

Imagine this for your red blood cells

The first and only targeted PK deficiency treatment

Jim, 22
Takes PYRUKYND®

All patients photographed may or may not still be on treatment.

Introducing PYRUKYND, a treatment of hemolytic anemia for adults with pyruvate kinase (PK) deficiency that targets the underlying cause of the disease and activates the defective enzyme.



Talk to your doctor about what PYRUKYND can do for you.

WHAT IS PYRUKYND?

PYRUKYND is a prescription medicine used to treat low red blood cell counts caused by the early breakdown of red blood cells (hemolytic anemia) in adults with pyruvate kinase (PK) deficiency.

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

IMPORTANT SAFETY INFORMATION

PYRUKYND may cause serious side effects, including:

- **Rapid breakdown of red blood cells (acute hemolysis)** has happened after suddenly interrupting or stopping treatment with PYRUKYND. **You should not suddenly stop taking PYRUKYND.** If you have to stop your treatment with PYRUKYND, your healthcare provider should monitor you closely. Tell your healthcare provider right away if you develop any signs or symptoms of breakdown of red blood cells including yellowing of the skin or the whites of your eyes (jaundice), dark colored urine, dizziness, confusion, feeling tired, or shortness of breath

Please see additional Important Safety Information throughout and full Prescribing Information, including Patient Information, for PYRUKYND in pocket.


pyrukynd[®]
(mitapivat) tablets
5 • 20 • 50 mg

What is PK deficiency?

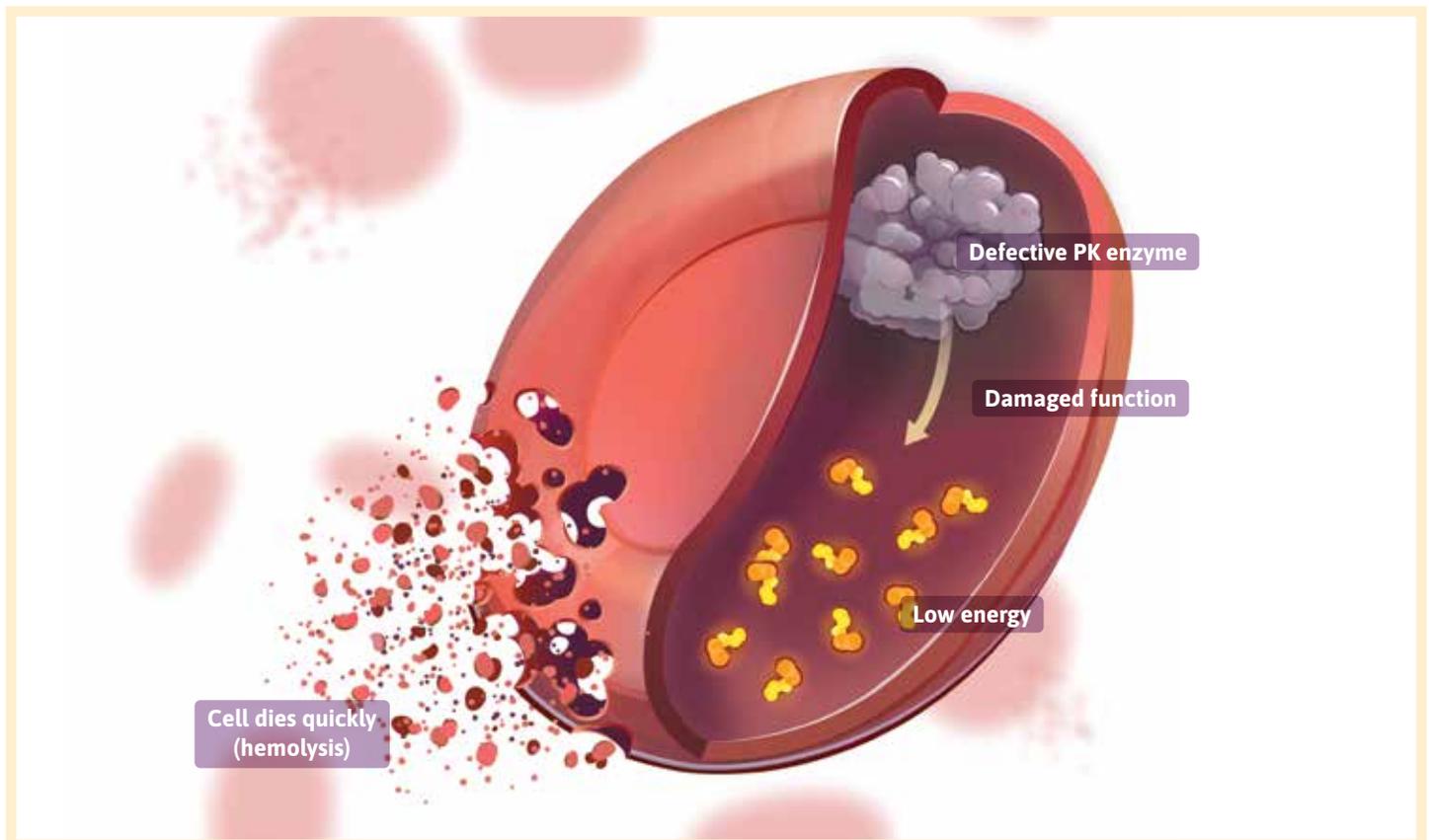
Understand the role that the PK enzyme plays in the health of your red blood cells (RBCs)

PK deficiency is a rare, inherited enzyme defect that causes RBCs to break down faster than they are made, which leads to lifelong hemolytic anemia.

