

## Patient Medication Information

### READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

Pr **SEPHIENCE™**

#### **sepiapterin for oral suspension**

This Patient Medication Information is written for the person who will be taking **SEPHIENCE**. This may be you or a person you are caring for. Read this information carefully. Keep it as you may need to read it again.

This Patient Medication Information is a summary. It will not tell you everything about this medication. If you have more questions about this medication or want more information about **SEPHIENCE**, talk to a healthcare professional.

#### **What SEPHIENCE is used for:**

SEPHIENCE is used to lower blood levels of phenylalanine (Phe) in adults and children 1 month of age and older with phenylketonuria (PKU) who have shown they respond to sepiapterin, the medicinal ingredient in SEPHIENCE. It is used together with a Phe-restricted diet.

Your healthcare professional will test you over a 14 consecutive day evaluation period to determine if SEPHIENCE is right for you.

#### **How SEPHIENCE works:**

Our bodies break down the protein in foods into amino acids. Phenylketonuria (PKU) is an inherited disease where people cannot break down the amino acid phenylalanine (Phe), causing a buildup in the blood and brain, which can be harmful. SEPHIENCE contains the medicinal ingredient sepiapterin, which is used by the body to help break down Phe. This reduces the harmful excess of Phe in the blood.

#### **The ingredients in SEPHIENCE are:**

Medicinal ingredient: sepiapterin

Non-medicinal ingredients: colloidal silicon dioxide, croscarmellose sodium, isomalt, magnesium stearate, mannitol, microcrystalline cellulose, sucralose, and xanthan gum

#### **SEPHIENCE comes in the following dosage forms:**

Powder: 250 mg and 1000 mg

#### **Do not use SEPHIENCE if:**

- you are allergic to sepiapterin or any of the non-medicinal ingredients in SEPHIENCE (see **The ingredients in SEPHIENCE are:**)

**To help avoid side effects and ensure proper use, talk to your healthcare professional before you take SEPHIENCE. Talk about any health conditions or problems you may have, including if you:**

- have a rare hereditary intolerance to fructose as SEPHIENCE contains isomalt as a non-medicinal ingredient

- are taking medicines called “dihydrofolate reductase (DHFR) inhibitors” that affect how your body uses the B vitamin folate, such as methotrexate, pemetrexed, pralatrexate, or trimetrexate, which are used for cancer treatment and to treat some immune system disorders
- have liver or kidney problems
- are taking levodopa, used to treat Parkinson’s disease. Taking SEPHIENCE with levodopa can cause over-stimulation, irritability or seizures or make seizures worse.
- are pregnant or planning to become pregnant
- are breastfeeding or planning to breastfeed

**Other warnings you should know about:**

- **Risk of bleeding:** SEPHIENCE can increase your risk of bleeding. This can include bruising or red or purple skin marks, bleeding that lasts longer than usual or does not stop, nose bleeds and heavy menstrual bleeding. If you notice any unusual bleeding while you are taking SEPHIENCE talk to your healthcare professional.
- **Low blood Phe (hypophenylalaninemia):** This is common during treatment and can be severe. Your healthcare professional will check your blood Phe levels before you start taking SEPHIENCE. They will monitor your blood Phe levels along with your dietary protein and Phe intake frequently while you are being treated with SEPHIENCE.

**Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements, or alternative medicines.**

**The following may interact with SEPHIENCE:**

- medicines called “DHFR inhibitors” that are used to suppress the immune system or for treatment of cancer, such as trimethoprim, methotrexate, pemetrexed, pralatrexate, trimetrexate
- medicines called “sepiapterin reductase (SR) inhibitors” used for the treatment of inflammation, such as sulfasalazine, or for the treatment of bacterial infections, such as sulfamethoxazole
- medicines used to prevent and treat chest pain (angina), such as glyceryl trinitrate (GTN), isosorbide dinitrate (ISDN), sodium nitroprusside (SNP), molsidomin
- medicines used to treat erectile dysfunction, such as sildenafil, vardenafil, tadalafil
- minoxidil, used to stimulate hair growth and slow down balding
- levodopa, used to treat Parkinson’s disease

**How to take SEPHIENCE:**

- **Always take this medicine exactly as your healthcare professional has told you.** Check with your healthcare professional if you are not sure.
- **Do not** stop taking SEPHIENCE or change your dose without talking to your healthcare professional, as phenylalanine levels in your blood may increase.
- Your healthcare professional will do blood tests before and during your treatment with SEPHIENCE to check your blood Phe levels.
- Your healthcare professional may change your dose, temporarily stop, or permanently stop treatment with SEPHIENCE if your blood tests show it is not working or if you have certain side effects.
- Your healthcare professional may change your diet during treatment. Follow your healthcare professional’s instructions and do not make any changes to your diet without first talking to your healthcare professional.

