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The 261 enrolled patients were aged 16 to 55 years (mean: 29 years) and had a baseline mean (range) blood phenylalanine of 1,233 (285, 2330) micromol/L. One hundred forty nine out of 261 (57%) patients were taking medical food at baseline and 41 out of 261 patients (16%) were on a protein-restricted diet at baseline (defined as receiving greater than 75% of total protein intake from medical food). Patients were randomized (1:1) to one of two target maintenance dosage arms: 20 mg once daily or 40 mg once daily. Patients were titrated to reach their randomized target dosage of 20 mg once daily or 40 mg once daily. The duration of titration varied among patients and was based on patient tolerability. Of the 261 enrolled patients, 195 (75%) patients reached their randomized maintenance dosage (103 in the 20 mg once daily arm, 92 in the 40 mg once daily arm). Among the patients who reached their randomized maintenance dosage, patients in the 20 mg once daily randomized arm reached their maintenance dosage at a median time of 10 weeks (range: 9 to 29 weeks) and patients in the 40 mg once daily arm reached their maintenance dosage at a median time of 11 weeks (range: 10 to 33 weeks).

Of the 261 patients who enrolled in Study 301, 54 (21%) patients discontinued treatment during Study 301, 4 patients completed Study 301 and did not continue to Study 165-302 (referred to as Study 302, NCT01889862), 152 patients continued to the eligibility period of Study 302, and 51 patients continued directly from Study 301 into the long-term treatment period of Study 302.

#### Study 302: Efficacy Assessment

A total of 164 adult patients with PKU who were previously-treated with Palynziq (152 patients from Study 301 and 12 patients from other Palynziq trials) enrolled in Study 302 and continued treatment with Palynziq in Study 302 for up to 13 weeks to assess eligibility for randomized withdrawal period.

#### *Randomized Withdrawal Period*

Following this period of up to 13 weeks of additional Palynziq treatment in Study 302, eligibility for entry into the efficacy assessment period (randomized withdrawal period) was determined by whether a patient achieved at least a 20% reduction in blood phenylalanine concentration from pre-treatment baseline (when in previous studies). Eighty-six out of 164 patients (52%) met this response target and continued into the randomized withdrawal period. In the double-blind, placebo-controlled, randomized withdrawal period, patients were randomized in a 2:1 ratio to either continue their maintenance Palynziq dosage or to receive matching placebo for a total of 8 weeks. The treatment difference in least squares (LS) mean change in blood phenylalanine concentration from the Study 302 randomized withdrawal baseline to randomized withdrawal Week 8 for each randomized study arm is shown in Table 5. Mean blood phenylalanine concentrations at pre-treatment baseline (Study 301 or other Palynziq trials) are also shown in Table 5. At Study 302 randomized withdrawal Week 8, Palynziq-treated patients (20 mg once daily or 40 mg once daily) maintained their blood phenylalanine concentrations as compared to their randomized withdrawal baseline, whereas patients randomized to matching placebo (20 mg once daily or 40 mg once daily) returned to their pretreatment baseline blood phenylalanine concentrations (Figure 1).

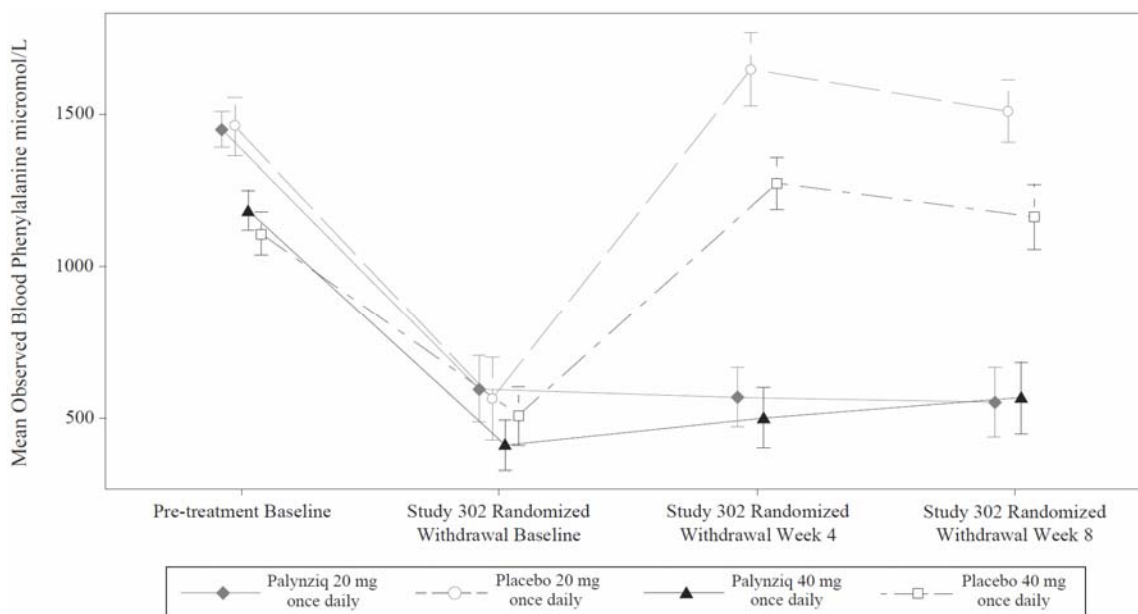
**Table 5: Primary Endpoint: LS Mean Change in Blood Phenylalanine Concentration from Randomized Withdrawal Baseline to Week 8 in Adult Patients with PKU – Efficacy Assessment in Study 302**