The life of healthy RBCs

- After healthy RBCs are produced, they travel through the lungs, where oxygen binds to a molecule in each of the RBCs called hemoglobin
- The RBCs then transport oxygen to the rest of the body
- Healthy RBCs have enough ATP, or energy, made by the pyruvate kinase R (PKR) enzyme to survive this trip throughout the body
- Each RBC lives for about 120 days before being broken down and removed from circulation

PK-Deficient RBC



- People with PK deficiency have a PK enzyme that has a defect, causing their RBCs to break down sooner than normal. When RBCs break down, it's called hemolysis
- If PK deficiency is left untreated, RBCs continue to break down, and this may lead to symptoms of anemia like extreme fatigue, yellow skin/eye tone (jaundice), and complications like iron overload

KEY TERMS

Red blood cells

Cells that carry oxygen throughout the body

Anemia

A condition in which the blood has lower-than-normal levels of RBCs or hemoglobin

Hemoglobin (Hb)

A protein that helps RBCs carry the oxygen your body needs

Hemolytic anemia

A type of anemia that is caused by the early breakdown of RBCs in the bloodstream or by the spleen

Hemolysis

The breakdown of RBCs, which leads to the release of hemoglobin and bilirubin into the blood

Glycolysis

The process of RBCs converting glucose (sugar) into pyruvate and ATP

Enzyme

A protein that catalyzes chemical reactions that occur inside the body

PKR

The pyruvate kinase enzyme found in red blood cells

Adenosine triphosphate (ATP)

The primary source of energy for cells

Iron overload

An excess of iron in the body



If you have questions about the details of PK deficiency, a myAgios® Patient Support Manager is available to help at **1-800-951-3889**, Mon-Fri, 8 AM to 6 PM ET.

It's important to speak up about your PK deficiency symptoms

When talking with your doctor it can be helpful to prepare ahead of each appointment by knowing the key information to bring up.

Answer these questions about your PK deficiency journey to help guide the conversation.



What are your Hb levels?

How do these signs and symptoms affect you?



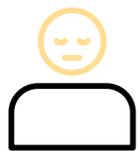
FATIGUE AND TIREDNESS

0	1	2	3	4	5
Not at all		Mild	Moderate		Severe



SHORTNESS OF BREATH

0	1	2	3	4	5
Not at all		Mild	Moderate		Severe



YELLOWING OF THE SKIN/EYES (JAUNDICE)

0	1	2	3	4	5
Not at all		Mild	Moderate		Severe

Do you have a history with transfusions? Yes No

If yes, when was the last one you received?

Think about different areas of your life and note any impact you feel due to PK deficiency:

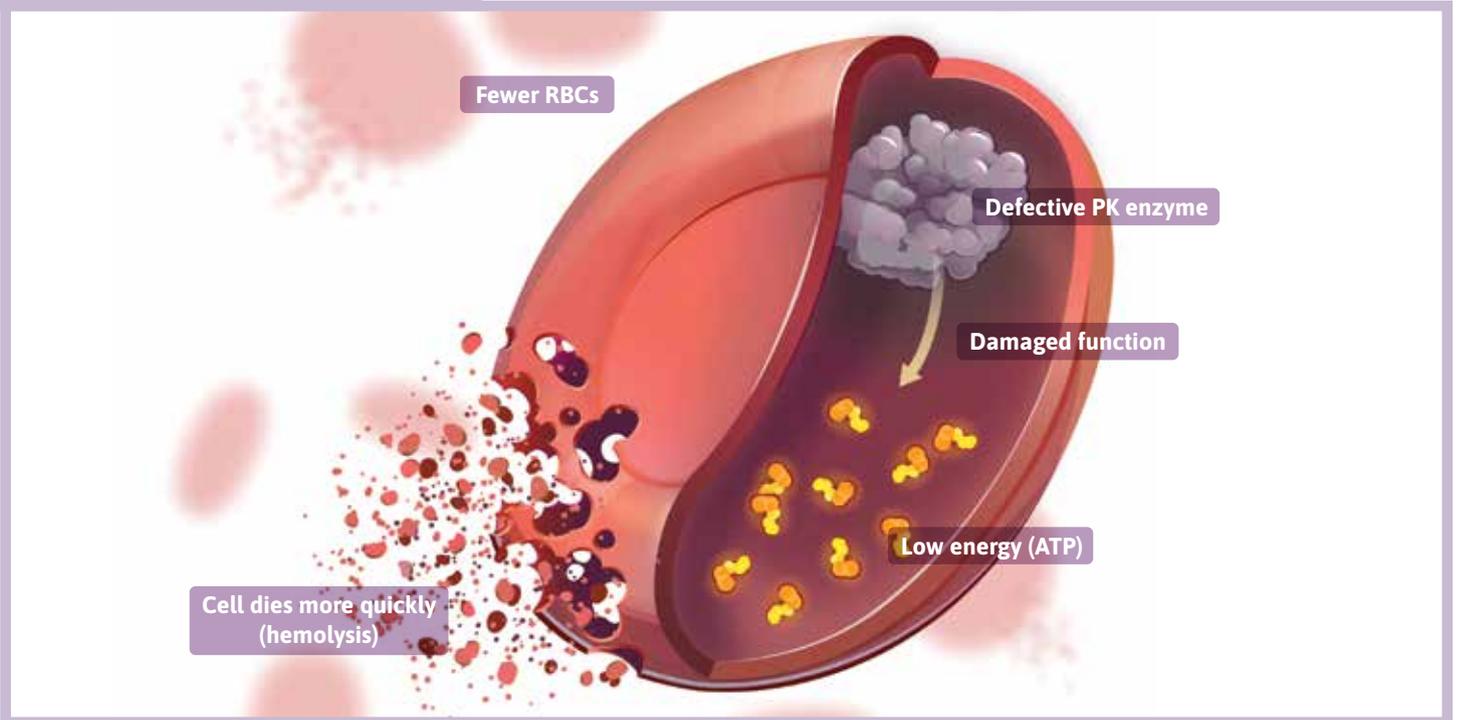


Bring this form to your next appointment to help paint a full picture of your PK deficiency experience for your doctor.