- Take SEPHIENCE orally, once daily with food.
- SEPHIENCE can be mixed in water, apple juice, or soft foods such as apple sauce or jam. The dose is based on age and body weight. Your healthcare professional will tell you:
  - which sachet dose to use (250 mg or 1000 mg)
  - the amount of water, apple juice, or soft foods to be added to SEPHIENCE
  - the amount you will need to take for your prescribed dose
- **For patients less than 6 months of age:** SEPHIENCE should be mixed only in water. Do not mix with soft foods, such as apple sauce or strawberry jam, or with apple juice.
- **For patients 6 months to 2 years of age:** SEPHIENCE should be mixed in water or apple juice.
- The powder should be mixed well for at least 30 seconds with water or apple juice and for at least 60 seconds with soft food. Once mixed, the dose should be taken immediately.
- If the dose is not taken immediately, the liquid and soft food mixtures can be used within 6 hours when stored between 20°C and 25°C or within 24 hours when stored in the refrigerator. Before giving the dose, the liquid mixture or soft food mixture should be stirred once again for at least 30 seconds or 60 seconds, respectively.
- An accurate measuring device (e.g. oral dosing syringe or medicine cup) with suitable graduations should be used to make sure the dose contains the appropriate volume of liquid mixture.
- Please see the **Instructions for Use** at the end of this leaflet for complete instructions on how to prepare and administer SEPHIENCE.

**Usual dose:**

The dose depends on your age and weight in kilograms (kg), and this will be calculated by your healthcare professional who prescribes it for you (or your child).

The starting dose is:

**Children younger than 2 years**

- Under 6 months: 7.5 mg / kg body weight once a day
- Between 6 and 12 months: 15 mg / kg body weight once a day
- Between 12 and 24 months: 30 mg / kg body weight once a day

Some patients may need an increase in their dose. This will be determined by your healthcare professional. The maximum dose is 60 mg / kg.

**Adults and children 2 years of age and older**

- The starting, recommended and maximum dose is 60 mg / kg body weight once a day.

**Overdose:**

If you think you, or a person you are caring for, have taken too much SEPHIENCE, contact a healthcare professional, hospital emergency department, regional poison control center or Health Canada’s toll-free number, 1-844 POISON-X (1-844-764-7669) immediately, even if there are no signs or symptoms.

**Missed Dose:**

If you missed a dose of this medication, take it as soon as you remember on the same day. Then go back to your normal dosing schedule on the next day. Do not take two doses at the same time.

### Possible side effects from using SEPHIENCE:

These are not all the possible side effects you may have when taking SEPHIENCE. If you experience any side effects not listed here, tell your healthcare professional.

#### Side effects may include:

- diarrhea
- nausea, vomiting
- stomach pain
- unusual-coloured feces (yellow or orange)
- headache
- fatigue

#### Serious side effects and what to do about them

Frequency/Side Effect/Symptom	Talk to your healthcare professional		Stop taking this drug and get immediate medical help
	Only if severe	In all cases	
<b>Unknown</b>			
<b>Bleeding problems:</b> bruising, red or purple skin marks, bleeding that lasts longer than usual or does not stop, nose bleeds, heavy menstrual bleeding		√	

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

#### Reporting side effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting ([canada.ca/drug-device-reporting](http://canada.ca/drug-device-reporting)) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your healthcare professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

#### Storage:

Store at room temperature (15°C to 25°C).

Keep out of reach and sight of children.

After mixing the medicine, take it immediately. If not, the solution or mixture may be covered and stored up to 24 hours in the refrigerator (2°C to 8°C) or up to 6 hours between 20°C and 25°C.

