALYNZIQ REMS at 1-866-713-8421.**

**PALYNZIQREMS.com
Phone: 1-855-758-REMS (1-855-758-7367)
Fax: 1-866-713-8421**

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Palynziq®
(pegvaliase-pqpz) Injection



PALYNZIQ REMS Pharmacy Enrollment Form

PALYNZIQ® (pegvaliase-pqpz) is available only through the PALYNZIQ REMS, a restricted distribution program. Only prescribers, patients, and a limited network of certified pharmacies enrolled in the program are able to prescribe, receive, and dispense PALYNZIQ.

If you have questions, please contact the PALYNZIQ REMS at 1-855-758-REMS (1-855-758-7367). Please complete the form below and fax to 1-866-713-8421.

AUTHORIZED PHARMACY REPRESENTATIVE RESPONSIBILITIES:

I am the authorized representative designated by my Pharmacy to coordinate the activities of the PALYNZIQ REMS. By signing this form, I agree, on behalf of myself and the Pharmacy, to comply with the following program requirements:

- I will oversee implementation of and ensure my pharmacy's compliance with the PALYNZIQ REMS requirements
- I have reviewed the *REMS Program Overview* and will ensure that all relevant staff involved in the dispensing of PALYNZIQ are trained on the PALYNZIQ REMS requirements and that a record of training is maintained
- Only certified pharmacies can dispense PALYNZIQ
- PALYNZIQ is only available through the PALYNZIQ REMS and the pharmacy must comply with the REMS requirements to dispense PALYNZIQ
- I will ensure that prior to dispensing PALYNZIQ, my pharmacy will document and verify:
 - The patient has auto-injectable epinephrine
 - The prescriber is certified
 - The patient is enrolled
- This pharmacy will ensure that anaphylaxis episodes are reported by the Pharmacy to the PALYNZIQ REMS
- This pharmacy will not distribute, transfer, loan, or sell PALYNZIQ, except to certified pharmacies
- This pharmacy will maintain and make available appropriate documentation reflecting that all processes are in place and being followed for the PALYNZIQ REMS and provide copies of such documentation upon request to BioMarin or any third party acting on behalf of BioMarin
- This pharmacy will comply with audits by BioMarin or a third party acting on behalf of BioMarin, to ensure compliance with the PALYNZIQ REMS
- This pharmacy will ensure that if the pharmacy designates a new authorized representative, the new authorized representative must complete a new *Pharmacy Enrollment Form*
- I understand that non-compliance with the requirements of the PALYNZIQ REMS will result in decertification of my Pharmacy and termination of the authorization to dispense PALYNZIQ

PHARMACY INFORMATION (please print)

* indicates a REQUIRED field

Pharmacy Name:*				
Pharmacy Address:*		City:*	State:*	ZIP Code:*
Pharmacy Identifiers:	NPI:*	NCPDP:		

PHARMACY AUTHORIZED REPRESENTATIVE INFORMATION (please print)

* indicates a REQUIRED field

First Name:*		Middle Initial:	Last Name:*	
Phone Number:*		Alternate Phone Number:		Fax Number:*
Email:*		Preferred Method of Communication: * <input type="checkbox"/> Phone <input type="checkbox"/> Email <input type="checkbox"/> Fax		
Authorized Pharmacy Representative Signature:*				Date:*

Access this form at PALYNZIQREMS.com.
To submit this form via fax, please complete all required fields and fax to PALYNZIQ REMS at 1-866-713-8421.

For additional information, visit PALYNZIQREMS.com or call the PALYNZIQ REMS at 1-855-758-REMS (1-855-758-7367)

For information on 340B, contact the PALYNZIQ REMS at 1-855-758-7367.

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Palynziq®
(pegvaliase-pqpz) Injection

PALYNZIQ

REMS Prescriber Guide

What is PALYNZIQ?

PALYNZIQ® is indicated to reduce blood phenylalanine concentrations in adult patients with phenylketonuria (PKU) who have uncontrolled blood phenylalanine concentrations greater than 600 micromol/L on existing management.

Please see Prescribing Information, including **BOXED WARNING**, for additional Important Safety Information.

Serious Risk of Anaphylaxis

PALYNZIQ may cause anaphylaxis; patients may experience an anaphylaxis episode immediately or at any time after an injection of PALYNZIQ. Episodes of anaphylaxis are more common at the beginning of treatment, but can occur anytime during treatment.

In clinical trials of PALYNZIQ with induction/titration/maintenance dosing, 29 out of 285 (10%) patients experienced a total of 42 anaphylaxis episodes. Anaphylaxis generally occurred within 1 hour after injection (81%; 34/42 episodes); however, delayed episodes also occurred (up to 48 hours after PALYNZIQ administration). Most episodes of anaphylaxis occurred within the first year of dosing (69%; 29/42 episodes), but cases also occurred after one year of dosing and up to 1604 days (4.4 years) into treatment.

Twenty one out of the 29 (72%) patients who experienced anaphylaxis were rechallenged with PALYNZIQ and 6 out of the 21 (29%) had a recurrence of anaphylaxis. All anaphylaxis episodes resolved without sequelae.

The signs and symptoms of anaphylaxis can include:

- Syncope, hypotension
- Hypoxia, dyspnea, wheezing
- Chest discomfort/chest tightness
- Tachycardia
- Angioedema (swelling of the face, lips, eyes, tongue)
- Throat tightness
- Skin flushing
- Rash, urticaria, pruritus
- Gastrointestinal symptoms (vomiting, nausea, diarrhea)

Anaphylaxis requires immediate treatment with auto-injectable epinephrine. Prescribe auto-injectable epinephrine to all patients receiving PALYNZIQ and instruct patients to carry auto-injectable epinephrine with them at all times during PALYNZIQ treatment. Prior to the first dose, instruct the patient and adult observer (if applicable) to recognize the signs and symptoms of anaphylaxis, how to properly administer auto-injectable epinephrine, and to seek immediate medical care upon its use. Consider the risks associated with auto-injectable epinephrine use when prescribing PALYNZIQ. Refer to the auto-injectable epinephrine prescribing information for complete information.

Administer the initial dose of PALYNZIQ under the supervision of a healthcare provider equipped to manage anaphylaxis, and closely observe patients for at least 60 minutes following the injection. Prior to self-injection, confirm patient competency with self-administration, and patient's and adult observer's (if applicable) ability to recognize signs and symptoms of anaphylaxis and administer auto-injectable epinephrine, if needed.

Consider the risks and benefits of readministering PALYNZIQ following an episode of anaphylaxis. If the decision is made to readminister PALYNZIQ, readminister the first dose under supervision of a healthcare provider equipped to manage anaphylaxis and closely observe the patient for at least 60 minutes following the dose.

Palynziq[®]
(pegvaliase-pqpz) Injection

Additional Risks and Safety Information

The information presented in this document does not include a complete list of all safety information for PALYNZIQ. To review the complete safety information on PALYNZIQ, please refer to the Prescribing Information, including **BOXED WARNING**, for PALYNZIQ at PALYNZIQREMS.com

Clinical Considerations

Adult Observer

Prescribers may consider having an adult observer for patients who may need assistance in recognizing and managing anaphylaxis during PALYNZIQ treatment. If an adult observer is needed, the observer should be present with the patient during and for at least 60 minutes after PALYNZIQ administration, should be able to administer auto-injectable epinephrine, and call for emergency medical support upon its use.

Premedication

For hypersensitivity reactions, consider premedication with a H₁-receptor antagonist, H₂-receptor antagonist, and/or antipyretic prior to PALYNZIQ administration based upon individual patient tolerability.

What is the PALYNZIQ REMS?

