Patient Enrollment Form for Sapropterin Dihydrochloride Tablets or Powder for Oral Solution

Phone: +1 (888) 360-8482 **FAX: +1 (888) 385-8482**

All required fields are purple and noted with an asterisk*

PATIENT INFORMATION

Patient Last Name*		Patient First Name*	
Date of Birth*	Gender* ☐ Male ☐ Female ☐ Other	Parent/Guardian Name *(if patient is a minor)*	
Street Address*		Suite/Floor/Apt #	
City*		State*	Zip Code*

Preferred Method of Contact (please specify)*

☐ Cell Phone ☐ Alternate Phone

☐ Email

Language Preferred: ☐ English ☐ Spanish ☐ Other *(please specify):*

INSURANCE INFORMATION

Please attach a copy of the prescription insurance benefit card, front and back, or complete the following*

☐ Prescription insurance benefit card attached. ☐ Patient does not have a prescription.

Primary Insurance Company Name*		Secondary Insurance Company Name	
Primary Insurance Company Phone Number*		Secondary Insurance Company Phone Number	
Patient is Primary Cardholder*		Patient is Primary Cardholder	
Primary Insurance Member ID*	Group ID*	Secondary Insurance Member ID	Group ID
BIN*	PCN*	BIN	PCN

CLINICAL INFORMATION

Diagnosis ICD-10-CM* : _____

Please specify: _____

☐ Sapropterin Dihydrochloride Tablets for Oral Use and Powder for Oral Solution are indicated to reduce blood phenylalanine (Phe) levels in adult and pediatric patients one month of age and older with hyperphenylalaninemia (HPA) due to tetrahydrobiopterin- (BH4-) responsive Phenylketonuria (PKU). SAPROPTERIN DIHYDROCHLORIDE is to be used in conjunction with a Phe-restricted diet.

☐ Other Diagnosis *(please specify):* _____

Baseline Blood Phenylalanine (Phe) Levels *(before trial):*

Date: _____

I am prescribing Sapropterin Dihydrochloride for this patient and is medically necessary for the following reasons:

☐ To reduce blood Phe levels ☐ Other (please specify)_____

Additional Comments: _____

Patient Allergies*:

☐ No Known ☐ Known *(please list known allergies):*

_____

Patient Medications*:

☐ None ☐ Please list the names of other medications the patient is currently taking *(if any):*

_____

Patient Health Conditions*:

☐ No Known ☐ Please list the names of any other health conditions the patient currently has *(if any):*

_____

RDY-0222-391

Patient Full Name*	Date of Birth*

PRESCRIBER INFORMATION

Prescriber Last Name*	Prescriber First Name*	Prescriber Specialty: ☐ Genetics ☐ Internal Medicine ☐ Other *(please specify):*	
Prescriber Office/Site/Clinic*		Office Contact	Office Contact Phone Number
Prescriber Phone Number*		Prescriber Fax Number*	
Street Address*			
City*		State*	Zip Code*
NPI Number*			

PRESCRIPTION INFORMATION

☐ **Try Sapropterin – The Sapropterin Support Program for Sapropterin Dihydrochloride will provide up to a 30-day supply of Sapropterin Dihydrochloride for patients new to therapy.**

By checking this box, I, as the prescriber, with my signature below on this form, agree and attest that I will not submit a claim to or seek payment from the patient or any third-party payer (e.g., Medicaid, Medicare, private insurance, etc.) for payment/reimbursement for any free product(s) provided by the Sapropterin Support Program for Sapropterin Dihydrochloride. I agree and understand that any free product provided by the Sapropterin Support Program for Sapropterin Dihydrochloride may not be sold, traded, bartered, transferred, or returned for credit and will only be used for the patient named above on this form.

Current weight _____ kg. Dose per kg body weight: ☐ 10 mg/kg ☐ 20 mg/kg ☐ Other _____ mg/kg Number of days' supply/prescription: ☐ 30 days ☐ 90 days	Refill(s): ☐ One (1) Year
☐ Sapropterin Dihydrochloride, *Powder for Oral Solution / 100 mg (Single Unit Dose Packet)*	NDC Number: 43598-477-11 (Single Unit Dose Packet)
☐ Sapropterin Dihydrochloride, *Powder for Oral Solution / 100 mg (Carton of 30 Unit Dose Packets)*	NDC Number: 43598-477-30 (Carton of 30 Unit Dose Packets)
☐ Sapropterin Dihydrochloride, *Tablet 100 mg*	NDC Number: 43598-749-04

Only prescriptions filled with product NDC numbers listed above shall be eligible for the Sapropterin Support Program for Sapropterin Dihydrochloride (Eligible Products).