Randomized Study Arm	Blood Phenylalanine Concentration (micromol/L)			LS Mean Change from Study 302 Randomized Withdrawal Baseline to Week 8 (95% CI)	Treatment Difference in LS Mean Change (95% CI) P-value*
	Pre-treatment Baseline	Study 302 Randomized Withdrawal Baseline	Study 302 Randomized Withdrawal Week 8		
Palynziq 20 mg once daily	1450.2 (310.5) n = 29	596.8 (582.8) n = 29	553.0 (582.4) n = 26 <sup>†</sup>	-23.3 (-156.2, 109.7)	-973.0 (-1204.2, -741.9) p < 0.0001
Placebo 20 mg once daily	1459.1 (354.7) n = 14	563.9 (504.6) n = 14	1509.0 (372.6) n = 13 <sup>†</sup>	949.8 (760.4, 1139.1)	
Palynziq 40 mg once daily	1185.8 (344.0) n = 29	410.9 (440.0) n = 29	566.3 (567.5) n = 23 <sup>†</sup>	76.3 (-60.2, 212.8)	-588.5 (-830.1, -346.9) p < 0.0001
Placebo 40 mg once daily	1108.9 (266.8) n = 14	508.2 (363.7) n = 14	1164.4 (343.3) n = 10 <sup>†</sup>	664.8 (465.5, 864.1)	

\* Based on the mixed model repeated measures (MMRM) method, with treatment arm, visit, and treatment arm-by-visit interaction as factors adjusting for baseline blood phenylalanine concentration.

<sup>†</sup> Patients who did not complete phenylalanine assessment within the window for Week 8 (Day 43 to 56) were excluded.

**Figure 1: Observed Mean (SE) Blood Phenylalanine Concentrations Over Time in Adult Patients with PKU in Study 302**



**Study 301 and 302 Continuous Treatment**

Of 118 patients from Study 301 with a pre-treatment baseline blood phenylalanine concentration greater than 600 micromol/L who were randomized to and received at least one dose of 20 mg once daily Palynziq, 108 patients, 98 patients, and 51 patients were treated for at least 24 weeks, 48 weeks, and 96 weeks, respectively.

Of the 118 patients, 53 patients reached their first response (at least a 20% reduction in blood phenylalanine concentration from pre-treatment baseline or a blood phenylalanine concentration less than or equal to 600 micromol/L) by 4 weeks of treatment with 20 mg once daily and 28 patients reached their first response between Weeks 4 and 24 with 20 mg once daily. Of the 118 patients, 25 patients escalated their dosage from 20 mg once daily to 40 mg once daily before reaching a first response; of those 25 patients, 8 patients reached their first response by 4 weeks of treatment with 40 mg once daily and 6 patients reached their first response between Weeks 4 and 16 with 40 mg once daily.

## 16 HOW SUPPLIED/STORAGE AND HANDLING

### How Supplied

Palynziq (pegvaliase-pqpz) injection is supplied as a preservative-free, sterile, clear to slightly opalescent, colorless to pale yellow solution. All dosage strengths of Palynziq are provided in a 1 mL glass syringe with a 26 gauge, 0.5 inch needle.

Each carton contains 1 or 10 trays with single-dose prefilled syringe(s), Prescribing Information, Medication Guide, and Instructions for Use. The following packaging configurations are available.

**Table 6: Palynziq Packaging Configurations**

<b>Pegvaliase-pqpz 2.5 mg/0.5 mL</b>	1 syringe/carton	NDC 68135-058-90
<b>Pegvaliase-pqpz 10 mg/0.5 mL</b>	1 syringe/carton	NDC 68135-756-20
<b>Pegvaliase-pqpz 20 mg/mL</b>	1 syringe/carton 10 syringes/carton	NDC 68135-673-40 NDC 68135-673-45

### Storage and Handling

- Store in refrigerator at 36°F to 46°F (2°C to 8°C) in its original carton to protect from light.
- Do not freeze or shake.
- *For patients:* If needed, store Palynziq in the original carton at room temperature between 68°F to 77°F (20°C to 25°C) for up to 30 days. Record the date removed from refrigeration on the carton. Once stored at room temperature, do not return the product to the refrigerator.
- The shelf-life expires after storage at room temperature for 30 days, or after the expiration date on the product carton, whichever is earlier.

## 17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Medication Guide and Instructions for Use).

### Anaphylaxis and Other Hypersensitivity Reactions

- Advise patients that Palynziq may cause hypersensitivity reactions, including anaphylaxis that can occur at any time. Instruct patients to recognize the signs and symptoms of anaphylaxis [*see Warnings and Precautions (5.1, 5.3)*].
- Instruct patients to carry auto-injectable epinephrine with them at all times during Palynziq treatment. Instruct the patient and observer (if applicable) on the appropriate use of auto-injectable epinephrine for anaphylaxis [*see Warnings and Precautions (5.1)*].

- Instruct patients who experience anaphylaxis to seek immediate medical care, discontinue therapy, and resume treatment only at the instruction of a healthcare provider [see *Warnings and Precautions (5.1)*].