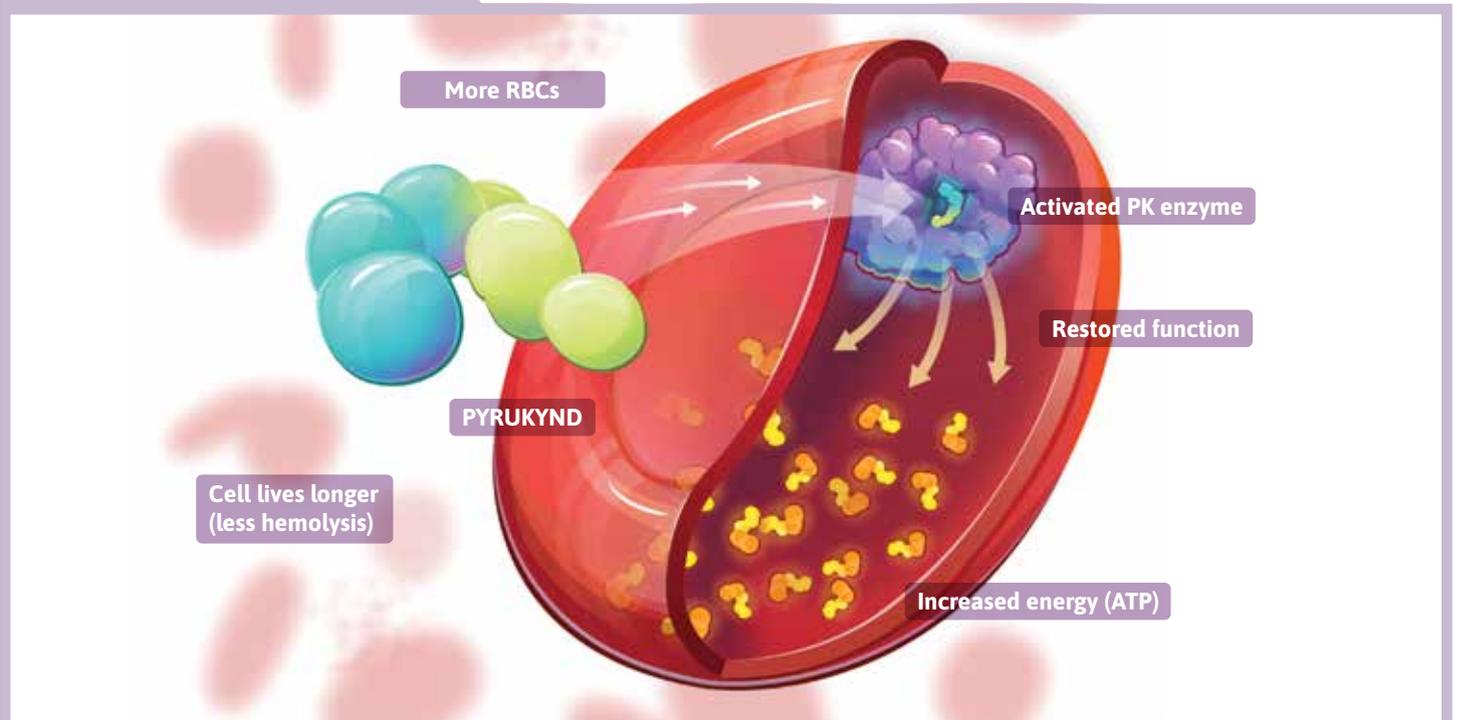
For more information about the symptoms and complications of PK deficiency, visit **KnowPKDeficiency.com**.

Imagine the first and only treatment to target the cause of your PK deficiency

WITHOUT PYRUKYND®



WITH PYRUKYND



By activating the defective PK enzyme that causes the rapid breakdown of RBCs (hemolysis), PYRUKYND may help your RBCs live longer

Take a closer look at how PYRUKYND is thought to work:



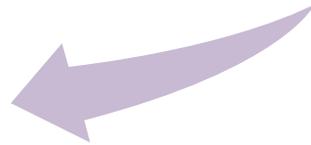
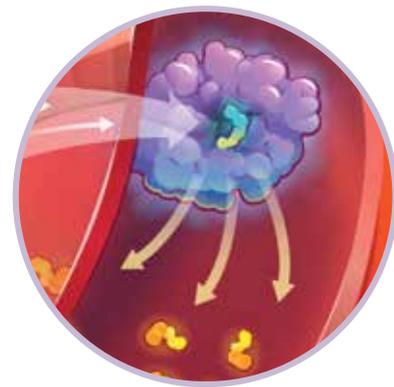
STEP ONE ATTACHES

PYRUKYND starts by attaching and binding to the defective PK enzyme



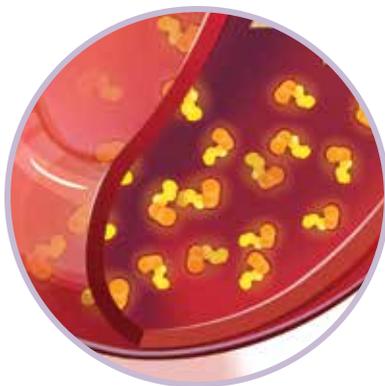
STEP TWO ACTIVATES

Once attached, PYRUKYND activates the PK enzyme to help improve its function, and increase energy, or ATP (as seen in healthy people without PK deficiency)



STEP THREE RESTORES ENERGY

Helps increase energy (ATP) to slow the process of RBC breakdown (hemolysis) and helps them live longer



IMPORTANT SAFETY INFORMATION (cont.)

The most common side effects of PYRUKYND were decrease in reproductive hormone (estrone) in men, increased salt from uric acid (urate) blood test, back pain, decrease in reproductive hormone (estradiol) in men, and joint pain (arthralgia).

These are not all the possible side effects of PYRUKYND. Call your healthcare provider for medical advice about side effects. You may report side effects to the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

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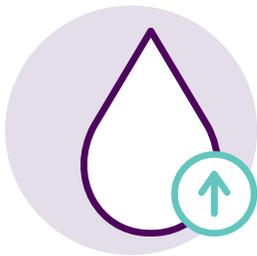
WHAT IS
PYRUKYND?

The safety and effectiveness of PYRUKYND[®] was studied in 2 clinical trials

STUDY 1 (ACTIVATE)

Adults with PK deficiency who were not regularly transfused
(defined as receiving 4 or fewer blood transfusions a year)

What were the main goals?