Patient Directions *(check all that apply):* ☐ Please contact your physician before starting use of the medication. ☐ Take _____ 100 mg Sapropterin Dihydrochloride (powder) once daily, as directed, with a meal, for a total dose of _____ mg/day. Note: Sapropterin Dihydrochloride powder for oral solution should be dissolved as directed by the physician before taking. ☐ Take _____ 100 mg Sapropterin Dihydrochloride (tablet) once daily, as directed, with a meal, for a total dose of _____ mg/day. ☐ Other: _____	Shipping Instructions *(check if applicable):* ☐ Dispensing pharmacy to notify prescriber when initial shipment is scheduled.

☐ **Bridge Prescription† - The Sapropterin Support Program for Sapropterin Dihydrochloride will provide up to a 30-day supply of Sapropterin Dihydrochloride for patients experiencing any disruption in therapy due to insurance coverage.**

By checking the box above for bridge prescription, I, as the prescriber, with my signature below on this form, agree and attest that I will not submit a claim to or seek payment from the patient or any third-party payer (e.g., Medicaid, Medicare, private insurance, etc.) for payment/reimbursement for any free product(s) provided by the Sapropterin Support Program for Eligible Products. I agree and understand that any free product provided by the Sapropterin Support Program for Eligible Products may not be sold, traded, bartered, transferred, or returned for credit and will only be used for the patient named above on this form. The Sapropterin Support Program for Eligible Products reserves the right to modify or terminate the program without notice at any time.

† Bridge prescription is at no cost, for eligible patients within labeled indication only, and not contingent on purchase of any kind. Bridge prescription is intended to support continuation of prescribed therapy if there is any disruption in therapy due to insurance coverage.

PRESCRIPTION DECLARATION

Prescriber Declaration: I understand and agree that, as the prescriber, I will comply with my state-specific prescription requirements such as e-prescribing, state-specific prescription form, fax language, etc. Non-compliance with state-specific requirements could result in outreach to me, as the prescriber. I verify that the patient and prescriber information contained in this enrollment form is complete and accurate to the best of my knowledge and that I have prescribed Sapropterin Dihydrochloride based on my professional judgment of medical necessity. I authorize the Sapropterin Support Program for Eligible Products, its affiliates, agents, and contractors (collectively, "The Sapropterin Support Program for Eligible Products to act on my behalf for the limited purposes of transmitting this prescription to the appropriate pharmacy designated by the above-named patient utilizing their benefit plan. I authorize the Sapropterin Support Program for Eligible Products, its affiliates, agents and contractors to perform any steps necessary to secure reimbursement for Sapropterin Dihydrochloride, including but not limited to insurance verification and case assessment. I understand that the Sapropterin Support Program for Eligible Products may need additional information, and I agree to provide it as needed for the purposes of securing reimbursement.

Prescriber Signature *(please select one of the options below)**	Date:
Prescriber Signature/Dispense as Written (DAW) (no stamps or initials)	Prescriber Signature/Substitution Permitted (no stamps or initials)

Patient Full Name*	Date of Birth*

Patient Authorization for Use and Disclosure of Personal Health Information (PHI)

I understand that I must complete this enrollment form before I can receive assistance through CYCLE Pharmaceuticals, Ltd., and the Sapropterin Support Program for Sapropterin Dihydrochloride. I understand that the Sapropterin Support Program for Sapropterin Dihydrochloride is only applicable for the Eligible Product. As part of this process, CYCLE and its agents and contractors (collectively, "CYCLE") will need to obtain, review, use and disclose PHI as described below.

To ensure I have access to the Sapropterin Support Program for Sapropterin Dihydrochloride benefits for which I may qualify AND to ensure my Personal Health Information (PHI) is appropriately protected in compliance with applicable federal laws and regulations:

- **I hereby authorize the Sapropterin Support Program for Sapropterin Dihydrochloride to contact me by mail, e-mail, text, phone, or any communication method I request for the purposes as described herein.**
- **I further authorize my healthcare providers (HCPs) and health plans to disclose my PHI as described below to an authorized CYCLE Health Care Professional (HCP) in connection with Sapropterin Support Program for Sapropterin Dihydrochloride, and I authorize CYCLE to use and disclose the information for the purposes stated in this authorization.**