Discard unused SEPHIENCE solution or mixture after 6 hours between 20°C and 25°C or after 24 hours if refrigerated.

**If you want more information about SEPHIENCE:**

- Talk to your healthcare professional.
- Find the full product monograph that is prepared for healthcare professionals and includes the Patient Medication Information by visiting the Health Canada Drug Product Database website: (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html>); or by calling 1-866-899-7002.

This leaflet was prepared by PTC Therapeutics International Limited.

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**INSTRUCTIONS FOR USE**  
**SEPHIENCE (seh-FIGH-ence)**  
**sepiapterin for oral suspension**

This Instructions for Use contains information on how to prepare, take, or give SEPHIENCE.

Ask your healthcare professional if you have any questions on how to prepare, take, or give SEPHIENCE.

**The preparation steps differ based on the prescribed dose. Follow the steps specific to the dose your healthcare professional has prescribed. See the section called:**

- **Instructions for SEPHIENCE Doses Less Than 1,000 mg or**
- **Instructions for SEPHIENCE Doses 1,000 mg or Greater**

**Each SEPHIENCE carton contains:**

- 30 SEPHIENCE 250 mg dose sachets **or**
- 30 SEPHIENCE 1,000 mg dose sachets

**Important information you need to know before taking or giving SEPHIENCE:**

- SEPHIENCE comes as a sachet containing powder.
- Take or give SEPHIENCE exactly as your healthcare professional tells you.
- Be sure that you know what dose of SEPHIENCE your healthcare professional has prescribed. Your healthcare professional will prescribe SEPHIENCE 250 mg sachet(s), SEPHIENCE 1,000 mg sachet(s), or both types of sachets to prepare your dose.
- Your healthcare professional may change your dose of SEPHIENCE depending on how you respond to treatment and based on your weight and age.
- Take or give SEPHIENCE 1 time each day with food. You must take or give more food after each SEPHIENCE dose.
- **Do not** use SEPHIENCE sachet(s) after the expiration date on the sachet(s) and box. The expiration date is the last day of the expiration month.
- **For SEPHIENCE doses less than 1,000 mg:** SEPHIENCE is to be mixed with water or apple juice before taking or giving. Follow the section called **Instructions for SEPHIENCE Doses Less Than 1,000 mg**.
- **For SEPHIENCE doses 1,000 mg or greater:** SEPHIENCE can be mixed with water, apple juice, strawberry jam, or applesauce before taking or giving. Follow the section called **Instructions for SEPHIENCE Doses 1,000 mg or Greater**.

## Instructions for SEPHIENCE Doses Less Than 1,000 mg:

### How to prepare SEPHIENCE mixture for doses less than 1,000 mg:

- The dose of SEPHIENCE is based on body weight. This will change as your child grows. Your healthcare professional will tell you:
  - the number of SEPHIENCE sachets needed for one dose,
    - For patients less than 6 months of age, SEPHIENCE should only be mixed in water.
    - For patients 6 months to 2 years of age, SEPHIENCE should be mixed in water or apple juice.
  - the amount of water or apple juice needed to mix one dose of SEPHIENCE, and
  - the amount of the mixture (powder and water or apple juice) to give your child for their prescribed dose.
- **You may need to measure a smaller amount of mixture than you prepared to take or give the correct prescribed dose of SEPHIENCE.**

### Supplies needed to mix and give SEPHIENCE doses less than 1,000 mg:

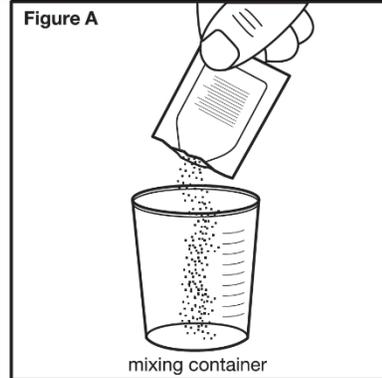
- The number of SEPHIENCE 250 mg sachet(s) needed for 1 dose, or one SEPHIENCE 1,000 mg sachet(s)
- 1 small cup of water **or** apple juice
- 1 mixing container
- 1 small spoon
- a 10 mL oral dosing syringe or recommended oral dosing syringe
- scissors (optional)

Ask your pharmacist for a container for mixing SEPHIENCE and an oral dosing syringe if you do not have these supplies.