#### Palynziq REMS Program

Palynziq is available only through a restricted program called the Palynziq REMS [see *Warnings and Precautions (5.2)*]. Inform the patient of the following notable requirements:

- Patients must be enrolled in the Palynziq REMS.
- Patients must be educated about the risk of anaphylaxis by a certified prescriber to ensure they understand the risks and benefits of treatment with Palynziq.
- Patients must fill a prescription for auto-injectable epinephrine and carry it with them at all times.
- Patients will be given a Palynziq Patient Wallet Card that they should carry with them at all times. This card describes symptoms which, if experienced, should prompt the patient and observer (if applicable) to immediately seek medical care. Advise the patient to show the Palynziq Wallet Card to other treating healthcare providers.

Palynziq is available only from certified pharmacies participating in the program. Therefore, provide patients with the telephone number and website for information on how to obtain the product.

#### Administration

- Advise patients to monitor their dietary protein and phenylalanine intake throughout treatment with Palynziq, and adjust intake as directed by their healthcare provider based on blood phenylalanine concentrations [see *Dosage and Administration (2.2)*].
- Provide appropriate instruction for methods of self-injection, including careful review of the Palynziq Medication Guide and Instructions for Use. Instruct patients in the use of aseptic technique when administering Palynziq [see *Dosage and Administration (2.4)*].
- Inform patients that a healthcare provider will show them or their caregiver how to prepare to inject Palynziq before self-administering.
- Advise patients not to inject into moles, scars, birthmarks, bruises, rashes, or areas where the skin is hard, tender, red, damaged, burned, inflamed, or tattooed.
- Advise patients to rotate areas of injection with each dose. Advise patients to check the injection site for redness, swelling, and tenderness, and to contact their healthcare provider if they have a skin reaction and it does not clear up, or worsens.
- Advise patients to follow sharps disposal recommendations [see *Instructions for Use*] patients on safe disposal procedures.
- Advise patients that the shelf-life expires after storage at room temperature for 30 days or after the expiration date on the product carton, whichever is earlier.

#### Pregnancy

- Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Advise females to inform their healthcare provider of a known or suspected pregnancy [see *Use in Specific Populations (8.1)*].
- 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. Encourage these patients to report their pregnancy to BioMarin (1-866-906-6100) [see *Use in Specific Populations (8.1)*].

Manufactured by:  
BioMarin Pharmaceutical Inc.  
Novato, CA 94949  
US License No. 1649

**Medication Guide**  
**Palynziq™ (Pal-lin-zeek)**  
**(pegvaliase-pqpz) injection**

**What is the most important information I should know about Palynziq?**

**Palynziq can cause a severe allergic reaction (anaphylaxis) that may be life-threatening and can happen any time during treatment with Palynziq.** Severe allergic reactions are a serious but common side effect of 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.
- If you have a severe allergic reaction during treatment with Palynziq, you will need to receive an auto-injection of epinephrine immediately and get emergency medical help right away.
- Your healthcare provider will decide if you (or your caregiver) are able to give the Palynziq injections, recognize the signs and symptoms of a severe allergic reaction, give an injection of epinephrine and call for emergency medical help, if needed.
- 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.

**Stop injecting Palynziq and get emergency medical care right away 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 an auto-injectable epinephrine for you and will teach you (or your caregiver) and your observer, if needed, when and how to use it if you have a severe allergic reaction. **Keep the auto-injectable epinephrine with you at all times during treatment with Palynziq.** Read the Patient Information that comes with the auto-injectable epinephrine that your healthcare provider prescribes for you for more information.
  - **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 medicines to take before your Palynziq injection that may 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.
  - **Your healthcare provider will give you a Palynziq Patient Wallet Card** that describes symptoms that you (or your caregiver), or your observer, should know that require you to get emergency medical care right away. **Carry this card with you at all times during treatment with Palynziq.** It is important to show your Palynziq Patient Wallet Card to any other healthcare provider who treats you.

**Palynziq is only available through a restricted program** called the Palynziq Risk Evaluation and Mitigation Strategy (REMS) Program. Before you can receive Palynziq, you must:

- enroll in this program.
- receive education about the risk of a severe allergic reaction (anaphylaxis) by a healthcare provider certified in the Palynziq REMS to be sure that you understand the risks and benefits of treatment with Palynziq.
- fill the prescription your healthcare provider gives you for the auto-injectable epinephrine and carry it with you at all times during treatment with Palynziq.
- carry the Palynziq Patient Wallet Card with you at all times.

Talk to your healthcare provider for more information about the Palynziq REMS and how to enroll.

**What is Palynziq?**

Palynziq is a prescription medicine used to lower blood levels of phenylalanine in adults with PKU (phenylketonuria) who have uncontrolled blood phenylalanine levels above 600 micromol/L (10 mg/dL) on their current treatment.

It is not known if Palynziq is safe and effective in children.

