

A PKU TREATMENT THAT HELPS FIND

LESS LIMITS. MORE POSSIBILITIES.

See what
SEPHIENCE
can offer.



IMPORTANT SAFETY INFORMATION

What is SEPHIENCE?

SEPHIENCE™ (sepiapterin) is a prescription medicine used to lower blood levels of phenylalanine (Phe) in adults and children 1 month of age and older with a certain type of Phenylketonuria (PKU). SEPHIENCE is used along with a Phe-restricted diet. It is not known if SEPHIENCE is safe and effective in children younger than 1 month of age.

What is the most important information I should know about SEPHIENCE?

SEPHIENCE may cause serious side effects, including:

- **increased bleeding problems.** SEPHIENCE may increase your risk of bleeding. Tell your healthcare provider if you develop any symptoms of bleeding including:
 - bruising or red or purple skin marks
 - menstrual bleeding that is heavier than normal
 - bleeding longer than usual or that does not stop
- **low blood Phe (hypophenylalaninemia).** Low blood Phe levels are common during treatment with SEPHIENCE and can be severe.

Please see full Important Safety Information on [pages 10-11](#) and the [Full Prescribing Information](#).


Sephience™
sepiapterin
250 mg | 1000 mg Oral Powder

Navigating life with PKU

Living with Phenylketonuria—better known as PKU—comes with daily challenges, like managing phenylalanine (Phe) levels. SEPHIENCE is used to help manage Phe levels in people with PKU, as part of a Phe-restricted diet, allowing you to focus on what's important to you.

What is PKU?

PKU is a genetic disorder characterized by the body's inability to break down an amino acid called Phe. When we consume high-protein foods, the body breaks it down into smaller components like amino acids. In people with PKU, the body has trouble processing Phe properly, causing it to build up in the blood—which can lead to irreversible brain damage and other serious health problems.

What's it called when Phe is high?

It's called hyperphenylalaninemia—when too much Phe builds up in the blood.



What's the recommended Phe range?

Experts recommend keeping Phe $\leq 360 \mu\text{mol/L}$ ($\leq 6 \text{ mg/dL}$) for lifelong brain health.



Diet matters. People with PKU need to avoid high-protein foods like meat, fish, eggs, dairy products, and nuts, as these can raise Phe levels.

IMPORTANT SAFETY INFORMATION (cont'd)

What is the most important information I should know about SEPHIENCE? (cont'd)

The most common side effects of SEPHIENCE include: diarrhea, headache, stomach (abdominal) pain, yellow or orange stool (feces), and throat pain.

Tell your healthcare provider if you have any side effect that bothers you or that does not go away. These are not all the possible side effects of SEPHIENCE. Call your healthcare provider for medical advice about side effects.

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What is SEPHIENCE™?

SEPHIENCE is a prescription medicine used along with a Phe-restricted diet to lower blood levels of Phe in adults and children 1 month of age and older with PKU. It contains sepiapterin, which your body converts into tetrahydrobiopterin (BH_4)—a key molecule that supports the enzyme that breaks down Phe and reduces its buildup.

How SEPHIENCE works



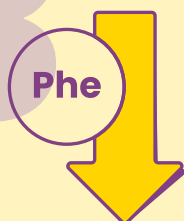
1 Taken as an oral powder



2 Converts to natural BH_4 , which aids Phe breakdown



3 Reduces Phe levels to help manage PKU



SEPHIENCE doesn't just add BH_4 —it helps your body make its own, supporting your natural process.



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

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Results with SEPHIENCE

SEPHIENCE was studied in APHENITY, a two-part clinical trial of people aged 1-61 years old living with PKU. During Part 1 of the trial, 156 participants received their age- and weight-specific dosage. In Part 2 of the trial, a total of 98 people with PKU, aged 2 years and older, who responded to SEPHIENCE in Part 1 were randomly assigned to receive either SEPHIENCE or a placebo for 6 weeks.

In Part 1 of the clinical trial,

SEPHIENCE began lowering blood Phe levels for many participants in the clinical trial after **2 weeks**.

66%

had $\geq 30\%$ reduction in Phe levels

73% had $\geq 15\%$ reduction in Phe levels



IMPORTANT SAFETY INFORMATION (cont'd)

What is the most important information I should know about SEPHIENCE? (cont'd)

Tell your healthcare provider about all medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. SEPHIENCE and other medicines may affect each other causing side effects. SEPHIENCE may affect the way other medicines work, and other medicines may affect how SEPHIENCE works. Especially tell your healthcare provider if you take:

- a medicine that contains levodopa
- an antifolate medicine
- another medicine also used to lower Phe
- medicines used to treat erectile dysfunction (phosphodiesterase 5 inhibitors or PDE5)

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In Part 2 of the clinical trial,

SEPHIENCE™ led to a significant reduction in blood Phe levels compared to placebo after **6 weeks**.

63%

reduction in Phe levels in the study population

Individual results may vary.



IMPORTANT SAFETY INFORMATION (cont'd)

What is the most important information I should know about SEPHIENCE? (cont'd)

Know the medicines you take. Keep a list of them with you to show your healthcare provider and pharmacist when you get a new medicine.

