INDICATION

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

BOXED WARNING: RISK OF ANAPHYLAXIS

- **Anaphylaxis has been reported after administration of PALYNZIQ and may occur at any time during treatment**
- **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 injection. Prior to self-injection, confirm patient competency with self-administration, and patient's and observer's (if applicable) ability to recognize signs and symptoms of anaphylaxis and to administer auto-injectable epinephrine, if needed**
- **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 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**
- **Prescribe auto-injectable epinephrine. Prior to the first dose, instruct the patient and observer (if applicable) on its appropriate use. Instruct the patient to seek immediate medical care upon its use. Instruct patients to carry auto-injectable epinephrine with them at all times during PALYNZIQ treatment**
- **PALYNZIQ is available only through a restricted program called PALYNZIQ REMS (Risk Evaluation and Mitigation Strategy). Further information, including a list of qualified pharmacies, is available at www.PALYNZIQREMS.com or by telephone at 1-855-758-REMS (1-855-758-7367)**

WARNINGS AND PRECAUTIONS

Anaphylaxis

- Signs and symptoms of anaphylaxis reported 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, and gastrointestinal symptoms (vomiting, nausea, diarrhea)
- Anaphylaxis generally occurred within 1 hour after injection; however, delayed episodes occurred up to 48 hours after PALYNZIQ administration
- 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 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
- 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 observer (if applicable) on how 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
- Consider the risks and benefits of readministering PALYNZIQ following an episode of anaphylaxis. If the decision is made to readminister PALYNZIQ, administer the first dose under the supervision of a healthcare provider equipped to manage anaphylaxis and closely observe the patient for at least 60 minutes following the dose. Subsequent PALYNZIQ dose titration should be based on patient tolerability and therapeutic response
- Consider premedication with an H_1-receptor antagonist, H_2-receptor antagonist, and/or antipyretic prior to PALYNZIQ administration based upon individual patient tolerability

Other Hypersensitivity Reactions

- Hypersensitivity reactions other than anaphylaxis have been reported in 204 of 285 (72%) patients treated with PALYNZIQ in clinical trials
- Management of hypersensitivity reactions should be based on the severity of the reaction, recurrence of the reaction, and the clinical judgment of the healthcare provider, and may include dosage adjustment, temporary drug interruption, or treatment with antihistamines, antipyretics, and/or corticosteroids

ADVERSE REACTIONS

- The most common adverse reactions (at least 20% of patients in either treatment phase) were injection site reactions, arthralgia, hypersensitivity reactions, headache, generalized skin reactions lasting at least 14 days, nausea, abdominal pain, vomiting, cough, oropharyngeal pain, pruritus, diarrhea, nasal congestion, fatigue, dizziness, and anxiety
- Of the 285 patients exposed to PALYNZIQ in an induction/titration/maintenance regimen in clinical trials, 44 (15%) patients discontinued treatment due to adverse reactions. The most common adverse reactions leading to treatment discontinuation were hypersensitivity reactions (6% of patients) including anaphylaxis (3% of patients), angioedema (1% of patients), arthralgia (4% of patients), generalized skin reactions lasting at least 14 days (2% of patients), and injection site reactions (1% of patients)
- The most common adverse reactions leading to dosage reduction were arthralgia (15% of patients), hypersensitivity reactions (9% of patients), injection site reactions (4% of patients), alopecia (3% of patients), and generalized skin reactions lasting at least 14 days (2% of patients)
- The most common adverse reactions leading to temporary drug interruption were hypersensitivity reactions (14% of patients), arthralgia (13% of patients), anaphylaxis (4% of patients), and injection site reactions (4% of patients)
- Angioedema and serum sickness: In clinical trials, 22 out of 285 (8%) patients experienced 45 episodes of angioedema (symptoms included: pharyngeal edema, swollen tongue, lip swelling, mouth swelling, eyelid edema, and face edema) occurring independent of anaphylaxis. In clinical trials, serum sickness was reported in 7 out of 285 (2%) patients

Blood Phenylalanine Monitoring and Diet

- Obtain blood Phe concentrations every 4 weeks until a maintenance dosage is established. Periodically monitor blood Phe concentrations during maintenance therapy
- Counsel patients to monitor dietary protein and Phe intake, and adjust as directed by their healthcare provider

DRUG INTERACTIONS

Effect of PALYNZIQ on Other PEGylated Products

- In a single-dose study of PALYNZIQ in adult patients with PKU, two patients receiving concomitant injections of medroxyprogesterone acetate suspension (a formulation containing PEG 3350) experienced a hypersensitivity reaction. One of the two patients experienced anaphylaxis
- The clinical effects of concomitant treatment with different PEGylated products are unknown. Monitor patients treated with PALYNZIQ and concomitantly with other PEGylated products for hypersensitivity reactions including anaphylaxis

USE IN SPECIFIC POPULATIONS

Pregnancy and Lactation

- PALYNZIQ may cause fetal harm when administered to a pregnant woman
- Advise women who are exposed to PALYNZIQ during pregnancy or who become pregnant within one month following the last dose of PALYNZIQ that there is a pregnancy surveillance program that monitors pregnancy outcomes. Healthcare providers should report PALYNZIQ exposure and encourage these patients to report their pregnancy to BioMarin (1-866-906-6100)
- Monitor blood Phe levels in breastfeeding women treated with PALYNZIQ

Pediatric Use

- The safety and effectiveness of PALYNZIQ in pediatric patients have not been established

Geriatric Use

- Clinical studies of PALYNZIQ did not include patients aged 65 years and older

You are encouraged to report suspected adverse reactions to BioMarin at 1-866-906-6100, or to the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see included full Prescribing Information, with Boxed Warning for risk of anaphylaxis, and Medication Guide.

BIOMARIN®

Palynziq® (pegvaliase-pqpz) Injection

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