A Risk Evaluation and Mitigation Strategy (REMS) is a strategy to manage known or potential serious risks associated with a drug product and is required by the U.S. Food and Drug Administration (FDA) to ensure the benefits of a drug continue to outweigh its risks.

Because of the risk of anaphylaxis, PALYNZIQ is only available through a restricted program called the PALYNZIQ REMS. The goal of the REMS is to mitigate the risk of anaphylaxis associated with PALYNZIQ by:

- Ensuring that prescribers are educated on the risk of anaphylaxis associated with the use of PALYNZIQ
- Ensuring that prescribers are educated and adhere to the following:
 - Counsel patients on how to recognize and respond to signs and symptoms of anaphylaxis
 - Enroll patients in the PALYNZIQ REMS
 - Prescribe auto-injectable epinephrine with PALYNZIQ
- Ensuring that PALYNZIQ is only dispensed to patients with documentation of safe use conditions including:
 - Patient education and enrollment
 - Having auto-injectable epinephrine available at all times
- Ensuring that patients are educated on the following:
 - How to recognize and respond to signs and symptoms of anaphylaxis
 - The need to carry auto-injectable epinephrine with them at all times

Risk Evaluation and Mitigation Strategy

PALYNZIQ REMS Overview for Prescribers

- PALYNZIQ is only available through a restricted program called the PALYNZIQ REMS
- Prescribers must be certified in the PALYNZIQ REMS and comply with the REMS requirements to prescribe PALYNZIQ
- All PALYNZIQ patients must be enrolled in the PALYNZIQ REMS to receive PALYNZIQ
- Prescribers must educate and counsel patients on the risks of PALYNZIQ, including the risk of anaphylaxis
- Prescribers must prescribe auto-injectable epinephrine and counsel patients on the need to carry auto-injectable epinephrine at all times



Prescriber Responsibilities

Prescribers must complete the following steps in the PALYNZIQ REMS

To prescribe PALYNZIQ:

- 1** Become certified by completing a one-time certification process
- 2** As you start patients on PALYNZIQ, counsel and enroll them into the PALYNZIQ REMS, prescribe PALYNZIQ and prescribe auto-injectable epinephrine
- 3** Report any anaphylaxis episodes to the PALYNZIQ REMS

How Does a Prescriber Become Certified in the PALYNZIQ REMS?

Before prescribing PALYNZIQ:

- Read the **PALYNZIQ Prescribing Information, REMS Program Overview**, and this guide to understand the PALYNZIQ REMS and the risk of anaphylaxis associated with PALYNZIQ treatment
- Complete and submit the **Prescriber Knowledge Assessment and Prescriber Enrollment Form**
- Once completed, the PALYNZIQ REMS will contact you within two business days to confirm your enrollment and certification in the PALYNZIQ REMS

Before starting each patient on PALYNZIQ:

- Assess the patient's need for an adult observer (An observer is an adult who can be present with the patient during and for at least 60 minutes after PALYNZIQ administration and is able to recognize signs and symptoms of anaphylaxis, administer auto-injectable epinephrine as required, and call for emergency medical support)
- Counsel your patient about the risk of anaphylaxis associated with PALYNZIQ treatment and about the PALYNZIQ REMS
 - Advise all patients that PALYNZIQ is only available through a restricted program called the PALYNZIQ REMS
 - Review the **Patient Guide: What You Need to Know**, **Wallet Card**, and **Safety Video** with each patient
 - Provide each patient with the **Patient Guide: What You Need to Know** and the **Wallet Card**, and **direct the patient to PALYNZIQREMS.com to view the Safety Video**
- Enroll all patients into the PALYNZIQ REMS
 - Confirm the patient agrees to comply with the PALYNZIQ REMS requirements and has signed the form where indicated
 - Submit a completed **Patient Enrollment Form** for each patient,

provide a copy of the form to the patient, and store a copy in the patient's records. Your patient can expect to be contacted by the PALYNZIQ REMS

- Provide a prescription for auto-injectable epinephrine to accompany the prescription for PALYNZIQ
- Educate the patient on when and how to use auto-injectable epinephrine and the need to carry it with them at all times

During treatment, before each prescription:

- Assess the patient for anaphylaxis episodes
- Assess the patient's supply of auto-injectable epinephrine
- Provide a prescription for auto-injectable epinephrine if the patient's supply is inadequate

At all times:

- Report anaphylaxis episodes to the PALYNZIQ REMS
- Report to the PALYNZIQ REMS if an enrolled patient is no longer under your care or has discontinued therapy

Enrollment can be completed online at PALYNZIQREMS.com; or forms can be downloaded, completed, and faxed to the PALYNZIQ REMS Fax at 1-866-713-8421 or mailed to the PALYNZIQ REMS at 200 Pinecrest Plaza, Morgantown, WV 26505

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(pegvaliase-pqpz) Injection

Additional Questions:

Please visit PALYNZIQREMS.com or call the PALYNZIQ REMS at 1-855-758-REMS (1-855-758-7367) for more information about the PALYNZIQ REMS.

Please see the Prescribing Information, including **BOXED WARNING**, for more information.

PALYNZIQ REMS Prescriber Knowledge Assessment

To become a Certified Prescriber in the PALYNZIQ® (pegvaliase-pqpz) Risk **E**valuation and **M**itigation **S**trategy (REMS), you must complete this **Prescriber Knowledge Assessment** and the **Prescriber Enrollment Form**. You must answer ALL 8 questions correctly on this assessment.

- You may complete the **Prescriber Knowledge Assessment** and **Prescriber Enrollment Form** online at PALYNZIQREMS.com.
You may also fax the completed forms to the PALYNZIQ REMS at 1-866-713-8421.
- You will receive correspondence from the PALYNZIQ REMS within 2 business days via email or fax confirming your certification in the PALYNZIQ REMS or providing instructions on how to retake your Knowledge Assessment if necessary.

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Assessment Questions

- 1** The goal of the PALYNZIQ REMS is to mitigate the risk of anaphylaxis.
- True
 - False
- 2** In order to receive PALYNZIQ, patients must enroll in the PALYNZIQ REMS.
- True
 - False
- 3** PALYNZIQ is indicated to reduce blood phenylalanine concentrations in adult patients with phenylketonuria (PKU) who have uncontrolled blood phenylalanine concentrations greater than 600 micromol/L on existing management.
- True
 - False
- 4** When is anaphylaxis more common?
- At the beginning of treatment
 - After >1 year of treatment
 - Anaphylaxis never occurs
- 5** The signs and symptoms of anaphylaxis may include:
- Syncope
 - Hypotension
 - Hypoxia, dyspnea, wheezing
 - Chest discomfort/chest tightness
 - Tachycardia
 - Angioedema (swelling of face, lips, eyes, tongue)
 - Throat tightness
 - Skin flushing
 - Rash, urticaria, pruritus
 - Gastrointestinal symptoms (vomiting, nausea, diarrhea)
 - All of the above
- 6** Prescribers may consider an observer for patients during PALYNZIQ treatment. An observer is
- An adult who enrolls in the PALYNZIQ REMS
 - An adult who is an authorized representative of the patient
 - An adult who can be present with the patient during and at least one hour after PALYNZIQ injection and is able to recognize signs and symptoms of anaphylaxis, call for emergency medical support, and administer auto-injectable epinephrine as required
- 7** Before prescribing PALYNZIQ, prescribers must read the Prescribing Information, *Prescriber Guide*, and *REMS Program Overview*, and then complete and submit the *Prescriber Enrollment Form* and *Prescriber Knowledge Assessment*.
- True
 - False
- 8** Prescribers must provide a prescription for auto-injectable epinephrine to accompany the prescription for PALYNZIQ to all patients, educate patients on when and how to use auto-injectable epinephrine, and the need to carry it with them at all times.
- True
 - False

Please provide your name and NPI number so we can associate your progress with your stakeholder record.