How should I take or give SEPHIENCE?

- Take or give SEPHIENCE exactly as your healthcare provider tells you. Your healthcare provider will tell you how much SEPHIENCE to take or give.
- Your healthcare provider may change your or your child's dose of SEPHIENCE depending on your weight and age.
- Take or give SEPHIENCE 1 time each day with food. You must take or give more food after the SEPHIENCE dose.

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Additional results with SEPHIENCE

Results across different types of PKU

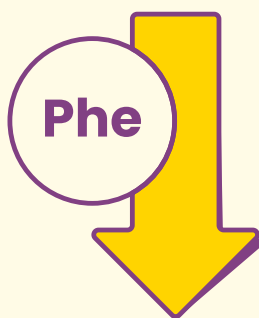
As part of the APHENITY study, SEPHIENCE was studied in people with different types of PKU, including those with classical PKU and those who had not responded to BH_4 treatment in the past. Classical PKU is the most severe form of PKU. People with classical PKU have had very high levels of blood Phe ($\geq 1200 \mu\text{mol/L}$) at some point in their lives, even if their levels are lower now. In both groups, SEPHIENCE significantly lowered the amount of Phe in the blood, showing it worked across a wide range of people with PKU.

For people with classical PKU

Blood Phe was reduced by

69%

on SEPHIENCE



For people not helped by BH_4 treatment in the past

Blood Phe was reduced by

54%

on SEPHIENCE

These findings help demonstrate the potential for SEPHIENCE to support people with PKU regardless of prior treatment experience or PKU type.

Individual results may vary. This information is based on clinical trial data but is not included in the approved full Prescribing Information for SEPHIENCE. Talk to your doctor if you have any questions.

IMPORTANT SAFETY INFORMATION (cont'd)

How should I take or give SEPHIENCE? (cont'd)

- SEPHIENCE comes as a packet containing oral powder.
 - For SEPHIENCE doses **less than** 1,000 mg: mix SEPHIENCE oral powder with water or apple juice before giving or taking.
 - For SEPHIENCE doses 1,000 mg or **greater**: SEPHIENCE oral powder can be mixed with water, apple juice, strawberry jam, or applesauce before taking or giving.
 - **See the detailed Instructions for Use that comes with SEPHIENCE for information about the correct way to prepare, take, or give a dose of SEPHIENCE oral powder.**

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Achieving recommended Phe levels

SEPHIENCE™ was studied to see how well it helps people with PKU reach blood Phe level targets recommended by experts.

These targets, set by the American College of Medical Genetics and Genomics, recommend maintaining a blood Phe level of ≤ 360 $\mu\text{mol/L}$ (or ≤ 6 mg/dL).

In the APHENITY trial:

84%

of participants taking SEPHIENCE reached that expert-recommended target

Only 9% of participants who took placebo achieved the same goal

Maintaining Phe levels within this recommended range is important for supporting brain development and long-term cognitive health.

IMPORTANT SAFETY INFORMATION (cont'd)

How should I take or give SEPHIENCE? (cont'd)

- If you or your child miss a dose of SEPHIENCE, take or give it as soon as possible. Do not take 2 doses in a day. Continue with your normal dosing schedule the following day.
- During treatment with SEPHIENCE, you or your child will have regular check-ups with your healthcare provider.
- Your healthcare provider will do blood tests before and during your treatment with SEPHIENCE to check your blood Phe levels.

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What to expect with SEPHIENCE

SEPHIENCE has been shown to provide effective management of Phe levels in clinical trials of people with PKU spanning a range of age groups.

SEPHIENCE may cause serious side effects, including an increased risk of bleeding or bruising. One person in the APHENITY trial experienced non-life-threatening bruising and prolonged bleeding, which resolved after treatment was discontinued. Contact your doctor if you notice any unusual bleeding. In children with PKU, it can sometimes cause very low levels of Phe in the blood, so regular monitoring is important. For those taking levodopa, your doctor should monitor for any side effects such as seizures, irritability, or feeling overly stimulated.

Side effects with SEPHIENCE may affect each person differently. Information on the long-term use of SEPHIENCE is limited.



IMPORTANT SAFETY INFORMATION (cont'd)

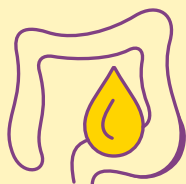
How should I take or give SEPHIENCE? (cont'd)

- Your healthcare provider may change your dose, temporarily stop, or permanently stop treatment with SEPHIENCE if you have certain side effects.
- Your healthcare provider may change your diet during treatment. Follow your healthcare provider's instructions and do not make any changes to your diet without first talking to your healthcare provider.