**Before injecting Palynziq, tell your healthcare provider about all of your medical conditions, including if you:**

- cannot or are not willing to use auto-injectable epinephrine to treat a severe allergic reaction.
- are pregnant or plan to become pregnant. Palynziq may harm your unborn baby. Tell your healthcare provider right away if you become pregnant or think you might be pregnant while taking Palynziq.
  - If your phenylalanine levels are too high or too low during pregnancy, this may also affect your unborn baby. You and your healthcare provider can decide the best way for you to manage your blood phenylalanine levels and discuss the risks and benefits of taking Palynziq during pregnancy to you and your unborn baby. It is very important to keep your phenylalanine levels at the levels your healthcare provider recommends during pregnancy.
  - **Pregnancy Surveillance Program.** There is a pregnancy surveillance program for females who take Palynziq during

pregnancy, or who become pregnant while receiving Palynziq or within 1 month after their last dose of Palynziq. The purpose of this program is to collect information about the health of you and your baby while taking Palynziq. Talk to your healthcare provider about how you can take part in this program or call BioMarin at 1-866-906-6100.

- are breastfeeding or plan to breastfeed. It is not known if Palynziq passes into your breast milk. Talk to your healthcare provider about the best way to feed your baby if you take Palynziq.

**Tell your healthcare provider about all the medicines you take**, including prescription or over-the-counter medicines, vitamins, or herbal supplements.

#### **How should I take Palynziq?**

- Your healthcare provider will give you the Palynziq injection until they decide that you (or your caregiver) can give it. See **“What is the most important information I should know about Palynziq?”**
- Your healthcare provider may prescribe medicine for you to take before your Palynziq injection to help reduce the symptoms of an allergic reaction.
- If your healthcare provider decides that you (or your caregiver) can give your Palynziq injections, you (or your caregiver) will be shown how to prepare and give your Palynziq injections. See the “Instructions for Use” for detailed instructions on how to prepare and give an injection of Palynziq.
- Use Palynziq exactly as your healthcare provider tells you to. Your healthcare provider will tell you how much Palynziq to inject and when to inject it.
- Palynziq comes in prefilled syringes with 3 different strengths (2.5 mg, 10 mg, or 20 mg). You may need more than 1 Palynziq prefilled syringe for your prescribed dose.
- Monitor the amount of protein and phenylalanine that you eat or drink. Your healthcare provider may change the amount of protein and phenylalanine you should have in your diet during treatment with Palynziq, depending on the levels of phenylalanine in your blood. Follow your healthcare provider’s instructions about the amount of protein and phenylalanine you should have in your diet.
- If you miss a dose, take your next dose at the regular time. Do not take two doses of Palynziq to make up for a missed dose.

#### **What are the possible side effects of Palynziq?**

**Palynziq may cause serious side effects, including:**

- See **“What is the most important information I should know about Palynziq?”**
- **Other allergic reactions to Palynziq** can happen during treatment with Palynziq. **Contact your healthcare provider right away if you have any of the following symptoms of an allergic reaction including:** rash, itching, or swelling of the face, lips, eyes, or tongue. Your healthcare provider may change your dose of Palynziq, stop your treatment with Palynziq for a period of time, or prescribe medicine for you to take before your Palynziq injection to help reduce the symptoms of an allergic reaction.

**The most common side effects of Palynziq include:**

- injection site reactions, such as redness, itching, pain, bruising, rash, swelling, tenderness
- joint pain
- headache
- skin reactions that spread on your skin and last at least 14 days, such as itching, rash, redness
- itching
- nausea
- stomach pain
- mouth and throat pain
- vomiting
- cough
- diarrhea
- feel very tired
- low levels of phenylalanine in your blood

These are not all the possible side effects of Palynziq. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

#### **How should I store Palynziq?**

- Store Palynziq in the refrigerator at 36°F to 46°F (2°C to 8°C).
- If needed, you may store Palynziq at room temperature between 68°F to 77°F (20°C to 25°C) for up to 30 days.
  - Write the date that you remove Palynziq from the refrigerator on the carton.
  - If stored at room temperature, do not put Palynziq back in the refrigerator.
- **Keep Palynziq in the original carton to protect from light.**
- **Do not** freeze or shake Palynziq.
- Throw away Palynziq if it has been kept at room temperature for 30 days and has not been used, or after the expiration date on the carton, whichever comes first.

**Keep Palynziq and all medicines out of the reach of children.**

#### **General Information about the safe and effective use of Palynziq.**

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use Palynziq for a condition for which it was not prescribed. Do not give Palynziq to other people, even if they have the same symptoms that you have. It may harm them. You can ask your pharmacist or healthcare provider for information about Palynziq that is written for health professionals.

#### **What are the ingredients in Palynziq?**

**Active ingredients:** pegvaliase-pqpz

**Inactive ingredients:** sodium chloride, *trans*-cinnamic acid, tromethamine, and tromethamine hydrochloride

Manufactured by: BioMarin Pharmaceutical Inc. Novato, CA 94949 US License No. 1649

For more information, go to <http://www.Palynziq.com/> or call 1-866-906-6100.

This Medication Guide has been approved by the U.S. Food and Drug Administration.

Issued: May 2018



**Instructions for Use**  
**Palynziq (Pal-lin-zeek)**  
**(pegvaliase-pqpz)**  
**injection**  
**prefilled syringe**

Read this Instructions for Use before you start using the Palynziq prefilled syringe and each time you get a new prescription. There may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or your treatment.