1. **<u>Information to Be Disclosed</u>: Personal health information (PHI), including information about me (for example, name, mailing address, financial information, and insurance), my past, current and future medical condition and information provided on this form to include information concerning Adverse Events (AE).**
2. **<u>Persons Authorized to Disclose My Information</u>: My HCPs, including any pharmacy that fills my prescription medication, and any health plans or programs that provide me healthcare benefits.**
3. **<u>Persons to Whom My Information May Be Disclosed</u>: A qualified HCP, a nurse, individuals representing CYCLE, including third-party administrator responsible for the administration of the Sapropterin Support Program for Sapropterin Dihydrochloride, appropriate third parties under contract to CYCLE, such as the CYCLE Pharmacovigilance Agency and product manufacturer(s) to properly address any Adverse Event (AE). I understand my PHI will only be shared in accordance with my consent as described within this form.**
4. **<u>Purposes for Which the Disclosures Are to Be Made</u>: Disclosures of PHI may be made to CYCLE so that CYCLE may use and disclose the PHI for purposes of completing the enrollment process, verifying my enrollment form and establishing my eligibility for Sapropterin Support Program for Sapropterin Dihydrochloride and benefits that may include:**
    a. **<u>Insurance and Reimbursement Assistance</u>: Authorization allows for professional assistance at no charge on Patient's behalf for Claims Settlement, Claims Submission – to**

health insurers (for payment); communication of relevant claim information to/from HCPs and Insurance carriers.

b. Reimbursement Support: Financial Assistance, including CYCLE's sponsored Co-Pay Assistance, is available only for eligible patients. Co-Pay assistance allows CYCLE Pharmaceuticals LTD. to pay associated Co-Payments due to Insurance providers on behalf of the Patient.

c. Patient Benefits Investigation & Payer Prior-Authorization Support: Sapropterin Support Program for Sapropterin Dihydrochloride will contact, investigate, and arrange for Patient's eligible coverage with their respective Health Insurer and/or PBM (Pharmacy Benefit Manager), as well as support and appropriately assist with Prior-Authorizations.

d. Patient Education and Information: CYCLE and the Sapropterin Support Program for Sapropterin Dihydrochloride will provide Patients with full education on Sapropterin Support Program for Sapropterin Dihydrochloride administration, relevant disease area information and product information updates; in addition to pertinent updates and information on events for patients. This includes advocacy communication from national and international patient advocacy groups.

e. Access to Manufacturer / CYCLE: This will allow CYCLE to alert Patients receiving Sapropterin Support Program for Sapropterin Dihydrochloride about relevant product and market updates, product recalls, Adverse Event notifications, and available resources, including adherence tools and other programs to benefit patients with Hereditary Angioedema (HAE).

5. Limits of Protections after Disclosure. I understand that once my PHI has been disclosed hereunder, federal privacy law may no longer restrict its use or disclosure.
6. Option to Refuse. I understand I am not required to sign this Authorization as a condition to receive treatment with CYCLE's products, or payment for health care; enrolling in a health plan; or establishing eligibility for benefits. However, by refusing to authorize disclosure of my PHI to a qualified and authorized CYCLE HCP, I also understand that I am knowingly foregoing possible access to the Sapropterin Support Program for Sapropterin Dihydrochloride benefits.
7. Copy of Authorization and Ability to Cancel Authorization. I understand I will be given a copy of this Authorization after I sign it; and my Authorization shall remain in effect until it expires (i.e. 5 years from the date sign below unless a shorter period is required by the law of my state residence), or unless I revoke Authorization at any time by contacting the Sapropterin Support Program for Sapropterin Dihydrochloride on (toll-free), at +1 (888) 360-8482 (VITA) Monday through Friday, from 8:00am to 8:00pm EST, by FAX, at +1 (888) 385-8482 (VITA) or in writing to CYCLE Pharmaceuticals Ltd., PO Box 130059, Boston, MA 02113.
8. I understand that my pharmacy, health insurers and third-party vendors may receive payment from Manufacturer for product support provided to patients. My PHI is used for the sole purpose of providing me access to important patient support described within this enrollment form.

Patient Full Name*	Date of Birth*

9. **I understand that this program guarantees that I will receive Sapropterin Dihydrochloride [NDCs: 43598-477-11 / 43598-477-30 / 43598-749-04]. By signing, I elect to receive the generic product specified within this enrollment form. No substitutions will be made or given.**

PATIENT AUTHORIZATION **(To be completed by the Sapropterin Support Program for Sapropterin Dihydrochloride Patient):**

I have read and understood the Patient Authorization Information (starting on Page 3) and by signing this form authorize the use and disclosure of my health information as described above.

