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 PALYNIZQ 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 H_1-receptor antagonist, H_2-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

Risk
Evaluation and
Mitigation
Strategy

- 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

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

Palynziq®
(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.

BIOMARIN®

Palynziq®
(pegvaliase-pqpz) Injection