Sephience™
sepiapterin
250 mg | 1000 mg Oral Powder

FOR HEALTHCARE PROFESSIONALS

SEPHIENCE Dosing and Administration

Once-daily powder packets available in two strengths for flexible, weight-based adjustments as patients grow[1]

- **Once-daily dosing with liquid or soft food**
- **Age- and weight-based dosing**
- **Two strengths (250 mg | 1000 mg) for individualized dosing**

Product not shown at actual size.

INDICATION
SEPHIENCE™ (sepiapterin) is indicated for the treatment of hyperphenylalaninemia (HPA) in adult and pediatric patients 1 month of age and older with sepiapterin-responsive phenylketonuria (PKU). SEPHIENCE is to be used in conjunction with a phenylalanine (Phe)-restricted diet.

IMPORTANT SAFETY INFORMATION
Treatment with SEPHIENCE should be directed by physicians knowledgeable in the management of PKU. Biochemical response to SEPHIENCE can only be determined by a therapeutic trial with careful monitoring of ongoing dietary and nutritional balance to ensure adequate Phe control.

Please see additional Important Safety Information throughout and the Full Prescribing Information.

Designed for Every Age (>1 Month) and Every Stage

The patient's age determines the starting dose[1]

Recommended Starting Dose

FOR PATIENTS AGED	RECOMMENDED DOSE OF SEPHIENCE™*,†
<6 months	7.5 mg/kg/day
6 months to <1 year	15 mg/kg/day
1 year to <2 years	30 mg/kg/day
≥2 years	60 mg/kg/day

*For calculated daily doses less than 1000 mg, the final concentration of prepared SEPHIENCE liquid mixture is 25 mg/mL.
†60 mg/kg is the maximum daily dose for all patients.

Dose modifications based on weight are essential to maintain SEPHIENCE effectiveness

For SEPHIENCE doses ≥1000 mg

Daily dose (mg)	Number of 1000 mg packets[a]	Number of 250 mg packets[a]	Volume of water, apple juice, strawberry jam, or applesauce[b]
1000 mg to 1124 mg	1	0	2 Tbsp or 30 mL
1125 mg to 1374 mg	1	1	4 Tbsp or 60 mL
1375 mg to 1624 mg	1	2	
1625 mg to 1874 mg	1	3	
1875 mg to 2124 mg	2	0	
2125 mg to 2374 mg	2	1	6 Tbsp or 90 mL
2375 mg to 2624 mg	2	2	
2625 mg to 2874 mg	2	3	
2875 mg to 3124 mg	3	0	
3125 mg to 3374 mg	3	1	8 Tbsp or 120 mL
3375 mg to 3624 mg	3	2	
3625 mg to 3874 mg	3	3	
3875 mg to 4124 mg	4	0	
4125 mg to 4374 mg	4	1	10 Tbsp or 150 mL
4375 mg to 4624 mg	4	2	
4625 mg to 4874 mg	4	3	

Round calculated daily doses to the nearest 250 mg to determine the number of SEPHIENCE packets: round up if the dose is less than 1000 mg; round to the nearest 250 mg if 1000 mg or more

For patients under 2 years old, check Phe levels within 2 weeks of starting treatment and titrate as needed (up to 60 mg/kg/day)

Please see the full Prescribing Information for more information.

mg, milligrams; mL, milliliters; Tbsp, tablespoons.

[a]For calculated daily doses 1000 mg or greater, round the dose to the nearest 250 mg to determine the number of SEPHIENCE packets required.
[b]For each 1000 mg packet, add 2 Tbsp (30 mL) of water, apple juice, strawberry jam, or applesauce, and then add an additional quantity of 2 Tbsp (30 mL) for up to three 250 mg packet(s) and then mix.

IMPORTANT SAFETY INFORMATION (cont'd)

Warnings and Precautions

- **Increased Bleeding**: SEPHIENCE may increase the risk of bleeding. Bleeding events, including superficial hematomas, prolonged bleeding, and heavy menstrual bleeding have occurred in patients treated with SEPHIENCE. Inform patients about the risk of bleeding associated with SEPHIENCE and have patients follow up with their healthcare provider should such a bleeding event occur. Consider treatment interruption with SEPHIENCE in patients with active bleeding.

