Thiola® (tiopronin) tablets Rx Only — TOTAL CARE HUB

PATIENT ENROLLMENT FORM

PHONE: 844-4-THIOLA (844-484-4652) — FAX: 877-473-3167

For electronic version, visit www.THIOLAHub.com

Step 1: PATIENT INFORMATION

Name: _____
(First) (Middle) (Last)

Sex: ☐ Male ☐ Female DOB: _____ Height: _____ Weight: _____

Address: _____

City: _____ State: _____ Zip Code: _____

Phone: _____ Mobile Phone: _____

Method of Contact: ☐ Phone ☐ Mobile Phone E-mail: _____ Best Time to Call: _____

FOR PATIENTS UNDER 18:

Parent/Guardian Name: _____
(First) (Middle) (Last)

Address: _____

City: _____ State: _____ Zip Code: _____

Phone: _____ Mobile Phone: _____

Step 2: PRESCRIBER INFORMATION

Prescriber Name: _____
(First) (Last)

Email: _____ State License #: _____

Prescriber Address: _____

Prescriber Address #2: _____

City: _____ State: _____ Zip Code: _____

Phone: _____ Fax: _____ NPI #: _____

Physician Office Contact: _____ Phone: _____

Please complete and return Pages 1 and 2 of this form to THIOLA (tiopronin) Total Care Hub by faxing to (877) 473-3167

Step 3: PRESCRIPTION INFORMATION

℞ **THIOLA® (tiopronin) 100 mg tablets** Date: _____

DIAGNOSIS INFORMATION (This medical form is for insurance purposes only, not to suggest approved uses for promotion)

Diagnosis ☐ Cystinuria ICD-10-CM Code: E72.01

☐ Other Diagnosis _____ ☐ ICD-10-CM Code: _____

To expedite any insurance review process, please include the following information below:

Date of first cystine stone _____ # of historical stones _____ Most Recent Urine Cystine levels _____ Date _____

Has 24-hour urine test been completed? ☐ Yes ☐ No Date of Test _____ Please attach 24-hour urine test results

Failed therapies related to diagnosis of cystinuria (check all that apply):

☐ Conservative therapy (fluid, diet modifications) - Failure Date _____

☐ Potassium citrate - Failure Date _____ ☐ D-penicillamine/Cuprimine - Failure Date _____

☐ Other _____ - Failure Date _____

Recommended Initial Dosage

***Adult Dosage:** 800 mg/day given in 3 divided doses ***Pediatric Dosage:** Based on 15 mg/kg/day

_____ mg taken _____ times a day; Number of refills _____ Dispense 30 day supply

*Please see accompanying full Prescribing Information for Indications, complete Dosing Information and Important Safety Information.

NY Prescribers please submit prescription on an original NY State prescription blank. For all other states, if not faxed, prescription must be submitted on a state-specific blank, if applicable for your state. If required by your state, please indicate:

☐ Dispense as written ☐ Substitution allowed

Step 4: PRESCRIBER AUTHORIZATION — Required

Prescriber's full, usual, and actual signature is required-no stamps. This form cannot be processed without the prescriber's signature.

By signing below, I certify that (a) the above therapy is medically necessary and that I will supervise the patient's treatment accordingly; (b) I have received the necessary authorizations, including those required by state law and the Health Insurance Portability and Accountability Act of 1996 (HIPAA), to release the above information and other health and medical information of the patient to Travere Therapeutics, Inc. (Travere), and the company or companies that help Travere administer the THIOLA® Total Care Hub services; (c) I am prescribing the drug listed for the patient listed in this application based upon my independent medical judgment. By my signature below, I agree to receive certain reimbursement support services. I authorize Travere and Eversana, acting on behalf of Travere, to use the information contained in the prescription above, my name, and the name, address, and telephone number of my medical practice, and other applicable information, in order to provide me, my practice, and the patient listed in this application with the aforementioned reimbursement support services. I understand that participation in the THIOLA® Total Care Hub services described does not constitute a guarantee on the part of Travere or parties acting on its behalf that (1) the drug I have prescribed will be reimbursed by the patient's or any insurance program, or (2) the patient will be eligible for any patient assistance program. I appoint Travere and its agents to convey this prescription—electronically or otherwise—to the dispensing pharmacy.

Prescriber Signature: _____

Date: _____

Complete Information on following page →

Patient Name: _____
(First) (Middle) (Last)

Patient DOB: _____

Step 5: PRIMARY INSURANCE — Please attach a copy of both sides of the patient's insurance card

Insurance Carrier: _____ Phone: _____

Subscriber Name: _____

Subscriber Date of Birth:____ /___/_____

Relationship to Subscriber: ☐ Self ☐ Spouse ☐ Child ☐ Other: _____

Employer Name: _____ ID Number: _____

Policy #: _____ Group ID #: _____

PHARMACY BENEFITS-PRESCRIPTION DRUG CARD

Insurance Carrier: _____ Phone: _____

Rx BIN: _____ Rx PCN: _____

Rx ID #: _____ Group #: _____

(Pharmacy Benefits) section: _____

Step 6: PATIENT AUTHORIZATION–HIPAA Release

[Before signing, the patient and/or patient's authorized representative should review and understand the terms of this Authorization and Release ("Authorization") before signing. *If an authorized representative signs for the patient, please indicate the relationship to the patient.]*

I understand that the collection, use, and disclosure of the patient's health information are protected under law. Information contained in this Enrollment Form, such as the patient's name, address, insurance, prescription, and medical information, is "protected health information" ("PHI"). By signing this authorization, the patient agrees to the collection, use, and disclosure of the patient's PHI as described below.