You can provide this information below:

PRESCRIBER INFORMATION (please print) * indicates a REQUIRED field

First Name*:

Last Name*:

National Provider Identifier (NPI)*:

Phone:

Email*:

PALYNZIQREMS.com
Phone: 1-855-758-REMS (1-855-758-7367)
Fax: 1-866-713-8421

Access this form and enroll online at [PALYNZIQREMS.com](https://www.palynziqrems.com).
To submit this form via fax, please complete all required fields and fax to PALYNZIQ REMS at 1-866-713-8421.

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PALYNZIQ

REMS Patient Guide



What You Need to Know

Enroll

Before starting PALYNZIQ® (pegvaliase-pqpz)

- 1 Discuss** with your healthcare provider and understand:
 - The risks associated with PALYNZIQ, including a severe allergic reaction (anaphylaxis)
 - The need for auto-injectable epinephrine
- 2 Receive** and **read** the:
 - **Patient Guide: What You Need to Know**
 - **Wallet Card** (fill in your name and your doctor's information)
- 3 Watch** the **Safety Video**
- 4 Complete** the **Patient Enrollment Form** with your doctor
- 5 Receive** and **fill** a prescription for auto-injectable epinephrine

During Treatment

After starting PALYNZIQ

- 1 Carry** auto-injectable epinephrine with you at all times
- 2 Inform** your doctor if you have any signs or symptoms of a severe allergic reaction (anaphylaxis) after receiving PALYNZIQ and if you need more auto-injectable epinephrine
- 3 Show** the **Wallet Card** to your doctor or emergency responder when you have any medical treatment for any condition, even if it's not for your phenylketonuria (PKU). Inform all healthcare providers you are being treated with PALYNZIQ
- 4 Notify** the PALYNZIQ REMS if you change your PALYNZIQ doctor, if your contact information changes, or if you discontinue treatment with PALYNZIQ

Patients: Your doctor will go over this **Patient Guide** and **Safety Video** with you. It is important to ask any questions you may have at any time while receiving PALYNZIQ. Keep this guide for Important Safety Information about the serious risks of PALYNZIQ:

Prescribers: Review this **Patient Guide** and **Safety Video** with your patient and provide your patient a copy to take home.

Palynziq[®]
(pegvaliase-pqpz) Injection

Table of Contents:

What is PALYNZIQ?	2
What is the most serious risk of PALYNZIQ?	2
What is the PALYNZIQ REMS?	2
How do I enroll in the PALYNZIQ REMS and what is required of me?	3
After enrolling, what are the next steps?	3

What is PALYNZIQ?

PALYNZIQ is indicated to reduce blood phenylalanine concentrations in adult patients with phenylketonuria (PKU) who have uncontrolled blood phenylalanine concentrations greater than 600 micromol/L on existing management.

What is the Most Serious Risk of PALYNZIQ?

PALYNZIQ can cause a severe allergic reaction (anaphylaxis) that may be life-threatening and can happen anytime during treatment with PALYNZIQ. You will receive your first injection of PALYNZIQ in a healthcare setting where you will be closely watched for at least 1 hour after your injection for a severe allergic reaction.

Stop injecting PALYNZIQ and call 911 or go to the closest emergency medical center if you have any of the following symptoms of a severe allergic reaction during treatment with PALYNZIQ:

- fainting (passing out)
- dizziness or lightheadedness
- sudden confusion
- trouble breathing or wheezing
- chest discomfort or chest tightness
- fast heart rate
- swelling of your face, lips, eyes, or tongue
- throat tightness
- flushed skin
- skin rash, itching, or raised bumps on skin
- nausea, vomiting, or diarrhea
- losing control of urine or stools

Your healthcare provider will prescribe auto-injectable epinephrine and will teach you (or your caregiver) and your observer (if needed) when and how to use it if you should have a severe allergic reaction. **Keep the auto-injectable epinephrine with you at all times.** Read the Patient Information that comes with the auto-injectable epinephrine that your healthcare provider prescribes for you for more information.

Your healthcare provider may recommend that an adult observer (or your caregiver) be with you when you give your PALYNZIQ injection, and for at least 1 hour after your injection to watch you for signs and symptoms of a severe allergic reaction and, if needed, give you an injection of epinephrine and call for emergency medical help.

If you have a severe allergic reaction, do not continue to take PALYNZIQ until you talk with your healthcare provider. Tell your healthcare provider that you had a severe allergic reaction. Your healthcare provider will tell you if you can continue treatment with PALYNZIQ. Your healthcare provider may prescribe other medicine to take before your PALYNZIQ injection that help reduce the symptoms of an allergic reaction. If your healthcare provider decides that you can continue treatment with PALYNZIQ after a severe allergic reaction, you will receive your next injection of PALYNZIQ in a healthcare setting where you will be closely watched for at least 1 hour after your injection for a severe allergic reaction.

What is the PALYNZIQ REMS?

A Risk Evaluation and Mitigation Strategy (REMS) is a strategy to manage known or potential serious risks associated with a drug product and is required by the Food and Drug Administration (FDA) to ensure the benefits of a drug continue to outweigh its risks.

Because of the risk of a severe allergic reaction (anaphylaxis), PALYNZIQ is only available through a restricted program called the PALYNZIQ REMS.

The PALYNZIQ REMS educates patients and doctors about the risk associated with PALYNZIQ.

Requirements of the PALYNZIQ REMS include the following:

- Understand the risk of a severe allergic reaction (anaphylaxis) associated with PALYNZIQ
- You and your doctor must be enrolled in the PALYNZIQ REMS in order to receive and prescribe PALYNZIQ
- You must fill a prescription for auto-injectable epinephrine and carry auto-injectable epinephrine with you **at all times**
- PALYNZIQ is only available from pharmacies that participate in the PALYNZIQ REMS

How Do I Enroll in the PALYNZIQ REMS, and What is Required of Me?

- 1 Discuss** with your doctor and understand:
 - The risk of a severe allergic reaction (anaphylaxis)
 - The need to carry auto-injectable epinephrine with you **at all times**
- 2 Receive and read:**
 - This *Patient Guide*
 - The *Wallet Card* (fill in your name and your doctor's information)
- 3 Watch** the [Safety Video](#)
- 4 Complete** the *Patient Enrollment Form* with your doctor
- 5 Receive and fill** a prescription for auto-injectable epinephrine before your first dose of PALYNZIQ to ensure you have it available

After Enrolling, What Are the Next Steps? How Will I Receive PALYNZIQ?

Upon enrollment:

- A representative from the PALYNZIQ REMS will contact you to get you started
- The pharmacy will call you to schedule a shipment of PALYNZIQ that will come right to your home
 - PALYNZIQ is only available from pharmacies that participate in the PALYNZIQ REMS
 - The pharmacy will verify that you have received and filled a prescription for auto-injectable epinephrine and that you and your doctor are enrolled in the PALYNZIQ REMS

After starting PALYNZIQ:

- Carry auto-injectable epinephrine with you at all times
- Inform your doctor if you have any signs or symptoms of a severe allergic reaction (anaphylaxis) after receiving PALYNZIQ and if you need more auto-injectable epinephrine (if you needed to use it or if it expired)
- Show the *Wallet Card* to your doctor or emergency responder when you have any medical treatment, even if it is not for your PKU
- Notify the PALYNZIQ REMS if you change your PALYNZIQ doctor, if your contact information changes, or if you discontinue treatment with PALYNZIQ

Palynziq[®]
(pegvaliase-pqpz) Injection

Additional Questions:

If you have any questions regarding the PALYNZIQ REMS,
visit PALYNZIQREMS.com
or call 1-855-758-REMS **(1-855-758-7367)**.