Follow these instructions carefully while you are using Palynziq. If your healthcare provider decides that you (or your caregiver) can give the injections of Palynziq at home, your healthcare provider will show you (or your caregiver) how to inject Palynziq the right way. Your healthcare provider should watch you (or your caregiver) give the first Palynziq injection and monitor you for signs and symptoms of a severe allergic reaction (anaphylaxis). **Do not** inject Palynziq until your healthcare provider shows you (or your caregiver) how to inject Palynziq the right way and has watched you (or your caregiver) give your injection.

Talk to your healthcare provider if you (or your caregiver) have any questions about how to inject Palynziq the right way.

**Do not share your prefilled syringes with anyone else. You may give an infection to them or get an infection from them.**

**Store your Palynziq prefilled syringe(s) in its original carton in the refrigerator. See “Storage of Palynziq” at the end of this Instructions for Use.**

**Supplies you will need for each injection of Palynziq (See Figure A):**

- Palynziq prefilled syringe(s) in sealed tray(s). **Each tray contains 1 prefilled syringe. You may need more than 1 prefilled syringe for your prescribed dose.**
- 1 gauze pad or cotton ball
- 1 alcohol pad
- 1 bandage
- 1 puncture resistant or sharps disposal container. See “Dispose of the used prefilled syringes” at the end of this Instructions for Use.

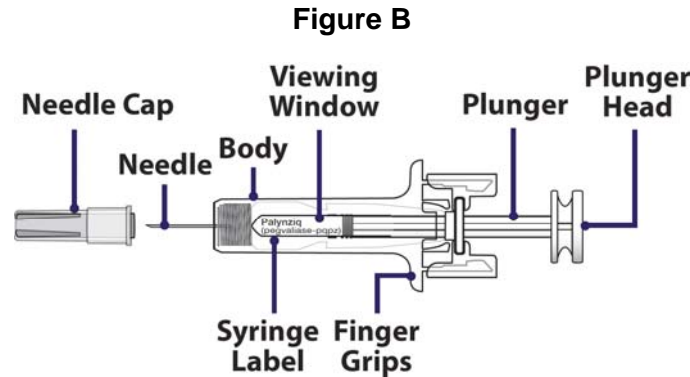
**Figure A**



## Important things to know about using your Palynziq prefilled syringe:

- Inject only 1 time with each Palynziq prefilled syringe. **Do not** use a Palynziq syringe more than 1 time.
- **Do not** pull back on the plunger at any time.
- **Do not** remove the needle cap until you are ready to inject.

Figure B below shows what the prefilled syringe looks like before use.

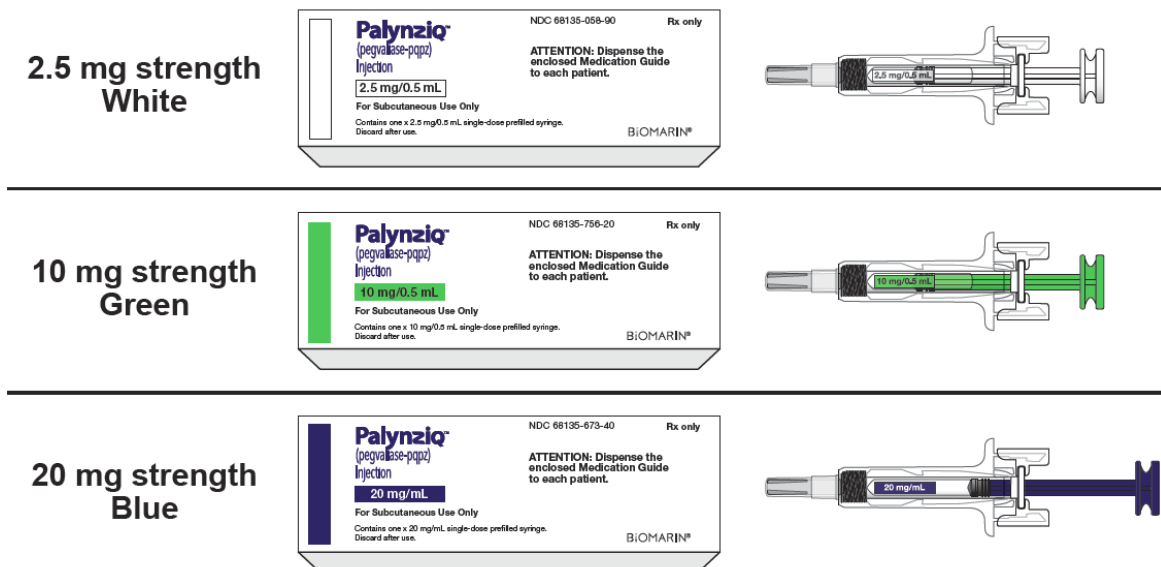


Select the correct Palynziq prefilled syringe(s) for your dose. You may need more than 1 prefilled syringe for your prescribed dose. Your healthcare provider will tell you which syringe(s) to use. Ask your healthcare provider if you have any questions.

When you receive your Palynziq prefilled syringe(s), check that the name “Palynziq” appears on the carton(s).

- Palynziq prefilled syringes come in 3 different strengths (See Figure C).
- Before you inject Palynziq, check each carton and syringe to make sure you have the right prefilled syringe for your prescribed dose.

**Figure C**



## Set up your injection

**Step 1:** Gather your supplies for the injection(s) (See Figure A) and place them on a clean flat surface.

Take out the number of cartons needed for your prescribed dose from the refrigerator.