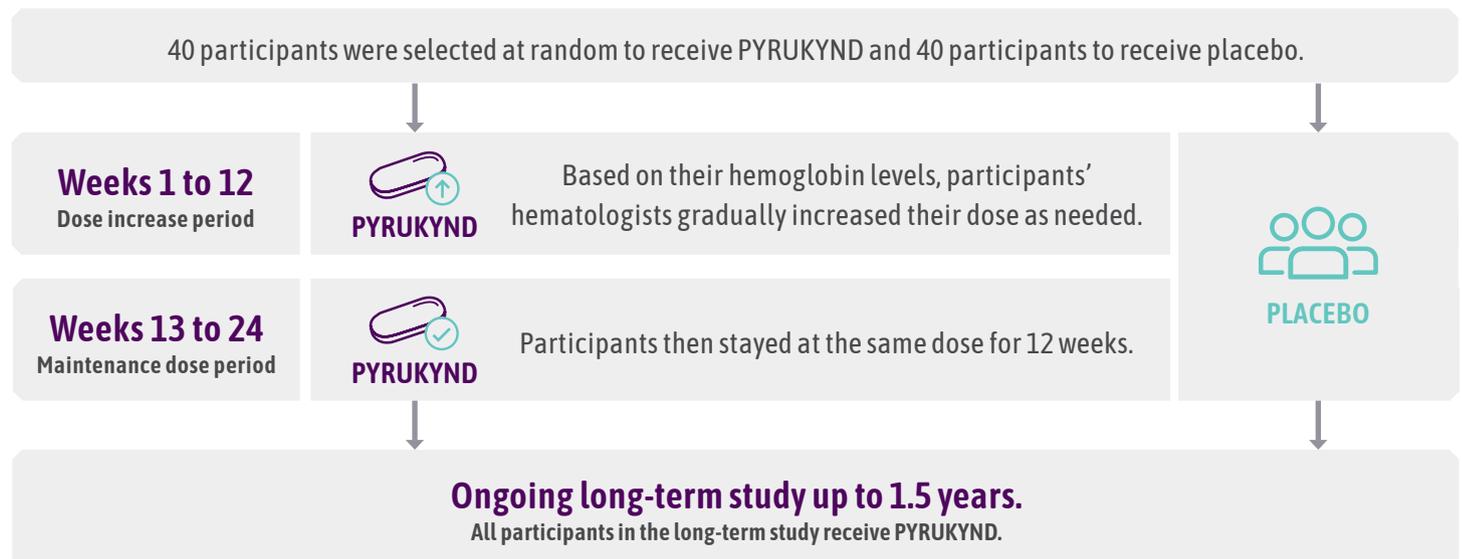


Study 1 measured:

- Changes in participants' hemoglobin and hemolysis levels
- Improvements in signs and symptoms of PK deficiency such as jaundice, tiredness, and shortness of breath

A response to PYRUKYND was measured by at least a 1.5 g/dL increase in hemoglobin during at least 2 of 3 checkups at weeks 16, 20, and 24.

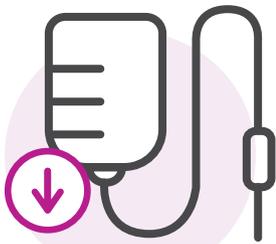
How was the study set up?



The safety of PYRUKYND has been studied up to 5 years in 4 clinical trials in 155 participants. Learn more about how PYRUKYND was studied at [PYRUKYND.com](https://www.pyrukynd.com).

STUDY 2 (ACTIVATE-T)**Adults with PK deficiency who were regularly transfused**

(defined as receiving 6 or more blood transfusions a year)

What was the main goal?**Study 2 measured changes in participants' need for transfusions**

A response to PYRUKYND was measured by at least a 33% reduction in the number of transfusions required during the final 24-week period.

Transfusion reductions were measured in comparison to the number of RBC units they received in the year before the study.

How was the study set up?

All 27 participants received PYRUKYND. None received placebo.

Weeks 1 to 16
Dose increase period



Participants' doses of PYRUKYND were gradually increased over the course of 16 weeks.

Weeks 17 to 40
Maintenance dose period



Participants were then given the same dose of PYRUKYND for the next 24 weeks.

Ongoing long-term study up to 1.8 years.



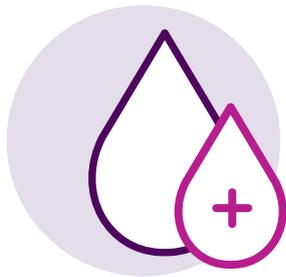
The most common side effects of PYRUKYND were decreases in reproductive hormones in males (estrone and estradiol), increased salt from uric acid (urate), back pain, and joint pain.

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What a change in hemoglobin levels means for your PK-deficient red blood cells

PYRUKYND® helps activate the PK enzyme to keep RBCs from breaking down too quickly and increase your hemoglobin (Hb) levels

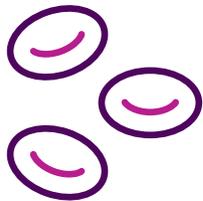
Increased hemoglobin levels are a sign that anemia is improving



40% of patients

out of the 40 participants in Study 1 (ACTIVATE) responded to PYRUKYND compared to 0% receiving placebo, meaning their Hb increased by 1.5 g/dL or greater during at least 2 of 3 checkups at weeks 16, 20, and 24.

In Study 1 (ACTIVATE), initial increases in average Hb levels were seen as early as 2 weeks after starting treatment, and improvements generally continued over the course of the 6-month period.



PYRUKYND was also shown to slow the process of RBC breakdown (hemolysis), which could help RBCs live longer.

Blood tests are used to measure levels of hemolysis. In clinical studies, **PYRUKYND noticeably improved***:

- Bilirubin
- Reticulocytes
- Haptoglobin
- Lactate dehydrogenase (LDH)

*Participants on PYRUKYND showed a -1.5 mg/dL reduction in bilirubin, a 15.8 mg/dL increase in haptoglobin, a -10% reduction in reticulocytes percentage, and a -71 U/L reduction in LDH.

IMPORTANT SAFETY INFORMATION (cont.)