**Step 1:** Find a clean, flat work surface. Place the following items on your clean, flat work surface:

- prescribed number of SEPHIENCE sachets for your daily dose
- a small cup of water **or** apple juice
- mixing container
- small spoon
- oral dosing syringe

**Step 2:** Check the label on the SEPHIENCE sachet(s) to make sure you have the number of sachets for the prescribed dose. Open the SEPHIENCE sachet(s) by folding and tearing at the tear notch, or using scissors to cut the sachet(s) open at the dotted line. Empty the entire contents of **each** SEPHIENCE sachet(s) into the mixing container (see **Figure A**).



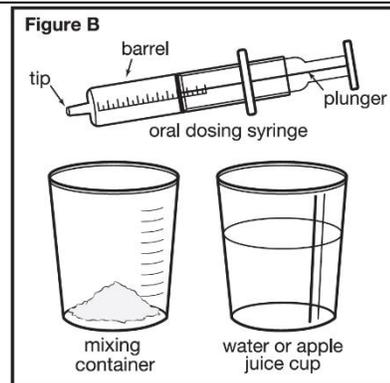
**Step 3:** Place the tip of the oral dosing syringe into the cup containing the water or apple juice. Pull back on the plunger and draw up the amount of water or apple juice needed to prepare the sachet(s) for the prescribed dose.

**Use 9 mL of water (if less than 6 months of age) or 9 mL of water or apple juice (if 6 months to 2 years of age) for each 250 mg sachet.** For example:

- If you are preparing 1 sachet of SEPHIENCE, you will need to add 9 mL of water or apple juice.
- If you are preparing 2 sachets of SEPHIENCE, you will need to add 18 mL of water or apple juice.
- If you are preparing 3 sachets of SEPHIENCE, you will need to add 27 mL of water or apple juice.
- If you are preparing 4 sachets of SEPHIENCE, you will need to add 36 mL of water or apple juice.

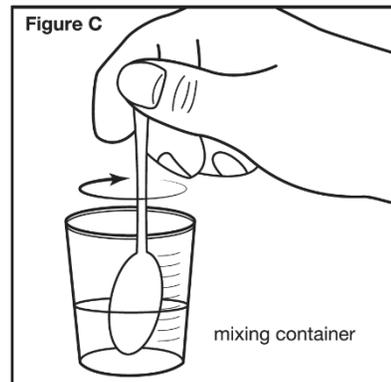
**If you are using one 1,000 mg sachet to prepare the prescribed dose, you will need to add 36 mL of water or apple juice.**

Slowly add the water or apple juice to the mixing container containing the SEPHIENCE powder. Repeat until the entire amount of water or apple juice that is needed to mix the number of SEPHIENCE sachets has been added to the mixing container (see **Figure B**).

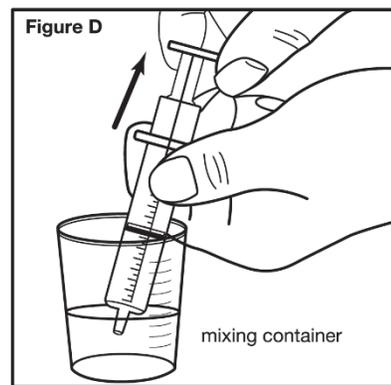


**Step 4:** Stir the SEPHIENCE mixed with water **or** apple juice well for 30 seconds or more with a small spoon until the SEPHIENCE mixture is free of lumps (see **Figure C**).

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



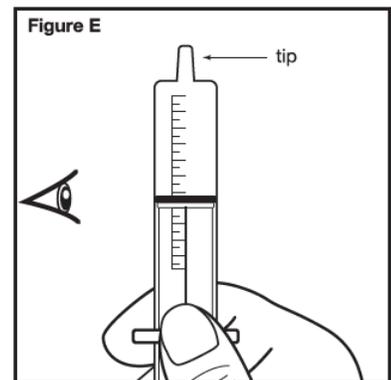
**Step 5:** Place the tip of the oral dosing syringe into the mixture inside the mixing container. Pull back on the plunger until the edge of the plunger lines up with the marking for the dose as instructed by your healthcare professional in mL (milliliters) (see **Figure D**).



