Pr Sephience™ sepiapterin

FOR HEALTHCARE PROFESSIONALS

SEPHIENCE™ (sepiapterin for oral suspension) Dosing and Administration Guide

Key information on dosing and administration to help you incorporate SEPHIENCE into your patients' treatment plans.

Dosing based on age and body weight

Once-daily oral administration taken with food

Powder available in 250 mg and 1000 mg sachets

INDICATION

SEPHIENCE™ (sepiapterin for oral suspension) 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 indicated in conjunction with a phenylalanine (Phe)-restricted diet.

Recommended Dosing by Age

The recommended dosage of SEPHIENCE is calculated based on age and body weight (kg) of the patient. The dose is administered orally once daily with food.

As children get older and gain weight, periodic dose adjustments will ensure the proper dosing of SEPHIENCE.

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.
*Maximum recommended daily dose.

Dietary Phe Intake

Patients treated with SEPHIENCE should undergo regular clinical assessments to align with their healthcare provider on appropriate dietary Phe intake.

Dose modifications based on weight are essential to maintain SEPHIENCE effectiveness

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 less than 2 years of age, check Phe levels within 2 weeks of starting treatment and titrate as needed (up to 60 mg/kg/day)

Steps for preparing SEPHIENCE—for all doses[1]

Doses <1000 mg (Liquid Prep):

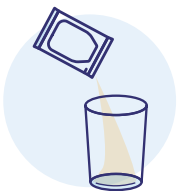
Number of SEPHIENCE Sachets and Volume to Prepare a SEPHIENCE Mixture of 25 mg/mL for Doses Less than 1000 mg

Daily dose (mg)	Number of 1000 mg sachets[a]	Number of 250 mg sachets[a]	Volume of water or apple juice (mL)[b]
250 mg or less	0	1	9 mL
251 mg to 500 mg	0	2	18 mL
501 mg to 750 mg	0	3	27 mL
751 mg to 999 mg	1	0	36 mL

Please see the full Product Monograph for more information.

mg- milligrams; mL- milliliters

[a] For calculated daily doses less than 1000 mg, round the dose up to the nearest 250 mg to determine the number of SEPHIENCE sachets and prepare each 250 mg sachet with 9 mL of water or apple juice.
[b] Patients younger than 6 months of age should only use water to mix with SEPHIENCE.



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. SEPHIENCE is not expected to dissolve completely. This is normal.

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

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

5 Draw up more water or apple juice into the oral syringe to catch residual. Repeat if particles remain.

Doses ≥1000 mg (Liquid or Soft Food):

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	
4875 mg to 5124 mg	5	0	
5125 mg to 5374 mg	5	1	12 Tbsp or 180 mL
5375 mg to 5624 mg	5	2	
5625 mg to 5874 mg	5	3	
5875 mg to 6124 mg	6	0	

Please see the full Product Monograph 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.

1 Round the dose to the nearest multiple of 250 mg.

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 above.

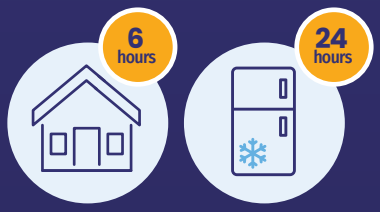
3 Stir for ≥30 seconds (liquid) or ≥60 seconds (soft food) until uniform. The oral powder is not expected to dissolve completely. This is normal.

4 Consume the entire mixture immediately. If any mixture remains in the container, rinse with water or apple juice and re-administer until no mixture remains.

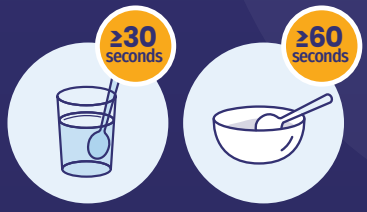
After Prep: Store Properly. Stir Before Use.

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

Each prepared dose is best administered immediately after preparation, if not:



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

Two doses should not be administered on the same day

SAFETY SUMMARY[1]

Adverse Reaction Overview:

- The safety profile of SEPHIENCE™ (sepiapterin for oral suspension) is based on clinical trials in pediatric and adult patients with PKU who received doses ranging from 7.5 to 60 mg/kg/day. The most frequently reported (≥2%) treatment-related adverse reactions (pooled across 2 clinical studies) were diarrhea, headache, feces discoloured, vomiting, nausea, upper abdominal pain, and fatigue. Cases of hypophenylalaninemia occurred more frequently in children, including some with multiple low blood Phe levels
- Five patients discontinued treatment due to adverse reactions, including: anxiety, vomiting, constipation, nausea, headache and hemorrhagic diathesis
- Long-term safety data are limited, especially for patients <2 years of age

Contraindications:

- SEPHIENCE is contraindicated in patients with hypersensitivity to sepiapterin or to any ingredient in the formulation, including any non-medicinal ingredient or component of the container

Relevant Warnings and Precautions:

- Patients treated with SEPHIENCE should undergo baseline and regular monitoring of blood Phe levels, along with appropriate dietary guidance from their healthcare provider and a dietitian, to maintain Phe within the desired range. Frequent monitoring is recommended, especially in pediatric patients
- Prolonged low blood Phe levels (hypophenylalaninemia) have been associated with protein catabolism and endogenous protein breakdown, which results in adverse developmental and neurodevelopmental outcomes
- Patients with rare hereditary fructose intolerance should not take this medicine due to isomalt content
- Increased bleeding: SEPHIENCE may increase the risk of bleeding. Bleeding events, including superficial hematomas, prolonged bleeding, epistaxis, and heavy menstrual bleeding have occurred in patients treated with SEPHIENCE. Advise patients to report bleeding and consider treatment interruption/discontinuation if active bleeding occurs
- The safety and efficacy of SEPHIENCE in patients with hepatic or renal impairment have not been established
- There are no adequate and well-controlled studies with SEPHIENCE in pregnancy or breastfeeding. Caution should be exercised when prescribing to these patients
- The safety and efficacy of SEPHIENCE in patients 65 years of age and older have not been established

Use Caution When Co-Administered With:

- Sepiapterin reductase (SR) inhibitors (e.g., sulfasalazine, sulfamethoxazole)
- Dihydrofolate reductase (DHFR) inhibitors (e.g., methotrexate, trimethoprim, pemetrexed, pralatrexate, trimetrexate)
- Drugs that cause vasodilation, including those administered topically, by affecting nitric oxide (NO) metabolism or action, including classical NO donors (e.g., glyceryl trinitrate, isosorbide dinitrate, sodium nitroprusside, molsidomin), PDE5 inhibitors (sildenafil, vardenafil, tadalafil), and minoxidil
- Levodopa, due to risk of seizures, excitability, or irritability

Patients receiving these drugs may require closer monitoring of blood Phe levels and/or blood pressure.

For More Information:

Please consult the Product Monograph at https://pdf.hres.ca/dpd_pm/00081969.PDF for important information about adverse reactions and drug interactions, how to calculate weight-based dosing, and instructions on preparing and administering each dose.

Reference:

1. SEPHIENCE Product Monograph. PTC Therapeutics; October 2025.

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