Before taking PYRUKYND, tell your healthcare provider about all of your medical conditions, including if you:

- have liver problems
- are pregnant or plan to become pregnant. It is not known if PYRUKYND will harm your unborn baby. Tell your healthcare provider right away if you become pregnant or think that you are pregnant during treatment with PYRUKYND
- are breastfeeding or plan to breastfeed. It is not known if PYRUKYND passes into your breast milk. Talk to your healthcare provider about the best way to feed your baby during treatment with PYRUKYND

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A great day is when I get to hang out with my dog and do the things that fuel me. With my hemoglobin levels improving, I can see the difference.

—Jim, 22
Takes PYRUKYND



KEY TERMS

MEASURES OF HEMOLYSIS

Bilirubin

A substance released from RBCs when they break down, which can cause yellowing of the skin/eyes (jaundice). During hemolysis, bilirubin levels increase

Haptoglobin

A protein produced by the liver that the body uses to clear hemoglobin found outside of RBCs. During hemolysis, haptoglobin is low

Reticulocytes

RBCs that are still developing. During hemolysis, reticulocyte levels increase

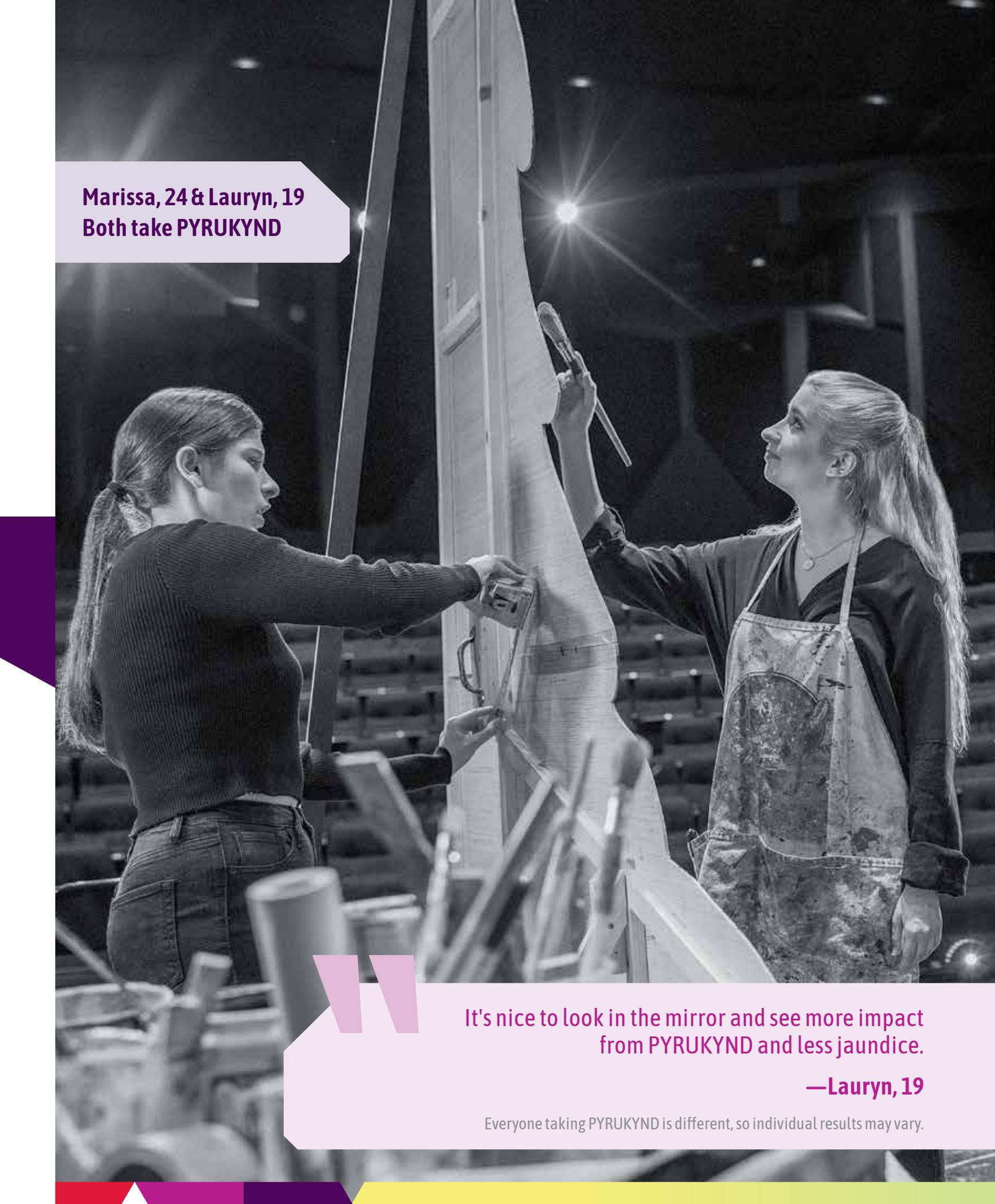
Lactate dehydrogenase (LDH)

An enzyme found in RBCs as well as other cells. A high LDH level is a sign of hemolysis, as it indicates that RBCs may be breaking apart

HOW PYRUKYND HELPS



Treatment experiences and results with PYRUKYND will be different for everyone.



**Marissa, 24 & Lauryn, 19
Both take PYRUKYND**

It's nice to look in the mirror and see more impact
from PYRUKYND and less jaundice.

—Lauryn, 19

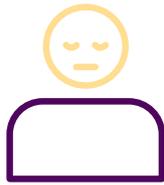
Everyone taking PYRUKYND is different, so individual results may vary.

A new day with PK deficiency and PYRUKYND[®]

Treating your PK deficiency with PYRUKYND may change the way you think about your daily symptoms

Patients taking PYRUKYND saw improvements in signs and symptoms of PK deficiency.

Over the course of the clinical study, the PK Deficiency Diary (PKDD) was used to help track changes in signs and symptoms of PK deficiency compared to placebo, such as:



JAUNDICE



TIREDNES



SHORTNESS OF BREATH

Before PYRUKYND, my day revolved around my PK deficiency, but now I feel less tired and my anemia has improved.

—Marissa, 24

Everyone taking PYRUKYND is different, so individual results may vary.



IMPORTANT SAFETY INFORMATION (cont.)