**Step 6:** Take the oral dosing syringe out of the mixing container. Carefully turn the oral dosing syringe so that the tip is pointing up. Check the syringe marking to make sure that the amount of SEPHIENCE mixture in the oral dosing syringe lines up with the prescribed SEPHIENCE dose in mL (milliliters) (see **Figure E**).

Your dose may be different than the dose shown in **Figure E**.

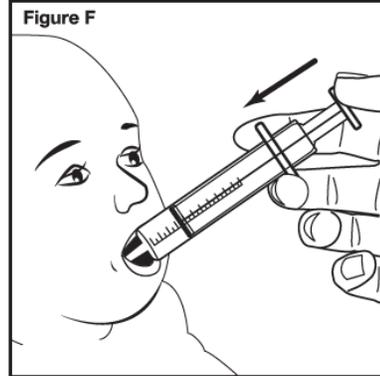
Give SEPHIENCE mixture right away after it is drawn up into the syringe.



**Step 7:** Place the tip of the oral dosing syringe into your child's mouth. Point the tip of the oral dosing syringe toward either cheek (see **Figure F**).

Push on the plunger slowly, until all the mixture in the oral dosing syringe is given.

If the prescribed dose is more than 10 mL, **repeat** Step 5 to Step 7 until you give the **total amount of prescribed dose in mL (milliliters)** by your healthcare professional.



**Step 8:** If there is any mixture left in the oral dosing syringe, draw up more water or apple juice into the oral dosing syringe and give until no mixture is left in the oral dosing syringe.

**Step 9:** Throw away (in household garbage) any SEPHIENCE mixture remaining in the mixing container.

Remove the plunger from the barrel of the oral dosing syringe. Wash the oral dosing syringe and mixing container with warm water and air dry. When the oral dosing syringe is dry, put the plunger back into the barrel. Store the oral dosing syringe and mixing container for the next use.

## Instructions for SEPHIENCE Doses 1,000 mg or Greater:

### How to prepare SEPHIENCE mixture for doses 1,000 mg or greater:

- Your healthcare professional will tell you the number of sachets, and the amount of water, apple juice, strawberry jam, or applesauce needed to mix 1 dose of SEPHIENCE per Table 1 below.

### Supplies needed to mix and take or give SEPHIENCE doses 1,000 mg or greater:

- The number of SEPHIENCE 250 mg sachet(s) and/or SEPHIENCE 1,000 mg sachet(s) needed for 1 dose
- a small cup of water, apple juice, strawberry jam, **or** applesauce
- 1 tablespoon to measure the water, apple juice, strawberry jam, **or** applesauce
- additional small cup of water **or** apple juice to rinse the mixing container
- 1 mixing container
- scissors (optional)

Ask your pharmacist for a container for mixing SEPHIENCE if you do not have one.

**Table 1: Number of SEPHIENCE Sachets to Prepare a SEPHIENCE Mixture for Doses of 1,000 mg or Greater**

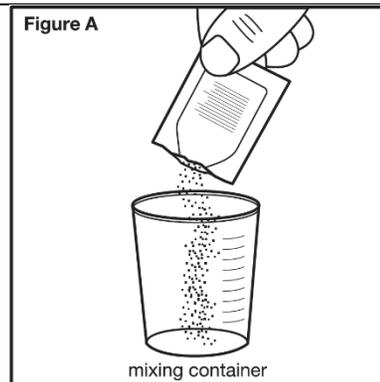
Find your prescribed number of sachets:		Choose one of the following:
Number of 1,000 mg sachets	Number of 250 mg sachets	<ul style="list-style-type: none"> <li>Water</li> <li>Apple juice</li> <li>Strawberry jam</li> <li>Applesauce</li> </ul>
		Amount of water, apple juice, strawberry jam, <b>or</b> applesauce to mix the sachet(s)
1	0	2 Tbsp or 30 mL
1	1	4 Tbsp or 60 mL
1	2	4 Tbsp or 60 mL
1	3	4 Tbsp or 60 mL
2	0	4 Tbsp or 60 mL
2	1	6 Tbsp or 90 mL
2	2	6 Tbsp or 90 mL
2	3	6 Tbsp or 90 mL
3	0	6 Tbsp or 90 mL
3	1	8 Tbsp or 120 mL
3	2	8 Tbsp or 120 mL
3	3	8 Tbsp or 120 mL