Fax: 1-866-713-8421

Mail: PALYNZIQ REMS, 200 Pinecrest Plaza, Morgantown, WV 26505-8065

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Palynziq[®]
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VISUAL NOTES	VOICE-OVER
Copy superimposed (SUPER) on screen fades in: This video is intended only to supplement your doctor's detailed instructions and in-person training.	[Upbeat music comes up and plays throughout.]
Animated introduction of PALYNZIQ logo.	If you are taking PALYNZIQ (pegvaliase-pqpz) Injection, you should know about the risks associated with your treatment. And you should also know there is a program designed to help you understand these risks.
	PALYNZIQ is a prescription medicine used to reduce blood phenylalanine concentrations

<p>The Indication comes up below the logo.</p> <p>SUPER: PALYNZIQ® (pegvaliase-pqpz) is indicated to reduce blood phenylalanine concentrations in adult patients with phenylketonuria (PKU) who have uncontrolled blood phenylalanine concentrations greater than 600 micromol/L on existing management.</p>	<p>...in adult patients with phenylketonuria (PKU) who have uncontrolled blood phenylalanine concentrations greater than 600 micromol/L on existing management.</p>
<p>Simple visual texture that mimics Blood Phe Icon.</p> <p>Typographic build of Risk Evaluation and Mitigation Strategy, which then simplifies down to PALYNZIQ REMS logo lockup.</p>	<p>PALYNZIQ is only available through a restricted program called...</p>
	<p>...the PALYNZIQ Risk Evaluation and Mitigation Strategy (REMS) Program...</p>
	<p>...This program makes sure you know about treatment risks</p>

Shapes start to transition off screen.	...and how to manage them.
Shapes continue to transition off screen.	
Shapes resolve into next scene.	
Animated icons of doctor and patient appear.	The PALYNZIQ REMS Program...
Doctor and patient speech bubbles appear to indicate they're talking.	...educates patients and doctors about the risks associated with PALYNZIQ. Also, PALYNZIQ is available only from pharmacies that participate in the PALYNZIQ REMS Program.
Shapes transition.	
Doctor and patient icons talk with each other, with the text "Anaphylaxis" in the bubble between them.	The most important risk of PALYNZIQ is a severe allergic reaction called anaphylaxis, that may be life threatening.

Transitional element begins to reveal form of auto-injectable epinephrine.	
Auto-injectable epinephrine appears and text bubble of “Auto-Injectable Epinephrine” appears above.	That is why your doctor will also prescribe auto-injectable epinephrine and teach you how and when to use it.
Shapes transition to iPad/tablet.	You may experience anaphylaxis soon after you inject a dose of PALYNZIQ...
“Symptoms include” bubble appears and body diagram appears on screen.	...and it can occur at any time during your treatment with PALYNZIQ. Common symptoms include:
Tablet rotates to landscape view.	
Areas highlight as voice-over calls out symptoms.	<ul style="list-style-type: none"> • Fainting (passing out) • Dizziness or lightheadedness • Sudden confusion • Trouble breathing or wheezing • Chest discomfort or chest tightness • Fast heart rate

<p>Areas highlight as voice-over calls out symptoms.</p>	<ul style="list-style-type: none"> • Swelling of your face, lips, eyes, or tongue • Throat tightness • Flushed skin • Skin rash, itching, or raised, bumps on skin • Nausea, vomiting, or diarrhea • Losing control of urine or stools
<p>Scene transitions to show patient in natural setting.</p>	<p>If you experience any of these symptoms...</p>
<p>Danger icon appears.</p>	<p>...stop taking PALYNZIQ...</p>
<p>Bevel of iPad/Tablet deforms, and shapes resolve to next scene.</p>	
<p>Shapes transition to patient swiping up and pushing e-contact button.</p>	<p>...and call 911...</p>
<p>Shapes transition.</p>	
<p>Shapes transition to an E.R. entrance.</p>	<p>...or go to the closest emergency room.</p>

<p>Shapes transition into the next scene.</p>	
<p>One of the cloud shapes transforms into auto-injectable epinephrine.</p>	<p>Use auto-injectable epinephrine as directed by your doctor.</p>
<p>Shapes transition to doctor and patient, with questions appearing in the bubble above them as called out by voice-over.</p>	<p>If you have any questions about...</p>
	<p>...PALYNZIQ...</p>
	<p>...or what to do if you have had a severe allergic reaction...</p>

	...anaphylaxis, reach out to your doctor.
Shapes resolve to show a doctor with a bubble that says "Prescription" above him. Next to him, a simple prescription pad builds.	Before receiving a PALYNZIQ prescription, you and your doctor will discuss the risk of anaphylaxis, and the need to carry auto-injectable epinephrine with you at all times. Your doctor will give you a prescription for auto-injectable epinephrine that you need to have filled.
The prescription pad transforms into the patient guide, with a "Patient guide" text bubble above.	You need to read the Patient Guide. It will tell you more about PALYNZIQ and about the most serious risks associated with it.
Shapes transition.	You will also learn more about what to expect when enrolled in the PALYNZIQ REMS Program.
Enrollment form builds onto screen.	Then you and your doctor will...
Doctor and patient sign the form.	...complete and sign the enrollment form.
Circular shapes transition to next environment.	

	which your doctor...
Enrollment form morphs into a paper airplane.	...will send to the REMS Program Coordinating Center and give you a copy to take home.
The paper airplane files into mailbox...	
...And morphs into phone	
Shapes form into a phone with the PALYNZIQ REMS calling.	A representative from the PALYNZIQ REMS will contact you to get you started.
Shapes resolve into a simple pharmacy icon	A pharmacy that participates in the PALYNZIQ REMS Program will schedule a shipment of your medicine right to your home.
Shapes transition	The pharmacy will verify that you have filled your prescription for auto-injectable epinephrine, and that you and your doctor are enrolled in the PALYNZIQ REMS Program.
Shapes assemble to form a delivery truck.	...and then send you your PALYNZIQ medicine.

Graphic treatment connecting delivery to patient.	
Background shapes transition to next scene.	
Wallet card icon resolves into frame.	You will also receive a wallet card that describes symptoms that you (or your caregiver), or your observer, should know that will require you to go to the emergency room right away.
Wallet card comes up, and the card appears above it.	Carry this card with you at all times during treatment with PALYNZIQ. Show this card to all of your doctors even if they are not your phenylketonuria (PKU) doctor.
The card slides downward into the wallet.	
Shield icon locks card into place.	
The patient grabs the wallet and card to end the animation.	
PALYNZIQ REMS logo animates back on. SUPER: 1-855-758 REMS (855-758-7367) PALYNZIQREMS.com	You can learn more about the PALYNZIQ REMS Program by calling 1-855-7-5-8 R-E-M-S or visiting PALYNZIQREMS.com .

SUPER: BioMarin Logo

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Thank you for watching this video.

- This patient has been prescribed PALYNZIQ for the treatment of phenylketonuria (PKU). Anaphylaxis has occurred in some patients during treatment with PALYNZIQ.**
- If this patient experienced anaphylaxis or an anaphylactic like reaction, please contact the prescribing physician as soon as possible
 - For more information about PALYNZIQ, please see the prescribing information, including BOXED WARNING, at PALYNZIQREMS.com
 - Please report any adverse events to the PALYNZIQ REMS at 1-855-758-REMS (1-855-758-7367)

PALYNZIQ Patient Wallet Card

Emergency Contact Information:

Patient's Name

PALYNZIQ Doctor's Name

PALYNZIQ Doctor's Phone Number
Reference ID: 4681560

Carry this card with you at all times. SHOW THIS CARD to all of your doctors or emergency responders involved in your medical treatment, even if it is not for your phenylketonuria (PKU).