***Signature NOT required to begin benefit investigation. Authorization may also be collected verbally upon completion of benefit investigation with Cycle Vita™.**

_____

Patient Name (Printed)

_____ _____

Signature of Patient **Date**

_____ _____

Signature of Patient Representative* **Date**

***If signed by Patient Representative, please explain authority / relation to act on behalf of patient:**

Please read the following statements and mark each box:

☐ **I hereby authorize the Cycle Vita™ –Sapropterin Support Program for Sapropterin Dihydrochloride to use my PHI to contact me by mail, e-mail, text, phone, or any communication method I request for the purposes as described herein.**

☐ **Further, I understand that this program guarantees that I will receive Cycle Vita™ – Sapropterin Support Program for Sapropterin Dihydrochloride [NDC: (43598-477-11 / 43598-477-30 / 43598-749-04)] rather than other products. By signing, I elect to receive the generic product specified within this enrollment form. No substitutions will be made or given.**

Patient Full Name*	Date of Birth*

INDICATION

SAPROPTERIN DIHYDROCHLORIDE Tablets for Oral Use and Powder for Oral Solution are indicated to reduce blood phenylalanine (Phe) levels in adult and pediatric patients one month of age and older with hyperphenylalaninemia (HPA) due to tetrahydrobiopterin-(BH4-) responsive Phenylketonuria (PKU). SAPROPTERIN DIHYDROCHLORIDE is to be used in conjunction with a Phe-restricted diet.

IMPORTANT SAFETY INFORMATION

Treatment with SAPROPTERIN DIHYDROCHLORIDE should be directed by physicians knowledgeable in the management of PKU. All patients with PKU who are being treated with sapropterin dihydrochloride should also be treated with a Phe-restricted diet, including dietary protein and Phe restriction. Prolonged exposure to elevated blood Phe levels can result in severe neurologic damage in PKU patients.

During treatment with Sapropterin Dihydrochloride, monitor blood Phe levels frequently to ensure adequate blood Phe level control, especially in pediatric patients. Also, active management of dietary Phe intake is required to ensure adequate Phe control and nutritional balance. Biochemical response to SAPROPTERIN DIHYDROCHLORIDE treatment should be determined through a therapeutic trial.

Patients should be advised to notify their physicians in cases of overdose.

WARNINGS AND PRECAUTIONS

- **Hypersensitivity Reactions Including Anaphylaxis:** SAPROPTERIN DIHYDROCHLORIDE is not recommended in patients with a history of anaphylaxis to SAPROPTERIN DIHYDROCHLORIDE. Hypersensitivity reactions, including anaphylaxis and rash, have occurred. Signs of anaphylaxis include wheezing, dyspnea, coughing, hypotension, flushing, nausea, and rash. Discontinue SAPROPTERIN DIHYDROCHLORIDE treatment in patients who experience anaphylaxis, and initiate appropriate medical treatment. Continue dietary protein and Phe restrictions in patients who experience anaphylaxis.
- **Upper Gastrointestinal Mucosal Inflammation:** Gastrointestinal (GI) adverse reactions suggestive of upper GI mucosal inflammation have been reported with SAPROPTERIN DIHYDROCHLORIDE. Serious adverse reactions included esophagitis and gastritis. If left untreated, these could lead to severe sequelae including esophageal stricture, esophageal ulcer, gastric ulcer, and bleeding, and such complications have been reported in patients receiving SAPROPTERIN DIHYDROCHLORIDE. Monitor patients for signs and symptoms of upper GI mucosal inflammation.
- **Hypophenylalaninemia:** Some patients receiving SAPROPTERIN DIHYDROCHLORIDE have experienced hypophenylalaninemia (low blood Phe) during treatment. Children younger than 7 years old treated with SAPROPTERIN DIHYDROCHLORIDE doses of 20 mg/kg per day are at an increased risk for low levels of blood Phe compared with older patients.
- **Monitoring Blood Phe Levels During Treatment:** Prolonged elevations of blood Phe levels in patients with PKU can result in severe neurologic damage, including severe intellectual disability, developmental delay, microcephaly, delayed speech, seizures, and behavioral abnormalities. Conversely, prolonged levels of blood Phe that are too low have been associated with catabolism and endogenous protein breakdown, which has been associated with adverse developmental outcomes.
  Active management of dietary Phe intake while taking sapropterin dihydrochloride is required to ensure adequate Phe control and nutritional balance. Monitor blood Phe levels during treatment to ensure adequate blood Phe level control. Frequent blood monitoring is recommended in the pediatric population.
- **Lack of Biochemical Response to SAPROPTERIN DIHYDROCHLORIDE:** Not all patients with PKU respond to treatment with SAPROPTERIN DIHYDROCHLORIDE. Biochemical response to SAPROPTERIN DIHYDROCHLORIDE treatment cannot generally be pre-determined by laboratory testing (e.g., molecular testing), and should be determined through a therapeutic trial (evaluation) of SAPROPTERIN DIHYDROCHLORIDE response.
- **Interactions with Levodopa:** There have been reports of interactions with levodopa causing seizures, exacerbation of seizures, over-stimulation, and irritability. Monitor patients who are receiving levodopa for a change in neurologic status during treatment with SAPROPTERIN DIHYDROCHLORIDE.
- **Hyperactivity:** There have been post-marketing reports of hyperactivity with administration of SAPROPTERIN DIHYDROCHLORIDE. Monitor patients for hyperactivity.