Tell your healthcare provider about all the medicines that you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. PYRUKYND and certain other medicines may affect each other causing side effects. PYRUKYND may affect the way other medicines work, and other medicines may affect how PYRUKYND works. Know the medicines you take. Keep a list of them to show your healthcare provider or pharmacist when you get a new medicine.

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Imagine an opportunity for fewer transfusions

Another possibility with PYRUKYND®

In some cases, people with PK deficiency receive regular transfusions. In Study 2 (ACTIVATE-T), the need for transfusions was evaluated in 27 participants who were regularly transfused.



Patients had the opportunity to have fewer transfusions.

33% of patients

experienced a $\geq 33\%$ reduction in the units transfused compared to their previous history*



And some were even transfusion free.

22% of patients

achieved transfusion-free status during the fixed-dose period of Study 2*

*Out of the 27 participants, 9 experienced a transfusion reduction and 6 became transfusion free.

IMPORTANT SAFETY INFORMATION (cont.)

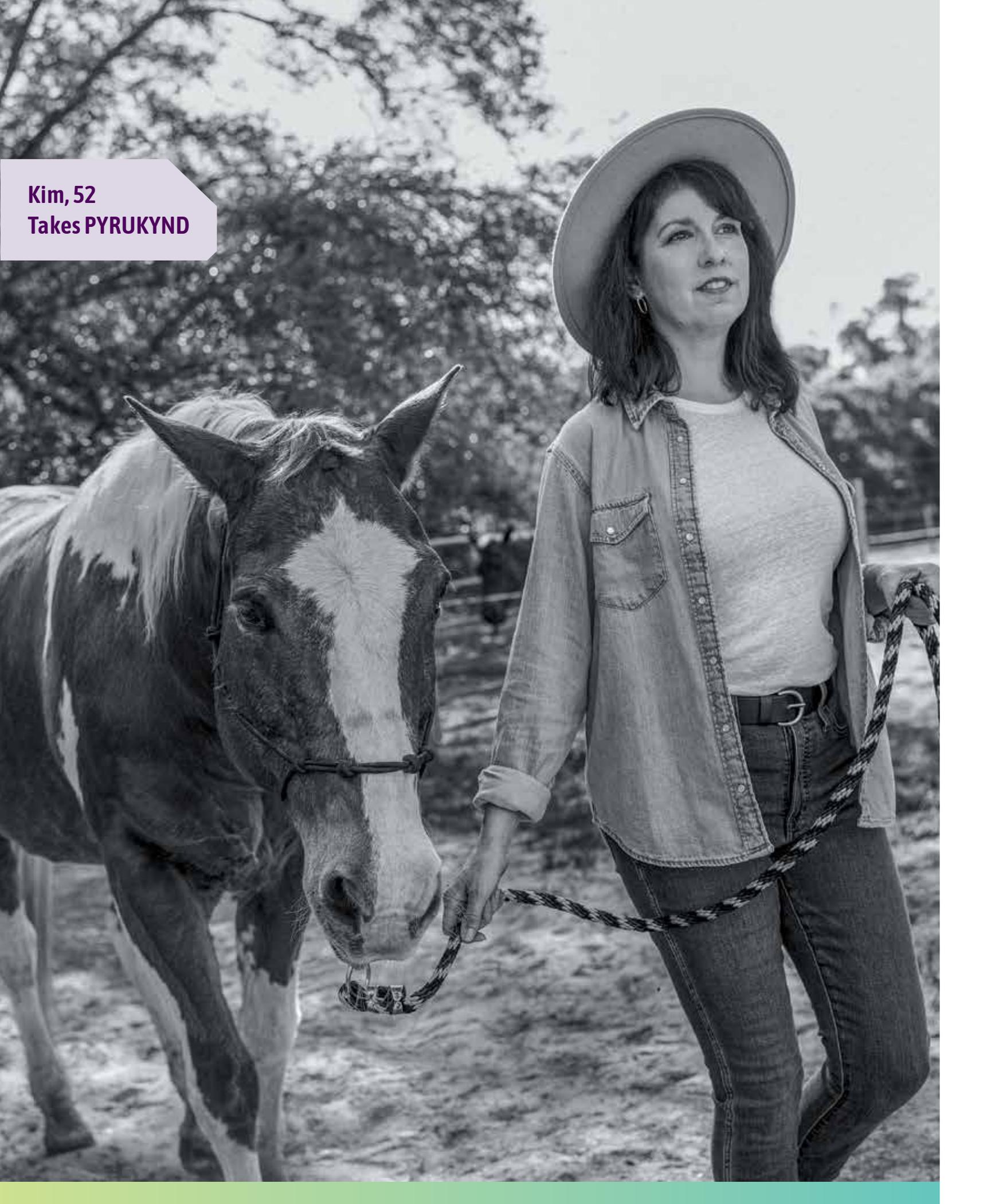
The most common side effects of PYRUKYND were decrease in reproductive hormone (estrone) in men, increased salt from uric acid (urate) blood test, back pain, decrease in reproductive hormone (estradiol) in men, and joint pain (arthralgia).