Palynziq
(pegvalase-pqpz) Injection

PALYNZIQ® (pegvaliase-pqpz) may cause a severe allergic reaction (anaphylaxis) that may be life-threatening. You may experience a severe allergic reaction (anaphylaxis) right after you inject a dose of PALYNZIQ or at any time after you inject PALYNZIQ.

Stop injecting PALYNZIQ and call 911 or go to the closest emergency medical center if you have any of the following signs or symptoms:

- fainting (passing out)
- dizziness or lightheadedness
- sudden confusion
- trouble breathing or wheezing
- chest discomfort or chest tightness
- fast heart rate
- swelling of your face, lips, eyes, or tongue
- throat tightness
- flushed skin
- skin rash, itching, or raised bumps on skin
- nausea, vomiting, or diarrhea
- losing control of urine or stools

Use auto-injectable epinephrine as directed by your doctor.

Palynziq REMS Program Overview

Risk Evaluation and Mitigation Strategy

This overview describes the requirements of the PALYNZIQ® (pegvaliase-pqpz) REMS and the responsibilities of prescribers, pharmacies, and patients.

If you have any questions regarding the PALYNZIQ REMS, please visit PALYNZIQREMS.com or call 1-855-758-REMS (1-855-758-7367).

Please see Prescribing Information, including **BOXED WARNING**, for additional Important Safety Information

Palynziq[®]
(pegvaliase-pqpz) Injection

Table of Contents

What is the PALYNZIQ REMS?	1
How Does the PALYNZIQ REMS Work?	2
What are the Requirements of the PALYNZIQ REMS?	2
– Prescriber	3
– Pharmacy	3
– Patient	4
PALYNZIQ REMS Resources	4

What is the PALYNZIQ REMS?

- A Risk Evaluation and Mitigation Strategy (REMS) is a strategy to manage known or potential serious risks associated with a drug product and is required by the Food and Drug Administration (FDA) to ensure the benefits of a drug continue to outweigh its risks.
- **Due to the risk of anaphylaxis, PALYNZIQ is available only through a restricted program called the PALYNZIQ REMS.**

PALYNZIQ may cause anaphylaxis; patients may experience an anaphylaxis episode immediately or at any time after an injection of PALYNZIQ. Episodes of anaphylaxis are more common at the beginning of treatment, but they can also occur anytime during treatment.

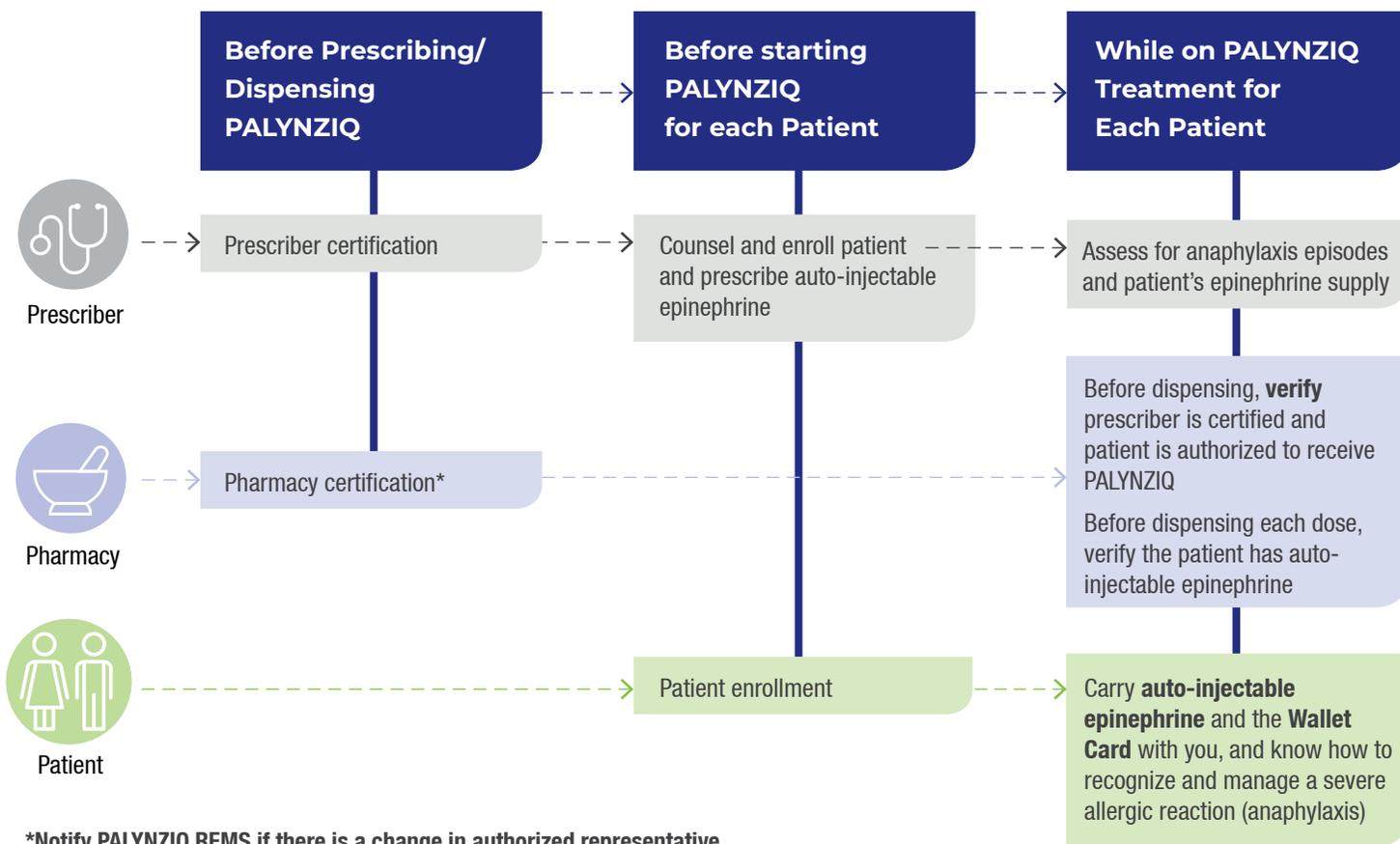
Anaphylaxis can be life-threatening and can occur quickly; inform your patients of the signs and symptoms, the appropriate use (when and how to use) auto-injectable epinephrine, and when to seek immediate medical care.

Anaphylaxis has been reported in patients who have used PALYNZIQ. The signs and symptoms of anaphylaxis may include:

- Syncope, hypotension
- Hypoxia, dyspnea, wheezing
- Chest discomfort/chest tightness
- Tachycardia
- Angioedema (swelling of the face, lips, eyes, tongue)
- Throat tightness
- Skin flushing
- Rash, urticaria, pruritus
- Gastrointestinal symptoms (vomiting, nausea, diarrhea)