Patient Full Name*	Date of Birth*

ADVERSE REACTIONS

- **Most common:** The most common adverse reactions (incidence ≥4%) were headache, rhinorrhea, pharyngolaryngeal pain, diarrhea, vomiting, cough, and nasal congestion.

The following adverse reactions have been reported during post-approval use of sapropterin dihydrochloride:

- **Hypersensitivity reactions** including anaphylaxis and rash. Most hypersensitivity reactions occurred within several days of initiating treatment;
- **Gastrointestinal reactions:** esophagitis, gastritis, oropharyngeal pain, pharyngitis, esophageal pain, abdominal pain, dyspepsia, nausea, and vomiting;
- **Hyperactivity**

DRUG INTERACTIONS

- **Levodopa -** Sapropterin Dihydrochloride may increase the availability of tyrosine, a precursor of levodopa. Neurologic events were reported post-marketing in patients receiving sapropterin and levodopa concomitantly for a non-PKU indication. Monitor patients for a change in neurologic status.
- **Inhibitors of Folate Synthesis -** Drugs that inhibit folate synthesis may decrease the bioavailability of endogenous BH4 by inhibiting the enzyme dihydrofolate reductase, which is involved in the recycling (regeneration) of BH4. This reduction in net BH4 levels may increase Phe levels. Frequently monitor blood Phe levels when co-administering SAPROPTERIN DIHYDROCHLORIDE with medications known to inhibit folate synthesis, such as methotrexate, valproic acid, phenobarbital, trimethoprim.
- **Drugs Affecting Nitric Oxide-Mediated Vasorelaxation** – Both Sapropterin Dihydrochloride and PDE-5 inhibitors (such as sildenafil, vardenafil, or tadalafil) may induce vasorelaxation. A reduction in blood pressure could occur. Monitor patients for hypotension when co-administering SAPROPTERIN DIHYDROCHLORIDE with medications known to affect nitric oxide–mediated vasorelaxation such as PDE-5 inhibitors.

USE IN SPECIFIC POPULATIONS

- **Pregnancy:** There are no well-controlled clinical studies of Sapropterin Dihydrochloride in pregnant women.
- **Lactation:** There are insufficient data to assess the presence of sapropterin in human milk and no data on the effects on milk production.
- **Pediatric Use:** Pediatric patients with PKU, ages 1 month to 16 years, have been treated with sapropterin dihydrochloride in clinical trials. The efficacy and safety of sapropterin dihydrochloride have not been established in neonates.
- **Geriatric Use:** Clinical studies of sapropterin dihydrochloride in patients with PKU did not include patients aged 65 years and older. It is not known whether these patients respond differently than younger patients.

For more detailed information, please refer to the full Prescribing Information at https://www.drreddys.com/pi/sapropterin-tabs.pdf for Sapropterin Dihydrochloride Tablets for Oral Use, 100 mg.

For more detailed information, please refer to the full Prescribing Information at https://www.drreddys.com/pil/sapropterin_outsert_v_3.pdf for Sapropterin Dihydrochloride Powder for Oral Solution, 100 mg.

To report SUSPECTED ADVERSE REACTIONS, contact Dr. Reddy's Laboratories, Inc. at 1-888-375-3784 or by email: medinfo@drreddys.com, or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.