Sapropterin Support Program for Patients with Phenylketonuria (PKU)

Sapropterin Dihydrochloride Tablets for Oral Use, 100 mg
Sapropterin Dihydrochloride Powder for Oral Solution, 100 mg

Sapropterin Support Program for Sapropterin Dihydrochloride features:

HUB PRODUCT SUPPORT

- ✓ **4-Week Free Medication Trial.*** Available for eligible newly enrolled patients who have a prescription for Sapropterin Dihydrochloride therapy
- ✓ **Quick Start Program.**** Rapid supply of medication to eligible newly enrolled patients to ensure continuity of treatment for up to 28 days
- ✓ **Co-pay Assistance Program.**[§] Commercially insured eligible patients may pay as little as $0
- ✓ **Bridge Program.**[‖] Up to a 28-day medication supply is available to prevent therapy interruption for existing eligible patients due to a change in insurance
- ✓ **Reimbursement Research Product Support.** Including Benefit Investigation and Prior Authorization

NUTRITION PRODUCT SUPPORT

- ✓ **Dietary Product Support.** 24/7 product support from a Registered Dietitian to reinforce your clinic's dietary plan for existing consented and eligible patients. Informed patient consent is obtained by the patient signing the enrollment form.

*4-Week Free Medication Trial: The one-time 4-Week Free Trial of Sapropterin Dihydrochloride is only available to eligible commercially insured patients, who are United States residents, with a valid prescription, and who have never used Sapropterin Dihydrochloride previously. Subject to terms and conditions, eligibility criteria, and other federal and state law. **Quick Start Program is available to eligible commercially insured patients at initiation phase who pass an initial insurance screening for government insured patients, while the Sapropterin Support Program for Sapropterin Dihydrochloride is liaising with the relevant insurers. The Quick Start Program aims at providing medication to patients to ensure a rapid initiation without delays. The medication provided as part of the Quick Start Program is free of charge for up to 28 days and is not contingent on any purchase requirement. A prescription is required. Other specified limits and relevant terms and conditions apply. [§]Co-pay Assistance Program: for eligible commercially insured patients within specified limits and relevant terms and conditions. [‖]Bridge Program: Available at no cost, for eligible commercially insured patients within labelled indication only, and not contingent on purchase of any kind. Bridge Program is within specified limits and relevant terms and conditions.

Click here for more detailed information regarding additional terms and conditions.

To get started, please complete the Sapropterin Support Program Enrollment Form. If you have any questions, please contact the Sapropterin Support Program at 1-800-890-5732.

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

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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.

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.

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4 Week Medication Trial, Quick Start Program or Bridge Program

Eligibility Criteria include, but are not limited to the criteria set forth below. Please complete and submit the Patient Enrollment Form for Sapropterin Dihydrochloride Tablets or Powder for Oral Solution to determine full eligibility for patient. This offer is not health insurance*. No membership fees apply. Dr. Reddy's reserves the right to rescind, revoke, or amend this offer without notice.

Patients are not eligible for these programs if they are enrolled in a state or federally funded insurance program, including but not limited to Medicare, Medicaid, DOD, TRICARE, Veterans Affairs health care, a state prescription drug assistance program, or the Government Health Insurance Plan available in Puerto Rico

Patient is a US Resident with a valid prescription for Sapropterin Support Program eligible product**

Patient may experience a delay in commercial insurance coverage that would result in a gap or delay in access to prescribed Sapropeterin Support Program eligible product**

Co-Pay Program Eligibility, maximum annual and per claim limits apply and are subject to change, rescission, revocation at any time.

Patient is commercially insured

Patient is a US resident with a valid prescription from a US physician.

Patients are not eligible for these programs if they are enrolled in a state or federally funded insurance program, including but not limited to Medicare, Medicaid, DOD, TRICARE, Veterans Affairs health care, a state prescription drug assistance program, or the Government Health Insurance Plan available in Puerto Rico. Patient is not eligible if they reside in Massachusetts or California

*Dr. Reddy's does not guarantee coverage or and/or reimbursement for Sapropterin. Coverage, coding, and reimbursement policies vary significantly by payer, patient, and setting of care. Actual coverage and reimbursement decisions are made by individual payers following the receipt of claims. Patients and healthcare professionals should always verify coverage, coding, and reimbursement guidelines on a payer and patient specific basis.

**Eligible Products:

Sapropterin Dihydrochloride, ***Powder for Oral Solution / 100 mg (1st pack)***	NDC Number: 43598-477-11 (Single Unit Dose Packet)
Sapropterin Dihydrochloride, ***Powder for Oral Solution / 100 mg (Carton, 2nd pack)***	NDC Number: 43598-477-30 (Carton of 30 Unit Dose Packets)
Sapropterin Dihydrochloride, ***Tablet 100 mg***	NDC Number: 43598-749-04

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