

# 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:**

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#### 1. Healthcare Providers who prescribe PALYNZIQ must:

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| To become certified to prescribe         | <ol style="list-style-type: none"><li>1. Review the drug's Prescribing Information.</li><li>2. Review the following: <a href="#">Prescriber Guide</a> and <a href="#">REMS Program Overview</a>.</li><li>3. Successfully complete the <a href="#">Prescriber Knowledge Assessment</a> and submit it to the REMS program.</li><li>4. Enroll in the REMS by completing the <a href="#">Prescriber Enrollment Form</a> and submitting it to the REMS Program.</li></ol> |
| Before treatment initiation (first dose) | <ol style="list-style-type: none"><li>5. Assess the patient's need for an adult observer and for premedication as described in the <a href="#">Prescriber Guide</a>.</li></ol>   |
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	<ol style="list-style-type: none"> <li>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 <a href="#">Patient Guide</a>, <a href="#">Safety Video</a>, and <a href="#">Wallet Card</a>.</li> <li>7. Provide the patient with the <a href="#">Patient Guide</a> and <a href="#">Wallet Card</a>, and direct the patient to <a href="http://PALYNZIQREMS.com">PALYNZIQREMS.com</a> to view the <a href="#">Safety Video</a>.</li> <li>8. Enroll the patient in the REMS Program by completing and submitting the <a href="#">Patient Enrollment Form</a>. Provide a completed copy of the form to the patient and retain a completed copy in the patient's record.</li> <li>9. Provide the patient with a prescription for auto-injectable epinephrine to accompany the prescription for PALYNZIQ.</li> </ol>
During treatment; before each prescription	<ol style="list-style-type: none"> <li>10. Assess the patient for anaphylaxis episodes.</li> <li>11. Assess the patient's supply of auto-injectable epinephrine.</li> <li>12. Provide a prescription for auto-injectable epinephrine, if the patient's supply is inadequate.</li> </ol>
At all times	<ol style="list-style-type: none"> <li>13. Report anaphylaxis episodes to the REMS Program.</li> <li>14. Report treatment discontinuation or transfer of care to the REMS Program.</li> </ol>

## 2. Patients who are prescribed PALYNZIQ must:

Before treatment initiation	<ol style="list-style-type: none"> <li>1. Review the <a href="#">Patient Guide</a>, <a href="#">Safety Video</a>, and <a href="#">Wallet Card</a>.</li> <li>2. Enroll in the REMS Program by completing the <a href="#">Patient Enrollment Form</a> with the prescriber. Enrollment information will be provided to the REMS Program.</li> <li>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 <a href="#">Patient Guide</a>, <a href="#">Safety Video</a>, and <a href="#">Wallet Card</a>.</li> <li>4. Adhere to the safe use conditions including obtaining auto-injectable epinephrine.</li> </ol>
At all times	<ol style="list-style-type: none"> <li>5. Inform the prescriber if you have a severe allergic reaction (anaphylaxis).</li> <li>6. Inform the prescriber if you need more auto-injectable epinephrine.</li> <li>7. Have auto-injectable epinephrine and the <a href="#">Wallet Card</a> with you.</li> <li>8. Inform all doctors about this treatment.</li> <li>9. Report a change in prescriber or contact information to the REMS Program.</li> <li>10. Report treatment discontinuation to the REMS Program.</li> </ol>

## 3. Pharmacies that dispense PALYNZIQ must:

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

#### 4. Wholesalers that distribute PALYNZIQ must:

To be able to distribute	<ol style="list-style-type: none"> <li>1. Establish processes and procedures to ensure that the drug is distributed only to certified pharmacies.</li> <li>2. Train all relevant staff involved in distributing on the REMS Program requirements.</li> </ol>
At all times	<ol style="list-style-type: none"> <li>3. Distribute only to certified pharmacies and maintain records of all distributions.</li> <li>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.</li> </ol>

#### 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](#)