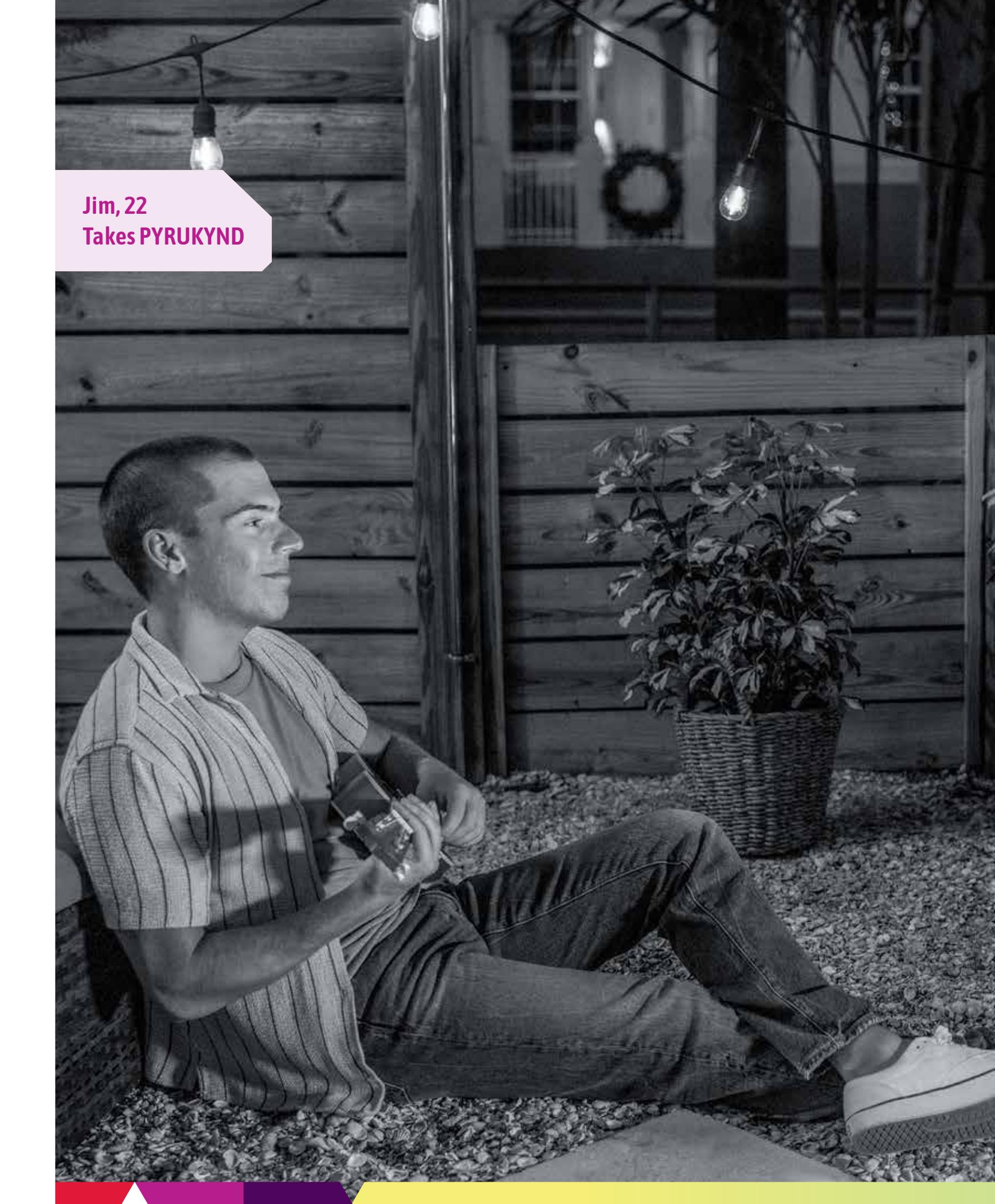
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Kim, 52
Takes PYRUKYND





Jim, 22
Takes PYRUKYND

What are the most common side effects of PYRUKYND®?

We know that starting a treatment can be overwhelming, especially if the treatment is new. As the first approved treatment for PK deficiency, PYRUKYND has been closely monitored through clinical studies.

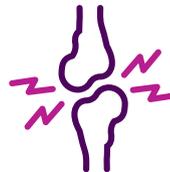
The most common side effects include:



decreases in reproductive hormones in males (estrone and estradiol)



increased salt from uric acid (urate)



joint pain



back pain



Tell your healthcare provider about the medicines you take.

PYRUKYND and certain other medicines may affect each other causing side effects.

PYRUKYND may affect the way other medicines work, and other medicines may affect how PYRUKYND works.

IMPORTANT SAFETY INFORMATION (cont.)

PYRUKYND may cause serious side effects, including:

- **Rapid breakdown of red blood cells (acute hemolysis)** has happened after suddenly interrupting or stopping treatment with PYRUKYND. **You should not suddenly stop taking PYRUKYND.** If you have to stop your treatment with PYRUKYND, your healthcare provider should monitor you closely. Tell your healthcare provider right away if you develop any signs or symptoms of breakdown of red blood cells including yellowing of the skin or the whites of your eyes (jaundice), dark colored urine, dizziness, confusion, feeling tired, or shortness of breath

The most common side effects of PYRUKYND were decrease in reproductive hormone (estrone) in men, increased salt from uric acid (urate) blood test, back pain, decrease in reproductive hormone (estradiol) in men, and joint pain (arthralgia).

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Getting started with PYRUKYND®



ONE ORAL TABLET, TWICE A DAY WITH OR WITHOUT FOOD

Check in with your doctor regularly to monitor your treatment progress and ask any questions you have while taking PYRUKYND.

Before starting PYRUKYND, your doctor will determine if your Hb is considered lower than normal and evaluate your need for transfusions. As you start treatment, your doctor may make adjustments as needed based upon changes in symptoms, Hb, need for transfusions, and potential side effects. If your Hb reaches a normal range, you'll stay at your current dose.

STEP ONE

Start at 5 mg twice a day

The starting dose for PYRUKYND is one 5-mg tablet taken orally twice daily for 4 weeks. Your doctor will assess your Hb after 3 weeks.

STEP TWO

Your doctor may increase your dose to 20 mg

After 4 weeks, your doctor may increase your dose of PYRUKYND to improve your body's Hb if:

- Your Hb stays below the normal range, or
- You've needed a transfusion within the last 8 weeks

If needed, your dose will increase from 5 mg twice daily to 20 mg twice daily.

STEP THREE

Your doctor may increase your dose to 50 mg

After 8 weeks, your doctor may increase your dose of PYRUKYND to 50 mg twice daily to increase your body's response if:

- Your Hb stays below the normal range after taking 20 mg of PYRUKYND twice daily, or
- You've needed a transfusion within the last 8 weeks

Your doctor will determine if other medications you're taking may cause your dosage to go above 50 mg twice daily.

Remember that PK deficiency is a chronic, genetic disease, which means it is persistent through life. Once treatment has started, it's important to continue with it.