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Most common side effects



Diarrhea
(7%)



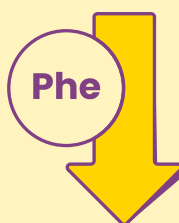
Headache
(7%)



Stomach pain
(5%)



Throat pain
(4%)

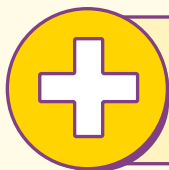


Low levels of Phe in the blood—
below the healthy range of
30–120 $\mu\text{mol/L}$ —also called
HypoPhe (4%)



Unusual-colored
feces
(4%)

These are not all the possible side effects of SEPHIENCE™. If you experience any side effects, talk to your doctor.



Talk to your doctor about your treatment and concerns—they're your best guide to managing PKU.

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- Your healthcare provider may change your diet during treatment. Follow your healthcare provider's instructions and do not make any changes to your diet without first talking to your healthcare provider.

To report an adverse event, please call [1-866-562-4620](tel:1-866-562-4620) or email at usmedinfo@ptcbio.com. You may also report side effects to FDA at [1-800-FDA-1088](tel:1-800-FDA-1088) or at www.fda.gov/medwatch.

Please see [Full Prescribing Information](#).



Once-daily dosing

Taking SEPHIENCE

- Take SEPHIENCE once a day, with food
 - Additional food intake is required after dosing
- It's best to take SEPHIENCE at the same time each day
- Your doctor will tell you the right dose based on your (or your loved one's) body weight and age

Mixing SEPHIENCE

- Comes in **250 mg** and **1000 mg** powder packets
- Mix with water, apple juice, or soft food (only for doses ≥ 1000 mg) like applesauce or strawberry jam
- May cause staining when in contact with certain surfaces. To minimize this risk, use as directed

Personalized dose tracking

Record the dose as discussed with your doctor and update it as needed. For additional dosing guidance, visit the [dose calculator on the SEPHIENCE website](#).

If the daily dose is: **<1000 mg**

Daily dose mg	Number of packets		Mix in mL of water or apple juice	Prescribed volume mL to be administered
	<input type="text"/> 250 mg	<input type="text"/> 1000 mg		

OR

If the daily dose is: **≥ 1000 mg**

Daily dose mg	Number of packets		Mix in mL or Tbsp of water, apple juice, strawberry jam, or applesauce	Administer the full volume
	<input type="text"/> 250 mg	<input type="text"/> 1000 mg		

AND/OR

IMPORTANT SAFETY INFORMATION (cont'd)

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Follow these steps to take SEPHIENCE™



Prepare

Mix the correct number of packets with water, apple juice, or soft food (only for doses ≥ 1000 mg), such as applesauce or strawberry jam



Mix until combined

- Stir liquids for at least 30 seconds
- Stir soft foods for at least 60 seconds

Note: oral powder is not expected to dissolve completely. This is normal.



Use as directed

- Drink or swallow the full amount
- For doses < 1000 mg: Use an oral syringe to draw up the prescribed dose and administer



Rinse & finish

- Rinse the cup or syringe with water or juice
- Swallow the rinse until clean to make sure you get the full dose



If you need to store it

- If not taken right away, cover and store the mix:
 - In the refrigerator (36°F to 46°F/2°C to 8°C) for up to 24 hours
 - At room temperature (68°F to 77°F/20°C to 25°C) for up to 6 hours
- Stir again before using (see step 2) for at least 30 to 60 seconds

Refer to Prescribing Information (page 18) for [Instructions for Use](#).

IMPORTANT SAFETY INFORMATION (cont'd)

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**WE'VE
GOT YOU
COVERED**

Not actual patients.

**Enroll in PTC Cares to get connected
with your dedicated Case Manager.**

PTC Cares Case Managers guide families through treatment, insurance, and medication access. Think of your Case Manager as your personal guide!

My Case Manager

Name

Phone Number

Have questions?

Contact PTC Cares at
1-844-4PTC-CARES
(1-844-478-2227)

Monday to Friday, 8am to 6pm (EST)



How we can help with PKU treatment costs

Our Case Managers explore every possible option to help you access the PKU medication your doctor prescribes. PTC Therapeutics offers several programs to help.



The Copay Assistance Program*†

May help qualified families who have commercial insurance get help covering out-of-pocket costs associated with treatment. Patients who qualify may pay as little as \$0 copay.



The Bridge Program*

May provide patients a temporary supply of PTC medication free of charge while they await verification of insurance coverage.



Patient Assistance Program (PAP)

May help patients without insurance, who are eligible, get access to treatment.

*Low to no out-of-pocket costs for most patients who qualify.

†Not valid for prescriptions eligible to be reimbursed, in whole or in part, by Medicaid or Medicare (including Medicare Part D), or where prohibited by law.

Join PTC Cares, treatment support for people and families living with PKU

To get started, simply sign the PKU Patient Consent for the PTC Cares Program online at PTCCares.com.



A PKU TREATMENT THAT HELPS FIND

LESS LIMITS. MORE POSSIBILITIES.

See what SEPHIENCE can offer.



Flexible once-daily dosing



Shown to reduce Phe levels
across all ages, from children
to adults



Support and resources
available at every step



Proven safety profile

Visit [SEPHIENCE.com](https://sephience.com) or speak
with your doctor for more information

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PTC
THERAPEUTICS

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Seth,
Living with PKU