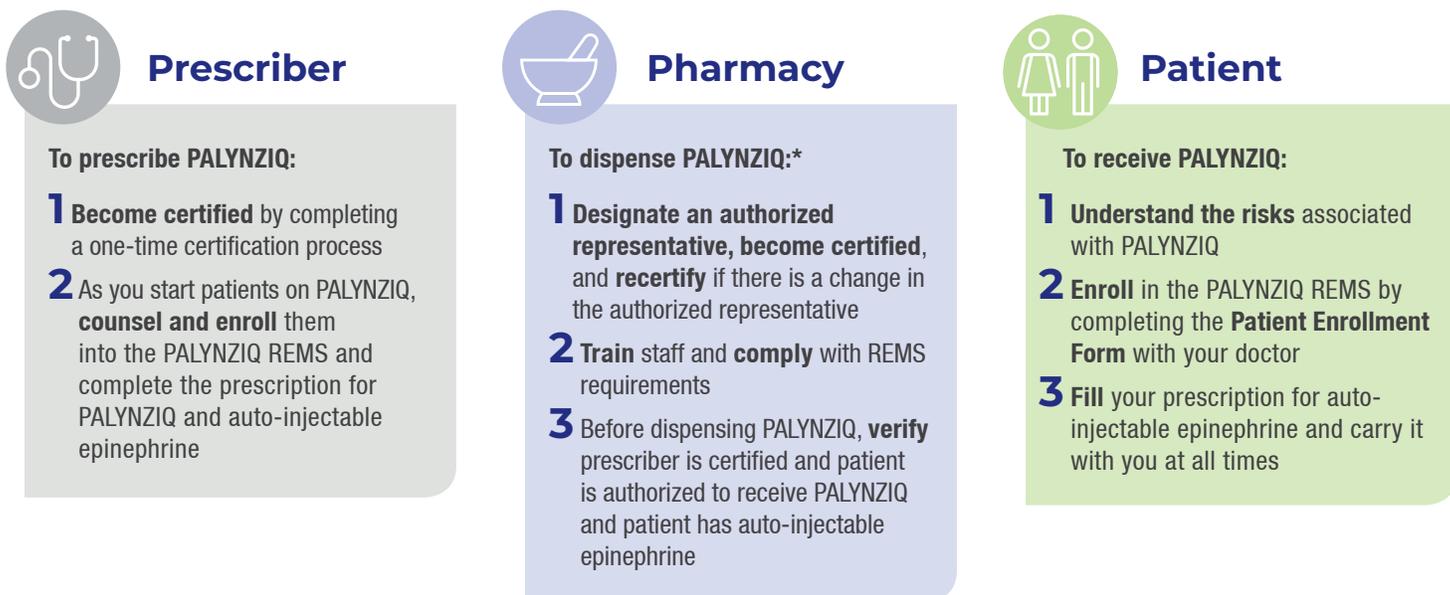
Palynziq[®]
(pegvaliase-pqpz) Injection

How Does the PALYNZIQ REMS Work?



What are the Requirements of the PALYNZIQ REMS?

In order to receive PALYNZIQ, prescribers, pharmacies, and patients must comply with the requirements of the PALYNZIQ REMS.



*PALYNZIQ is not available to all pharmacies. If you have any questions about the PALYNZIQ REMS or how to obtain PALYNZIQ, call 1-855-758-REMS (1-855-758-7367).



Prescriber Requirements

Become Certified (One-time)

Before prescribing PALYNZIQ

1 Review the following educational materials on PALYNZIQ to understand the risks of anaphylaxis and the need for auto-injectable epinephrine, and the PALYNZIQ REMS:

- Prescribing Information
- Prescriber Guide
- REMS Program Overview

2 Complete and submit using the submission details at the end of this document:

- Prescriber Knowledge Assessment
- Prescriber Enrollment Form

3 Once completed, the PALYNZIQ REMS will notify you that you are certified to prescribe PALYNZIQ

Enroll Your Patients

Before starting each patient on PALYNZIQ

1 Counsel your patient about the risks associated with PALYNZIQ, including anaphylaxis and the need for auto-injectable epinephrine and share the resources below:

- Patient Guide: What You Need to Know
- Safety Video
- Wallet Card

2 Submit a completed Patient Enrollment Form to the PALYNZIQ REMS. Provide a completed copy of the form to the patient and retain a copy in the patient's records

3 Prescribe auto-injectable epinephrine and instruct the patient on when and how to use it

4 Assess the patient's need for an adult observer and premedications as described in the Prescriber Guide

At All Times

Once your patient is on PALYNZIQ

1 Report any anaphylaxis episodes to the PALYNZIQ REMS. You will be contacted for more information about these episodes

2 Assess the patient's supply of auto-injectable epinephrine and provide the patient with a prescription for auto-injectable epinephrine refills as necessary

3 Inform the PALYNZIQ REMS if a patient is no longer under your care or has discontinued PALYNZIQ

The completed forms should be submitted to the PALYNZIQ REMS online, using the PALYNZIQ REMS Portal at PALYNZIQREMS.com, via fax to 1-866-713-8421, or by mail to 200 Pinecrest Plaza, Morgantown WV 26505.



Pharmacy Requirements

Become Certified

Before dispensing PALYNZIQ for the first time:

1 Designate an authorized representative for the pharmacy. He or she will need to review the *REMS Program Overview* and will oversee implementation and ensure compliance with the PALYNZIQ REMS requirements

2 Have the authorized representative complete and submit the Pharmacy Enrollment Form by fax

- Once this step is completed, the PALYNZIQ REMS will contact you to complete certification
- Dispensing of PALYNZIQ is limited to a small number of contracted pharmacies that will be certified

3 Have the authorized representative ensure that all relevant staff involved in dispensing of PALYNZIQ are trained on the PALYNZIQ REMS requirements and that a record of training is maintained by the pharmacy

Ensure Compliance with REMS Requirements

When dispensing PALYNZIQ:

1 Before dispensing PALYNZIQ, **verify** that the prescriber is certified and the patient is authorized to receive PALYNZIQ by accessing the PALYNZIQ REMS Portal or by calling the PALYNZIQ REMS

2 Confirm and **document** that patient has auto-injectable epinephrine

3 Report any anaphylaxis episodes to the PALYNZIQ REMS. You may be contacted for more information about these episodes

4 Maintain appropriate documentation that all processes and procedures are in place and are being followed so that it can be provided upon request to BioMarin or a third party acting on behalf of BioMarin

5 Recertify in the PALYNZIQ REMS if a new authorized representative is designated by completing and submitting the Pharmacy Enrollment Form

*PALYNZIQ is not available to all pharmacies. If you have questions about the PALYNZIQ REMS or how to obtain PALYNZIQ, call 1-855-758-REMS (1-855-758-7367).



Patient Requirements

Enroll

Before starting PALYNZIQ:

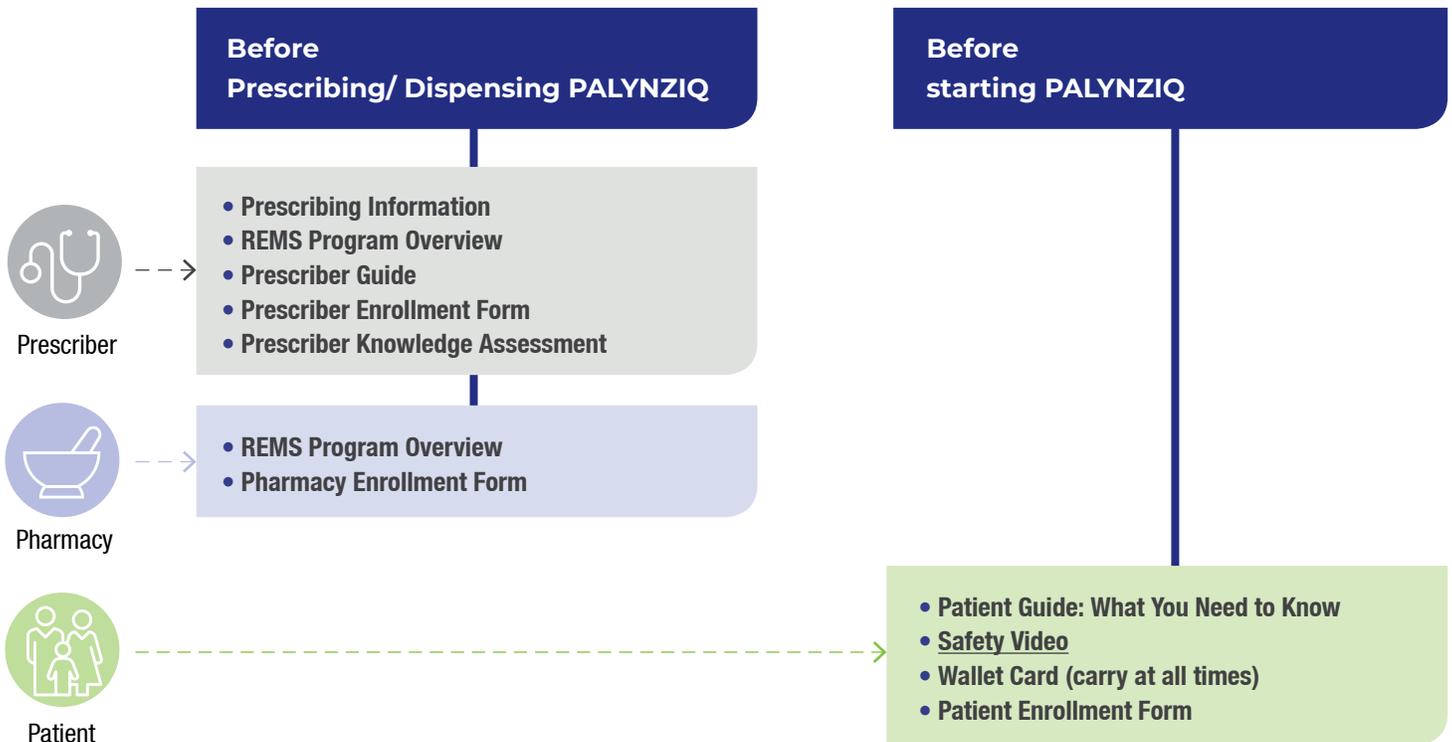
- 1 Discuss** with your doctor and understand:
 - The risks associated with PALYNZIQ, including anaphylaxis
 - The need for (including how and when to use) an auto-injectable epinephrine
- 2 Receive** and **read** the:
 - **Patient Guide: What You Need to Know**
 - **Wallet Card** (fill in your name and your doctor's information)
- 3 Watch** the **Safety Video**
- 4 Complete** the **Patient Enrollment Form** with your doctor
- 5 Receive** and **fill** a prescription for auto-injectable epinephrine

During treatment

After starting PALYNZIQ:

- 1 Carry** auto-injectable **epinephrine** with you at all times
- 2 Inform your healthcare providers** if you have any signs or symptoms of a severe allergic reaction (anaphylaxis) after receiving PALYNZIQ and if you need more auto-injectable epinephrine
- 3 Show** the **Wallet Card** to your doctor or emergency responder when you have any medical treatment for any condition, even if it's not for your phenylketonuria (PKU). Inform all doctors you are being treated with PALYNZIQ
- 4 Notify** the PALYNZIQ REMS if you **change your PALYNZIQ doctors** if your **contact information changes**, or if you **discontinue treatment with PALYNZIQ**

PALYNZIQ REMS Resources



PALYNZIQ is indicated to reduce blood phenylalanine concentrations in adult patients with phenylketonuria (PKU) who have uncontrolled blood phenylalanine concentrations greater than 600 micromol/L on existing management.

Please see the Medication Guide and Prescribing Information, including **BOXED WARNING**, for more information.

PALYNZIQ REMS Portal Overview

PALYNZIQREMS.com

- PALYNZIQ REMS Portal is a web-based tool designed to:
 - Provide real-time access to PALYNZIQ REMS patient, prescriber, and pharmacy information
 - Maintain compliance with the PALYNZIQ REMS
- PALYNZIQ REMS Portal allows prescribers to instantly certify themselves, enroll patients, and manage their patients online
- PALYNZIQ REMS Portal is accessed with secure username and password provided upon registration

Additional questions:

Please visit PALYNZIQREMS.com or call the PALYNZIQ REMS at 1-855-758-REMS (1-855-758-7367) for more information about the PALYNZIQ REMS.

Please see the Medication Guide and Prescribing Information, including **BOXED WARNING**, for more information.

PALYNZIQREMS.com

Phone: 1-855-758-REMS (1-855-758-7367) Fax: 1-866-713-8421

Mail: PALYNZIQ REMS, 200 Pinecrest Plaza, Morgantown WV 26505

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Palynziq[®]
(pegvaliase-pqpz) Injection

Welcome to the

PALYNZIQ REMS (Risk Evaluation and Mitigation Strategy) Program

A REMS is a strategy to manage known or potential serious risks associated with a drug product and is required by the Food and Drug Administration (FDA) to ensure the benefits of a drug outweigh its risks. Due to the risk of anaphylaxis, PALYNZIQ[®] (pegvaliase-pqpz) is only available through a restricted program called the PALYNZIQ REMS.

The goal of the REMS is to mitigate the risk of anaphylaxis associated with PALYNZIQ by:

- Ensuring prescribers are educated on the risk of anaphylaxis associated with the use of PALYNZIQ
- Ensuring that prescribers are educated and adhere to the following:
 - Counsel patients on how to recognize and respond to signs and symptoms of anaphylaxis
 - Enroll patients in the PALYNZIQ REMS
 - Prescribe auto-injectable epinephrine with PALYNZIQ
- Ensuring that PALYNZIQ is only dispensed to patients with documentation of safe use conditions:
 - Patient education and enrollment in the PALYNZIQ REMS
 - Having auto-injectable epinephrine available at all times
- Ensuring that patients are educated on the following:
 - How to recognize and respond to signs and symptoms of anaphylaxis
 - The need to carry auto-injectable epinephrine with them at all times

PALYNZIQ REMS Overview

- PALYNZIQ is only available through a restricted distribution program called PALYNZIQ REMS
- Prescribers must be certified in the PALYNZIQ REMS and comply with the REMS requirements to prescribe PALYNZIQ
- All PALYNZIQ patients must enroll in the PALYNZIQ REMS to receive PALYNZIQ
- Prescribers must educate and counsel patients on the risks of PALYNZIQ, including the risk of anaphylaxis
- Prescribers must counsel patients on the need to carry auto-injectable epinephrine with them at all times
- Pharmacies must be certified in the PALYNZIQ REMS to dispense PALYNZIQ
- Pharmacies must verify that PALYNZIQ is only dispensed to patients with documentation of safe use conditions

PALYNZIQ is not available to all pharmacies. If you have any questions about the PALYNZIQ REMS or need help enrolling, call 1-855-758-REMS (1-855-758-7367), Monday to Friday, 8:00 am to 8:00 pm (ET).

Indications

PALYNZIQ is indicated to reduce blood phenylalanine concentrations in adult patients with phenylketonuria (PKU) who have uncontrolled blood phenylalanine concentrations greater than 600 micromol/L on existing management.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

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Reference ID: 4681560

Prescribers

The goal of the PALYNZIQ REMS is to mitigate the risk of anaphylaxis associated with PALYNZIQ by:

- Ensuring prescribers are educated on the risk of anaphylaxis associated with the use of PALYNZIQ
- Ensuring that prescribers are educated and adhere to the following:
 - Counsel patients on how to recognize and respond to signs and symptoms of anaphylaxis
 - Enroll patients in the PALYNZIQ REMS
 - Prescribe auto-injectable epinephrine with PALYNZIQ
- Ensuring that PALYNZIQ is only dispensed to patients with documentation of safe use conditions:
 - Patient education and enrollment in the PALYNZIQ REMS
 - Having auto-injectable epinephrine available at all times
- Ensuring that patients are educated on the following:
 - How to recognize and respond to signs and symptoms of anaphylaxis
 - The need to carry auto-injectable epinephrine with them at all times

Only a limited number of certified pharmacies will dispense PALYNZIQ. Please contact the PALYNZIQ REMS for a list of certified pharmacies.