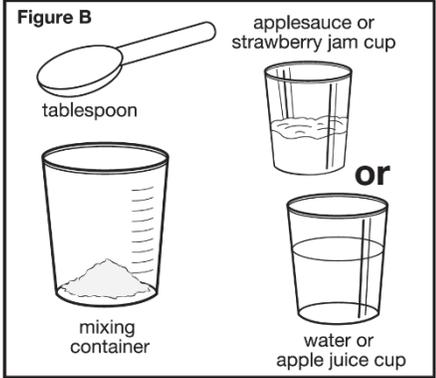
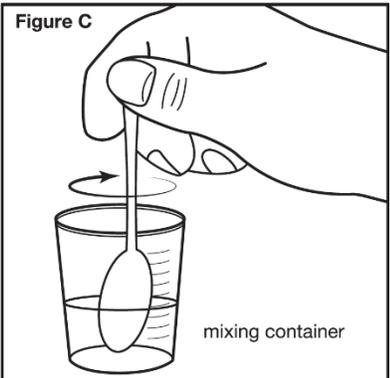
4	0	8 Tbsp or 120 mL
4	1	10 Tbsp or 150 mL
4	2	10 Tbsp or 150 mL
4	3	10 Tbsp or 150 mL
5	0	10 Tbsp or 150 mL
5	1	12 Tbsp or 180 mL
5	2	12 Tbsp or 180 mL
5	3	12 Tbsp or 180 mL
6	0	12 Tbsp or 180 mL

**Step 1:** Find a clean, flat work surface. Place the following items on your clean, flat work surface:

- prescribed number of SEPHIENCE sachets
- a small cup of water, apple juice, strawberry jam, **or** applesauce
- additional small cup of water **or** apple juice to rinse the cup (see **Step 6** below)
- tablespoon
- mixing container

**Step 2:** Check the label on the SEPHIENCE sachet(s) to make sure you have the number of sachets for the prescribed dose. Open the SEPHIENCE sachet(s) by folding and tearing at the tear notch or using scissors to cut the sachet(s) open at the dotted line. Empty the entire contents of **each** SEPHIENCE sachet(s) into the mixing container (see **Figure A**).



<p><b>Step 3:</b> Mix the SEPHIENCE sachet(s) with water, apple juice, strawberry jam, <b>or</b> applesauce. See Table 1 above.</p> <p>Slowly add the water, apple juice, strawberry jam, <b>or</b> applesauce to the mixing container containing the SEPHIENCE powder. Repeat until the entire amount of water, apple juice, strawberry jam, <b>or</b> applesauce that is needed to mix the number of SEPHIENCE sachets has been added to the mixing container (see <b>Figure B</b>).</p>	 <p><b>Figure B</b></p> <p>applesauce or strawberry jam cup</p> <p>tablespoon</p> <p>mixing container</p> <p>water or apple juice cup</p> <p><b>or</b></p>
<p><b>Step 4:</b> If you used water or apple juice to mix the SEPHIENCE sachet(s), stir the mixture well for 30 seconds or more with the tablespoon until the SEPHIENCE mixture is free of lumps (see <b>Figure C</b>).</p> <p>SEPHIENCE is not expected to dissolve completely.</p> <p style="text-align: center;"><b>or</b></p> <p>If you used strawberry jam or applesauce to mix the SEPHIENCE sachet(s), stir the mixture well for 60 seconds or more with the tablespoon.</p>	 <p><b>Figure C</b></p> <p>mixing container</p>
<p><b>Step 5:</b> Give or take all of the SEPHIENCE mixture from the mixing container.</p>	
<p><b>Step 6:</b> If any SEPHIENCE mixture remains in the mixing container, rinse the container with water or apple juice (at least 15 mL). Swallow the rinse right away. <b>Repeat this step until no mixture remains in the mixing container.</b></p>	
<p><b>Step 7:</b> Wash the mixing container with warm water and air dry. Store the mixing container for the next use.</p>	

Manufactured for:  
PTC Therapeutics International Limited  
Dublin 4, D04EE70, Ireland