Check the expiration date on the carton(s) (See Figure D).

- If the expiration date has passed, **do not** use the prefilled syringe(s) in that carton. Call BioMarin at 1-866-906-6100 or your healthcare provider for help with Palynziq.

**Step 2:** Open the carton(s) and take out the sealed tray(s) that you need for your prescribed dose (See Figure E). You may need more than 1 prefilled syringe for your prescribed dose.

Place the sealed tray(s) on a clean, flat surface out of reach of children and pets.

Put the carton with any remaining trays back in the refrigerator.

**Step 3:** Let the sealed tray(s) sit at room temperature for **at least 30 minutes**. Injecting Palynziq when cold can make the injection feel uncomfortable.

- **Do not** warm up the prefilled syringe in any other way other than letting it sit at room temperature. **Do not** warm in a microwave and **do not** place in hot water.

**Step 4:** Peel off the cover from the tray (See Figure F).

Figure D

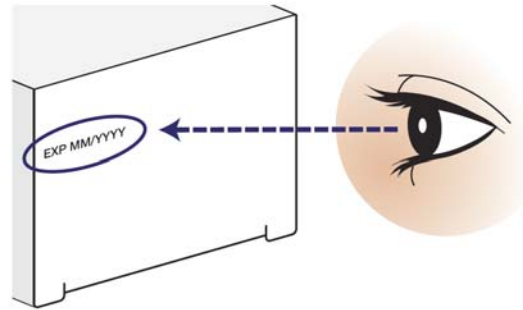
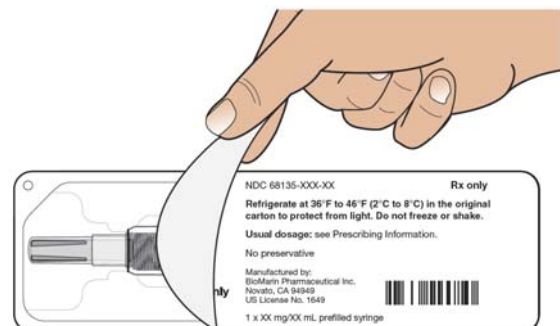


Figure E



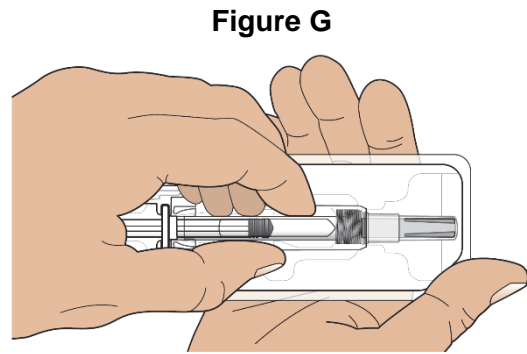
**Let the sealed tray(s) sit at room temperature for at least 30 minutes before opening.**

Figure F



**Step 5:** Hold the middle of the prefilled syringe body and remove the prefilled syringe from the tray (See Figure G).

- **Throw away** the prefilled syringe if it looks damaged or used, and use a new prefilled syringe for your injection. See “**Dispose of the used prefilled syringes**” at the end of this Instructions for Use. Call BioMarin at 1-866-906-6100 or your healthcare provider for help with Palynziq.
- **Do not** remove the needle cap from the prefilled syringe until Step 12.
- **Do not** shake or roll the syringe in your hands.



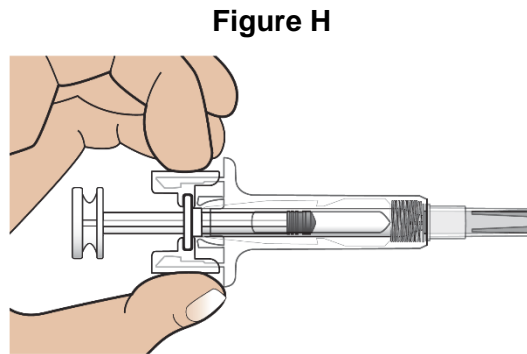
**Step 6:** Check the prefilled syringe label to make sure you have the correct strength for your prescribed dose.

**Check the prefilled syringe label to make sure you have the correct strength.**

**Step 7:** Look at the liquid through the viewing window (See Figure H).

- It is normal to see air bubbles. **Do not** flick or try to push the bubbles out.

The liquid should look clear and colorless to pale yellow. **Throw away** the prefilled syringe if the liquid is cloudy, discolored, or has particles in it and use a new prefilled syringe for your injection. See “**Dispose of the used prefilled syringes**” at the end of this Instructions for Use. Call BioMarin at 1-866-906-6100 or your healthcare provider for help with Palynziq.



## Choose and prepare injection site

### Step 8: Choose your injection site.

The recommended injection sites are:

- Front middle of the thighs.
- The abdomen except for the 2 inch (5 centimeter) area directly around the belly button (navel).

If a caregiver is giving the injection, the top of the buttocks and the back of the upper arms may also be used (See Figure I).

- **Do not** inject into moles, scars, birthmarks, bruises, rashes, or areas where the skin is hard, tender, red, damaged, burned, inflamed, or tattooed.
- If you need more than 1 injection for your dose, the injection sites should be at least 2 inches away from each other. The second injection site can be on the same part of the body or a different part of the body (See Figures I and J).
- For each injection, change (rotate) your injection sites. Choose an injection site that is at least 2 inches away from the injection site that you used for the last injection. It can be on the same part of the body or a different part of the body (See Figures I and J).