Missing a dose

- If you miss a dose of PYRUKYND, there are ways to get back on track. If it's been 4 hours or less since the time you usually take it, take your dose as soon as possible
- If it's been over 4 hours since your missed dose, wait until your next scheduled dose and then return to your normal schedule

Stopping treatment

- **Make sure to discuss any changes with your doctor before you stop taking PYRUKYND. If you stop treatment abruptly, there is a risk of acute hemolysis.** Acute hemolysis is when large numbers of red blood cells are destroyed over a short time
- If you and your doctor decide you should stop taking PYRUKYND, you'll follow a schedule that slowly decreases your doses



Contact your healthcare provider immediately if you discontinue treatment and develop signs or symptoms of acute hemolysis, which include yellowing of the skin or eyes, darkening of the urine, dizziness, confusion, fatigue, and shortness of breath



Your myAgios® Patient Support Manager is available to help you. They can provide tips to stay on track with dosing and offer support if you lose or forget your prescription.

To schedule a phone or video call with your Patient Support Manager, call **1-800-951-3889**, Mon-Fri, 8 AM to 6 PM ET.

IMPORTANT SAFETY INFORMATION (cont.)

Tell your healthcare provider about all the medicines that you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. PYRUKYND and certain other medicines may affect each other causing side effects. PYRUKYND may affect the way other medicines work, and other medicines may affect how PYRUKYND works. Know the medicines you take. Keep a list of them to show your healthcare provider or pharmacist when you get a new medicine.

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myAgios[®] Patient Support Services is here to help

A customized support program for people living with PK deficiency and being treated with PYRUKYND[®] (mitapivat) tablets

Nefar Moran

Patient Support Manager
Cambridge, MA



Elisabeth Herdic

Patient Support Manager
Cambridge, MA

What is myAgios?

It's a patient support program for people living with PK deficiency and their caregivers, including those prescribed PYRUKYND. Experienced Patient Support Managers are available to support you throughout your journey, whether you've just been diagnosed or have had the condition for a long time. This program is free of charge. Please call our Patient Support Managers when you're ready to enroll and participate in the program.

If you and your doctor agree PYRUKYND is the right medicine to treat your PK deficiency, your doctor will complete and fax the enrollment form to myAgios. Your signature is needed to finish the enrollment, so your Patient Support Manager will work with you to get your signature and begin the next steps to start treatment.

IMPORTANT SAFETY INFORMATION (cont.)

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How do Patient Support Managers help?

Your dedicated Patient Support Manager will listen to understand the challenges you experience living with PK deficiency and is here to provide tailored help, including:



Financial support

- Verifying coverage with your insurance company and out-of-pocket costs for PYRUKYND
- Connecting with your healthcare provider to discuss your health insurance company's requirements or questions your insurance company has while determining your coverage
- Discussing your eligibility for certain financial assistance programs



Patient support

- Support while on treatment with PYRUKYND, including tips to help you stay on track with your treatment



Building a community

- Helping you advocate for yourself and working with you to prepare for upcoming doctor's appointments with your hematologist and care team
- Connecting you with the PK deficiency community through a series of patient-focused webinars. You can sign up at PYRUKYND.com, KnowPKDeficiency.com, or by calling your Patient Support Manager directly at 1-800-951-3889, Mon-Fri, 8 AM to 6 PM ET



Staying informed

- Providing PK deficiency disease education and connecting you with educational resources through KnowPKDeficiency.com

The purpose of this program is NOT to offer medical or treatment-related advice.
For these types of questions, contact your doctor.



We're ready when you are.
Get your questions answered by calling
our Patient Support Managers at
1-800-951-3889, Mon-Fri, 8 AM to 6 PM ET.


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myAgios[®] financial assistance

Get the information and answers you need

If you do not have insurance, myAgios Patient Support Managers can assist you with financial and coverage support to help you access PYRUKYND[®]. Available information includes:



The PYRUKYND Copay Program

- If you're eligible, this program can lower the copay to \$0 per prescription
- Patients participating in government healthcare insurance are not eligible



The Patient Assistance Program

- For eligible patients, Agios' Patient Assistance Program can offer access to medication if you are uninsured or underinsured



Coverage Interruption

- If you are on PYRUKYND, but experience an interruption in prescription coverage by your health insurance, you may be eligible for the Coverage Interruption Program
- Patients participating in government healthcare insurance are not eligible



Please visit PYRUKYND.myAgios.com/financial-support to learn more about financial assistance options and to see full Terms and Conditions.

Please see full Terms and Conditions on myAgios.com/PYRUKYND.

The purpose of this program is NOT to offer medical or treatment-related advice. For these types of questions, contact your healthcare professional.

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A black and white photograph of a woman, Marissa, working in a clothing store. She is wearing a headset with a microphone and holding a clipboard with a pen. She is smiling and looking towards the camera. The background shows racks of clothing and a counter area.

Marissa, 24
Takes PYRUKYND



Reimagine your PK deficiency with PYRUKYND[®], the first and only targeted treatment



Increased hemoglobin levels and improved hemolytic anemia (see page 10)*



Showed improvements in signs and symptoms of PK deficiency (see page 13)*†



Reduced need for transfusions (see page 14)‡



PYRUKYND is an oral tablet taken twice a day



Learn more about PYRUKYND and explore additional resources at PYRUKYND.com.

*Study 1 (ACTIVATE) measured hemoglobin level changes in 80 adults who were not regularly transfused (4 or fewer blood transfusions a year). A hemoglobin increase of at least 1.5 grams per deciliter in at least 2 of the 3 checkups (at weeks 16, 20, or 24) was counted as a response. In Study 1, 40% of participants responded to PYRUKYND, compared to 0% receiving placebo.

†In Study 1 (ACTIVATE), changes in signs and symptoms of PK deficiency (jaundice, tiredness, and shortness of breath) were measured.

‡Study 2 (ACTIVATE-T) measured whether the need for transfusions changed in 27 regularly transfused adults (6 or more blood transfusions a year). Once they reached a maintenance dose of PYRUKYND, a 33% or greater decrease in the number of red blood cell units received was counted as a response. In Study 2, 33% of patients responded to PYRUKYND.

WHAT IS PYRUKYND?

PYRUKYND is a prescription medicine used to treat low red blood cell counts caused by the early breakdown of red blood cells (hemolytic anemia) in adults with pyruvate kinase (PK) deficiency.

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

IMPORTANT SAFETY INFORMATION (cont.)

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