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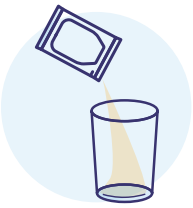
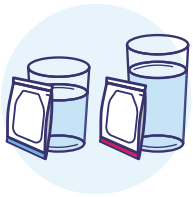
Made to Mix into Daily Routines

Clear steps for preparing SEPHIENCE—for all doses[1]

Doses <1000 mg (Liquid Prep):



1 Empty packet(s) into a cup



2

- Mix each 250 mg packet with 9 mL of water or apple juice

OR

- Mix one 1000 mg packet with 36 mL of water or apple juice

3 Stir for ≥30 seconds until uniform. The oral powder is not expected to dissolve completely. This is normal

4 Use an oral syringe to draw up the prescribed dose and administer the entire dose immediately

$$\text{Prescribed dose volume (mL)} = \frac{\text{SEPHIENCE calculated dose (mg)}}{25\ \text{mg/mL}}$$

5 Rinse the syringe with more liquid to catch residual. Repeat if particles remain

Doses ≥1000 mg (Liquid or Soft Food):

1 Round the dose to the nearest multiple of 250 mg or 1000 mg dose

2 Mix each 250 mg and 1000 mg packet with water, apple juice, strawberry jam, or applesauce. To determine the volume of liquid or soft food, refer to the table on the previous page or the full Prescribing Information

3 Stir for ≥30 seconds (liquid) or ≥60 seconds (soft food) until uniform. The oral powder is not expected to dissolve completely. This is normal

4 Consume the entire mixture immediately. Rinse the container with liquid and re-administer if particles remain

Careful mixing, dosing, and rinsing can help minimize the potential for staining from SEPHIENCE; following the instructions helps ensure proper administration.

IMPORTANT SAFETY INFORMATION (cont'd)

Warnings and Precautions (cont'd)

- **Hypophenylalaninemia:** Some pediatric patients receiving SEPHIENCE experienced hypophenylalaninemia. Monitor blood Phe levels during treatment and modify the dosage of SEPHIENCE and/or dietary protein and Phe intake as needed to ensure adequate blood Phe level control. Frequent blood monitoring is recommended in the pediatric population.

Please see additional Important Safety Information throughout and the Full Prescribing Information.

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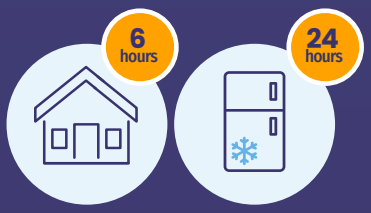
After Prep: Store Properly. Stir Before Use.

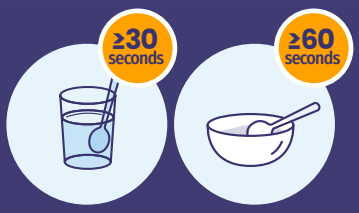
Proper handling helps to ensure dose accuracy and safety[1]

Storage Tips:

Use immediately after mixing



Store sealed mixture:
Room temp: up to 6 hours
Refrigerated: up to 24 hours



Stir again before administration:
Liquid: ≥30 seconds
Soft food: ≥60 seconds

Missed Dose?

Take as soon as remembered

Never double dose on the same day

Visit HCP.SEPHIENCE.com for more information

IMPORTANT SAFETY INFORMATION (cont'd)

Warnings and Precautions (cont'd)

- **Interaction with Levodopa**: In a 10-year post-marketing safety surveillance program for a non-PKU indication using another drug that is a phenylalanine hydroxylase (PAH) activator, 3 patients with underlying neurological disorders experienced seizures, exacerbation of seizures, over-stimulation, and irritability during co-administration with levodopa. Monitor patients who are receiving levodopa for changes in neurological status during treatment with SEPHIENCE.

Adverse Reactions

Most common adverse reactions with SEPHIENCE (≥2% and > placebo) were diarrhea, headache, abdominal pain, hypophenylalaninemia, feces discoloration, and oropharyngeal pain.

Drug Interactions

Avoid concomitant use of drugs known to inhibit folate synthesis dihydrofolate reductase (DHFR) (e.g., trimethoprim, methotrexate, trimetrexate, pemetrexed, pralatrexate, raltitrexed, and piritrexim) while taking SEPHIENCE. Concomitant administration of such drugs may reduce sepiapterin metabolism to BH_4. If concomitant use is not avoidable, monitor blood Phe levels.

SEPHIENCE and PDE-5 inhibitors (e.g., sildenafil, vardenafil, or tadalafil) induce vasorelaxation and may reduce blood pressure. Monitor for signs and symptoms of hypotension.

For medical information, product complaints, or to report an adverse event, please call 1-866-562-4620 or email at usmedinfo@ptcbio.com.

You may also report adverse events directly to FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see Full Prescribing Information.

Reference: 1. SEPHIENCE Prescribing Information. PTC Therapeutics. 2025.

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PTC THERAPEUTICS™