**Step 9:** Wash your hands well with soap and water before injecting Palynziq (See Figure K).

**Step 10:** Clean the chosen site with an alcohol pad. Let the skin air dry for at least 10 seconds before injecting Palynziq (See Figure L).

- **Do not** touch the cleaned injection site.
- **Do not** remove the needle cap until you are ready to inject Palynziq.

Figure I

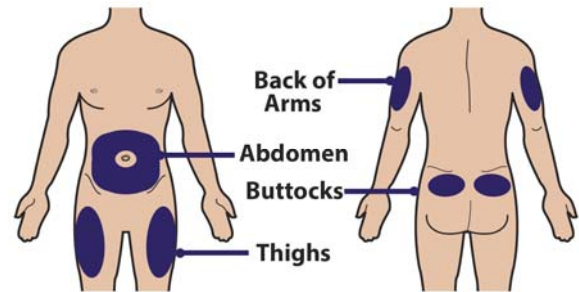


Figure J

Inject at least 2 inches apart

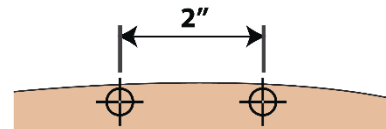


Figure K

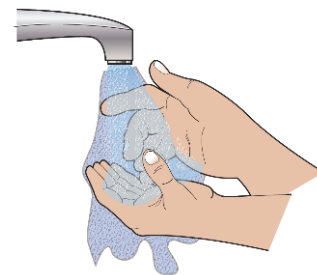
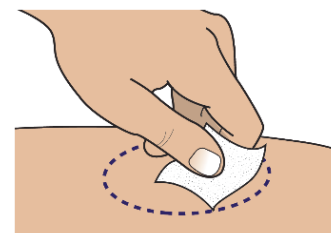


Figure L



## Inject Palynziq

**Step 11:** Hold the body of the prefilled syringe with one hand with the needle facing away from you (See Figure M).

- **Do not** use the prefilled syringe if it is dropped. **Throw away** the prefilled syringe if it is dropped and use a new prefilled syringe for your injection. See “**Dispose of the used prefilled syringes**” at the end of this Instructions for Use. Call BioMarin at 1-866-906-6100 or your healthcare provider for help with Palynziq.

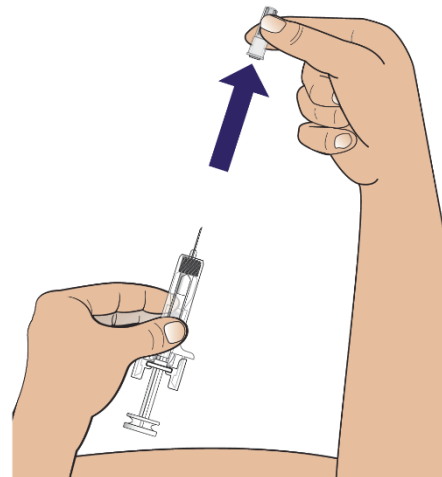
**Figure M**



**Step 12:** Pull the needle cap straight off the needle (See Figure N).

- **Do not** twist the needle cap during removal.
- **Do not** hold the prefilled syringe by the plunger or plunger head while taking the needle cap off.
- Before injecting Palynziq, check to make sure that the needle is not damaged or bent. Throw away the prefilled syringe if the needle is damaged or bent and use a new prefilled syringe for your injection. See “**Dispose of the used prefilled syringes**” at the end of this Instructions for Use. Call BioMarin at 1-866-906-6100 or your healthcare provider for help with Palynziq.

**Figure N**

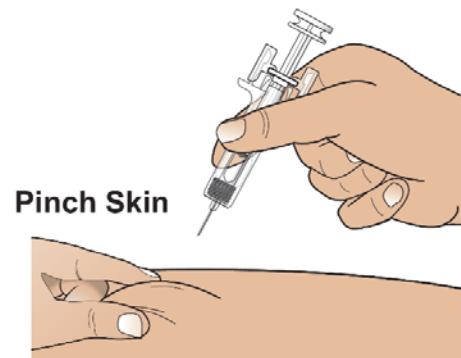


You may see a drop of liquid on the tip of the needle. This is normal. **Do not** wipe it away. Throw the needle cap away in a puncture resistant or sharps disposal container.

**Step 13:** Hold the body of the prefilled syringe in 1 hand between your thumb and index finger. Use your other hand to pinch up the skin around the injection site. Hold the skin firmly (See Figure O).

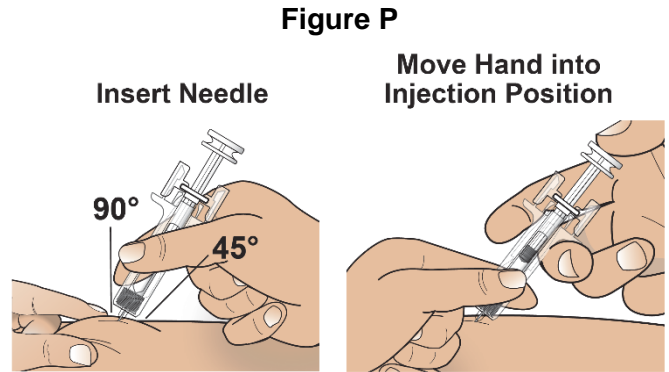
- **Do not** touch the plunger head while inserting the needle into the skin.

