

## Risk Mitigation Material

# Important Information for Patients for the Safe Use of PALYNZIQ® (pegvaliase injection) during Pregnancy

*This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effect(s) you may get in any of the following ways:*

- Contact BioMarin Pharmaceutical Inc. at 1-866-906-6100 or email [drugsafety@bmrn.com](mailto:drugsafety@bmrn.com)
- Report online to Health Canada at [www.healthcanada.gc.ca/medeffect](http://www.healthcanada.gc.ca/medeffect) or call toll-free 1-866-234-2345 [Visit the Web page on Adverse Reaction Reporting (<https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada.html>) for information on how to report online, by mail or by fax; or call toll-free at 1-866-234-2345].

This leaflet contains information on what is known about the risks of Palynziq treatment **during pregnancy** and what you can do to minimize these risks. It also contains guidance on what to do if you become pregnant while on Palynziq. Please read this carefully and keep it in a safe and easily accessible place.

There is a pregnancy surveillance registry for women who take Palynziq during pregnancy. The purpose of this registry is to collect information about the health of you and your baby. If you are pregnant or plan to become pregnant talk to your doctor. Your doctor will explain the purpose of this registry and how you can enroll in it.

### **Pregnancy**

There is limited experience from the use of Palynziq in pregnant women. Palynziq is **not recommended** during pregnancy, unless your clinical condition requires treatment with Palynziq and all alternative treatments to control phenylalanine levels (for example, a phenylketonuria [PKU] diet with or without sapropterin dihydrochloride) have been exhausted.

- The findings from animal studies suggest a potential for adverse outcomes in pregnant women on Palynziq treatment
- There are limited data from clinical trials because study protocols required patients to stop treatment with Palynziq if they were planning or became pregnant.
- You should discuss contraception with your doctor as part of your routine management of PKU

#### **What to do if you are planning or become pregnant while on Palynziq treatment**

- Discuss this with your physician and health care team to assure optimum conditions for your planned pregnancy. Careful, tight control of phenylalanine levels is an important part of these conditions.  
Increasing the frequency of your phenylalanine level monitoring prior to and during pregnancy should be part of your management.

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## **Foetal development toxicity associated with Phenylketonuria (PKU)**

Uncontrolled high blood phenylalanine levels (hyperphenylalaninaemia) before and during pregnancy are known to be associated with an increased risk for miscarriage, major birth defects including microcephaly (head much smaller than expected) and severe cardiac malformations, intrauterine foetal growth retardation (foetus does not grow as expected) and future intellectual disability with low intelligence quotient (IQ).

In the case of hypophenylalaninaemia (very low blood phenylalanine levels) during pregnancy, there is a risk of intrauterine foetal growth retardation. Additional risks to the unborn child due to hypophenylalaninaemia are not well known.

Thus, continued and stable control of phenylalanine levels and careful dietary management during pregnancy reduce the incidence of both high phenylalanine-induced and low phenylalanine related effects on your baby.

## **Non-clinical findings with Palynziq**

Palynziq was administered to pregnant rats and rabbits to determine its effect on the pregnant female and on the development of their offspring. The pregnant animals did not have PKU and, therefore, when they were given Palynziq, their blood levels of phenylalanine became very low (hypophenylalaninaemia), especially at higher doses of Palynziq. As a result, there were negative effects on the health of the pregnant female animals and on their developing foetuses.

Pregnant female rats and rabbits given Palynziq ate less food than un-treated animals and did not gain weight as expected. Effects on their offspring included increases in miscarriages, foetal death, smaller litter sizes, smaller foetuses, and alterations/malformations in development (birth defects). These effects in pregnant animals that did not have PKU and their offspring are thought to be due to the very low levels of phenylalanine in their blood after treatment but, but it is also possible that Palynziq directly caused negative effects on the pregnant animals and their offspring as well. Therefore, the degree to which these negative effects were due to very low blood phenylalanine levels were not fully proven.

## **Clinical findings with Palynziq**

No pregnancy studies have been conducted in humans receiving Palynziq. There is limited information from the use of Palynziq in pregnant women as the Palynziq clinical trials required pregnant women or those planning to become pregnant to stop treatment with Palynziq.

## **Contraception**

You should discuss the use of contraception with your doctor before starting and during treatment with Palynziq, as part of routine clinical management of your PKU. You should consider taking a pregnancy test if your contraception or that of your partner fails.

## **Regular monitoring of Phe levels prior to and during pregnancy**

If you become pregnant or are planning to become pregnant your blood phenylalanine levels (maternal) must be strictly controlled both **before** and **during** pregnancy.

You should have your blood phenylalanine levels frequently monitored during pregnancy and you should adjust the dosage of Palynziq or modify dietary protein and phenylalanine intake to avoid blood phenylalanine levels falling too low (i.e., below 30 micromol/L or 0.5 mg/dL).

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### **Pregnancy observational safety study**

There is a pregnancy surveillance program for Palynziq. Your PKU treating doctor will be provided with instructions on how to enrol into this study. For more information, visit [palominostudy.com](http://palominostudy.com) or contact 833-672-2203.

### **Reporting of pregnancies**

If you receive Palynziq during pregnancy, or if you become pregnant while receiving Palynziq or within one month following the last dose of Palynziq, your doctor should report Palynziq exposure by calling 1- 866-906-6100.

**If you are planning to become pregnant or become pregnant while taking Palynziq you should** talk with the doctor who prescribes you Palynziq. Tell your doctor if you are pregnant or planning to become pregnant. Your doctor will tell you if you should continue Palynziq treatment.

Please also read the **Patient Medication Information** document carefully. This is contained in each pack/carton of Palynziq.

**Palynziq 2.5 mg/0.5 mL DIN: 02526247**

**Palynziq 10 mg/0.5 mL DIN : 02526255**

**Palynziq 20 mg/1.0 mL DIN : 02526263**

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