To become certified to prescribe PALYNZIQ, prescribers must:

- Read the PALYNZIQ Prescribing Information (PI), *REMS Program Overview*, and the *Prescriber Guide*
- Enroll in the PALYNZIQ REMS by completing and submitting the *Prescriber Knowledge Assessment* and the *Prescriber Enrollment Form*:
 - Enroll online here
 - By fax at 1-866-713-8421
 - By mail at PALYNZIQ REMS, 200 Pinecrest Plaza, Morgantown, WV 26505-8065
- Receive an enrollment confirmation from the PALYNZIQ REMS verifying that enrollment has been completed

Before Treatment Initiation

- Assess the patient's need for an adult observer and for premedication as described in the Prescriber Guide
- Counsel the patient on the risk of anaphylaxis including how to recognize and respond to anaphylaxis using the *Patient Guide*, *Safety Video*, and *Wallet Card*
- Provide the patient with the *Patient Guide*, *Wallet Card*, and the link to access the *Safety Video*
- Enroll the patient in the PALYNZIQ REMS by completing and submitting the *Patient Enrollment Form*. Provide a completed copy of the form to the patient and retain a completed copy in the patient's record:
 - Enroll online here
 - By fax at 1-866-713-8421
- Provide the patient with a prescription for auto-injectable epinephrine to accompany the prescription for PALYNZIQ
- Educate the patient on when and how to use auto-injectable epinephrine and the need to carry it with them at all times

During Treatment, Before Each Prescription

- Assess the patient for anaphylaxis episodes
- Assess the patient's supply of auto-injectable epinephrine
- Provide a prescription for auto-injectable epinephrine if the patient's supply is inadequate

At All Times

- Report anaphylaxis episodes to the PALYNZIQ REMS
- Report treatment discontinuation or transfer of care to the PALYNZIQ REMS

Report anaphylaxis episodes to the PALYNZIQ REMS. Report if an enrolled patient is no longer under your care or has discontinued therapy to the PALYNZIQ REMS at 1-855-758-REMS (1-855-758-7367).

PDFs for Download

Materials for Healthcare Providers

- Prescriber Guide
- REMS Program Overview
- Prescriber Enrollment Form
- Prescriber Knowledge Assessment



Spanish Materials for Healthcare Providers

- Spanish Prescriber Guide
- Spanish REMS Program Overview
- Spanish Prescriber Enrollment Form
- Spanish Prescriber Knowledge Assessment

Materials for Patients

- Patient Enrollment Form
- Patient Guide: What You Need to Know
- Wallet Card
- Safety Video



Spanish Materials for Patients

- Spanish Patient Enrollment Form
- Spanish Patient Guide: What You Need to Know
- Spanish Wallet Card
- Spanish Safety Video

Pharmacies

PALYNZIQ is available only through the PALYNZIQ REMS. Only prescribers, patients, and a limited network of certified pharmacies enrolled are able to prescribe, receive, and dispense PALYNZIQ. If you have questions, please contact the PALYNZIQ REMS at 1-855-758-REMS (1-855-758-7367).

To become certified to dispense PALYNZIQ, pharmacies must:

- Designate an authorized representative to carry out the certification process and oversee implementation and compliance with the PALYNZIQ REMS on behalf of the pharmacy
- Have the authorized representative review the **REMS Program Overview**
- Have the authorized representative enroll in the PALYNZIQ REMS by completing and submitting the **Pharmacy Enrollment Form**
- Establish processes and procedures to verify and document the patient has auto-injectable epinephrine and report anaphylaxis episodes to the PALYNZIQ REMS/manufacturer/prescriber
- Train all relevant staff involved in the dispensing of PALYNZIQ on the program requirements using the **REMS Program Overview**

Before Dispensing:

- Verify and document that the patient has auto-injectable epinephrine through the processes and procedures established as a requirement of the PALYNZIQ REMS
- Obtain authorization to dispense each prescription by contacting the PALYNZIQ REMS to verify prescriber certification and patient enrollment

To Maintain Certification to Dispense:

- Have the new authorized representative enroll in the PALYNZIQ REMS by completing the **Pharmacy Enrollment Form** if the authorized representative changes

At All Times:

- Report anaphylaxis episodes to the PALYNZIQ REMS
- Do not distribute, transfer, loan, or sell PALYNZIQ except to certified dispensers
- Maintain records documenting staff's completion of REMS training and that all processes and procedures are in place and are being followed
- Comply with audits carried out by BioMarin or a third party acting on behalf of BioMarin to ensure that all processes and procedures are in place and are being followed

For information on 340B, contact the PALYNZIQ REMS at 1-855-758-7367.

PDFs for Download

Materials for Pharmacies

[REMS Program Overview](#)

[Pharmacy Enrollment Form](#)

Spanish Materials for Pharmacies

[Spanish REMS Program Overview](#)

[Spanish Pharmacy Enrollment Form](#)



Patients



PATIENT SAFETY VIDEO:
Patient must watch the SAFETY VIDEO before enrollment.

Requirements for receiving treatment with PALYNZIQ:

- Discuss the following with your doctor and make sure you understand:
 - The risks of PALYNZIQ, including severe allergic reaction (anaphylaxis)
 - The need to carry auto-injectable epinephrine with you at all times and when and how to use it
- Receive and read the *Patient Guide: What You Need To Know* and *Wallet Card* and view the *Safety Video*
 - The *Patient Guide: What You Need To Know* is your comprehensive guide to understanding treatment with PALYNZIQ
 - The *Wallet Card*, which is provided for you to carry during treatment, should be shared with your doctors or emergency responder
 - The *Safety Video* can be viewed to show you how to recognize and respond to signs and symptoms of a severe allergic reaction (anaphylaxis)
- Complete the *Patient Enrollment Form* with your doctor who will provide you with a copy of this form. You can expect to be contacted by the PALYNZIQ REMS
- Fill your prescription for auto-injectable epinephrine before your first dose to ensure that you have it available
 - Inform your doctor if you need more auto-injectable epinephrine if you needed to use it or if it becomes expired

It is important to tell your doctor if you have a severe allergic reaction (anaphylaxis). Carry the **Wallet Card and **auto-injectable epinephrine** with you at all times.**

Inform all doctors you are receiving PALYNZIQ.

Contact the PALYNZIQ REMS if you change doctors, if your contact information changes, or if you stop taking PALYNZIQ.

PDFs for Download

Materials for Patients

- [Patient Guide: What You Need to Know](#)
- [Wallet Card](#)
- [Safety Video](#)
- [Medication Guide](#)

Spanish Materials for Patients

- [Spanish Patient Guide: What You Need to Know](#)
- [Spanish Wallet Card](#)
- [Spanish Safety Video](#)
- [Spanish Medication Guide](#)



[HOME](#)

[PRESCRIBERS](#)

[PHARMACIES](#)

[PATIENTS](#)

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Contact Us

Phone

1-855-758-REMS
(1-855-758-7367)

Fax

1-866-713-8421

Hours of Operation

Monday - Friday
8:00 AM-8:00 PM
Eastern



To learn more about the serious risks associated with PALYNZIQ, please refer to the [Prescribing Information](#) including [Boxed Warning](#), [Medication Guide](#), [Prescriber Guide](#), [Patient Guide: What You Need to Know](#), and [REMS Program Overview](#).

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

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Login

Login

Your username was supplied to you via email when you registered. If you need assistance, please call 1-855-758-REMS (1-855-758-7367).

Please enter your username

[LOGIN](#)

OR

Do not have an online account?

Prescriber Registration

To create your prescriber web account for the PALYNZIQ REMS, please complete the fields below.

* NPI

[CONTINUE](#)

*Note online registration is for prescribers only. Pharmacy users must submit enrollment via fax and will receive username via email.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

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/s/

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