**Figure O**

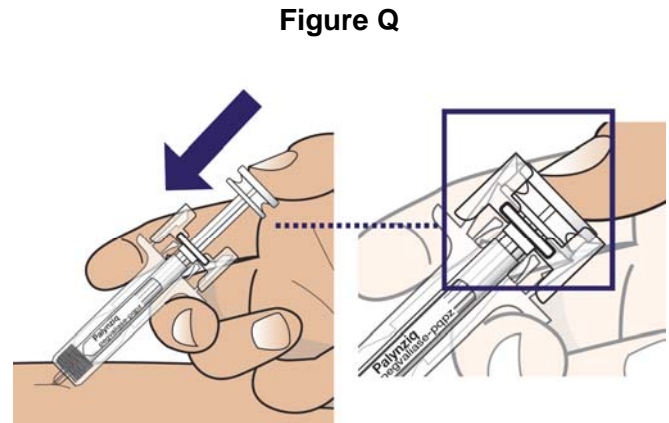


**Step 14:** Use a quick motion to fully insert the needle into the pinched skin at a 45 to 90 degree angle (See Figure P).

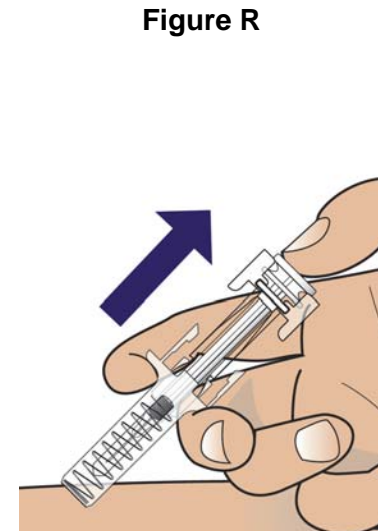
Release the pinch of skin. Use that hand to hold the bottom of the prefilled syringe steady. Place the thumb of your other hand on the plunger head and place your index and middle fingers under the finger grips (See Figure P).



**Step 15:** Use your thumb to push in the plunger slowly and steadily as far as it will go to inject all the medicine (See Figure Q). **More pressure on the plunger may be needed to inject all the medicine for the 10 mg and 20 mg strength prefilled syringes.**



**Step 16:** Slowly move your thumb up to release the plunger. The needle will automatically be covered by the prefilled syringe body (See Figure R).





## Treat injection site

**Step 17:** Treat injection site (if needed).

If you see drops of blood at the injection site, press a cotton ball or gauze over the injection site and hold for about 10 seconds. You may cover the injection site with a small adhesive bandage if needed.

**If more than 1 prefilled syringe is needed for your prescribed dose:**

**Step 18:** If your healthcare provider tells you to use more than one prefilled syringe for your prescribed dose, repeat Steps 4 to 17 listed above for each prefilled syringe that you use.

- **Note: Do not** give the injection in the same spot. The injection sites should be at least 2 inches away from each other. See Step 8 for information on choosing an injection site.

## Dispose of the used prefilled syringes

**Step 19:** Put your used prefilled syringes in a puncture resistant container, such as an FDA-cleared sharps disposal container immediately after use (See Figure S).

**Do not** throw away (dispose of) prefilled syringes in your household trash.

If you do not have an FDA-cleared sharps disposal container, you may use a household container that is:

- made of a heavy-duty plastic,
- can be closed with a tight-fitting, puncture-resistant lid, without sharps being able to come out,
- upright and stable during use,
- leak-resistant, and
- properly labeled to warn of hazardous waste inside the container.

When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be state or local laws about how you should throw away used needles and syringes. For more information about safe sharps disposal and for specific information about sharps disposal in the state that you live in, go to the FDA's website at:

<http://www.fda.gov/safesharpsdisposal>

**Do not** dispose of your used sharps disposal container in your household trash unless your community guidelines

**If you need to use more than 1 prefilled syringe for your prescribed dose, repeat Steps 4 to 17 right away for each prefilled syringe you use.**

**Figure S**





permit this. **Do not** recycle your used sharps disposal container.

**Note:** Keep sharps disposal container out of the reach of children and pets.

## Storage of Palynziq

- Store Palynziq in the refrigerator at 36°F to 46°F (2°C to 8°C) (See Figure T).
- If needed, you may store Palynziq at room temperature between 68°F to 77°F (20°C to 25°C) for up to 30 days.
  - Write the date that you remove Palynziq from the refrigerator on the carton.
  - If stored at room temperature, do not put Palynziq back in the refrigerator.
- **Keep Palynziq in the original carton to protect from light.**
- **Do not** freeze or shake Palynziq.
- Throw away Palynziq if it has been kept at room temperature for 30 days and has not been used, or after the expiration date on the carton, whichever comes first.

**Keep Palynziq and all medicines out of the reach of children.**

This Instructions for Use has been approved by the U.S. Food and Drug Administration.

Manufactured by:

BioMarin Pharmaceutical Inc.

Novato, CA 94949

U.S. License No. 1649

Issued: 05/2018

**Figure T**