I understand that I may decline to sign this Authorization, and that doing so will not affect the patient's ability to receive THIOLA® (tiopronin) or obtain insurance or insurance coverage.

I understand that once PHI about the patient is released based on this authorization, federal privacy laws may not prevent Travere Therapeutics, Inc. (Travere) and company or companies who administer the Total Care Hub Support Services ("Services") from further disclosing my information. However, I understand that such entities have agreed to use or disclose PHI they receive only for the purposes described in this authorization or as required by law.

I also understand that I may revoke (withdraw) this Authorization at any time by sending a signed, written statement to the THIOLA Total Care Hub by faxing it to (877) 473-3167.

Revoking this authorization will prohibit PHI disclosures after the date written revocation is received by the Total Care Hub, except to the extent that action has been taken already on this authorization. After I revoke this authorization, the patient's PHI may be disclosed among Travere and the company or companies that help Travere administer the services in order to maintain records of the patient's participation, but it will not be otherwise disclosed or used.

By signing below, I authorize Travere Therapeutics, Inc. (Travere) and the company or companies that help Travere administer the Services, to do the following:

1. Request and receive information from the patient's treating physician, healthcare provider, health insurer, or pharmacist necessary to investigate and resolve the patient's insurance coverage, coding, or reimbursement inquiry or to provide the reimbursement support service that I have requested. Information may include the patient's medical diagnosis, condition, and treatment (including prescription information), the patient's health insurance, name, address and telephone number;
2. Collect, use, and disclose to each other any patient information including PHI for the purpose of investigating and resolving the patient's insurance coverage, coding, or reimbursement inquiry or to administer the services, including entering and maintaining the patients in a database;
3. Contact me by mail, email, telephone, text or alternative communication to discuss and receive marketing communications, invitations to participate in research, educational materials, treatment support services and patient engagement initiatives designed for people taking THIOLA, including nutritional support and counseling;
4. Communicate with my healthcare providers and health plans about my insurance benefit and coverage status and product administration (e.g., prescription, dosing, refills);
5. Disclose information to the patient's treating physician, healthcare professional, or pharmacist as necessary to resolve the patient's insurance coverage, coding, or reimbursement inquiry. I also authorize my insurer, treating physician, healthcare provider, and pharmacist to release PHI about the patient's prescribed medications and medical condition requested by Travere and the company or companies that help Travere administer the services;
6. Contact the patient's insurer, other potential funding sources, social workers, patient advocacy organizations, or patient assistance programs (e.g., the Total Care Hub) on the patient's behalf to determine if the patient may be eligible for health insurance coverage or other funds, and disclose to them PHI about the patient's prescribed medications and medical condition that has been provided by the patient or patient's authorized representative or physician, healthcare provider, or pharmacist; and
7. Disclose any PHI obtained from the sources listed above to third parties, if required by law, and/or to conduct surveys, focus groups or interviews related to cystinuria and the effectiveness of the Total Care Hub program.

Patient/Guardian Signature: _____ **Date:** _____

Relationship to Patient: _____ **Date:** _____

Representative's Address: _____

Phone: _____ **Cell Phone:** _____

Please complete and return Pages 1 and 2 of this form to THIOLA (tiopronin) Total Care Hub by faxing to (877) 473-3167

Please see accompanying full Prescribing Information attached.

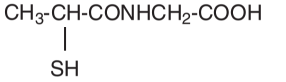
January 2021 THI010V6

THIOLA®

(Tiopronin) Tablets

FULL PRESCRIBING INFORMATION

DESCRIPTION: THIOLA® (Tiopronin) is a reducing and complexing thiol compound. Tiopronin is N-(2-Mercaptopropionyl) glycine and has the following structure:



Tiopronin has the empirical formula $C_5H_9NO_3S$ and a molecular weight of 163.20. In this drug product tiopronin exists as a dl racemic mixture.

Tiopronin is a white crystalline powder which is freely soluble in water.

THIOLA® tablets are white, sugar coated tablets, each containing 100 mg. of Tiopronin and are taken orally.

Inactive ingredients: Calcium carbonate, carnauba wax, ethyl cellulose, Eudragit E 100, hydroxypropyl cellulose, lactose, magnesium stearate, povidone, sugar, talc, titanium dioxide.

CLINICAL PHARMACOLOGY: THIOLA® is an active reducing agent which undergoes thiol-disulfide exchange with cystine to form a mixed disulfide of Thiola-cysteine.

Thiola Cystine ⇌ Thiola-cysteine

From this reaction a water-soluble mixed disulfide is formed and the amount of sparingly soluble cystine is reduced. When THIOLA® is given orally, up to 48% of dose appears in urine during the first 4 hours and up to 78% by 72 hours. Thus, in patients with cystinuria, sufficient amount of THIOLA® or its active metabolites could appear in urine to react with cystine, lowering cystine excretion.

The decrement in urinary cystine produced by THIOLA® is generally proportional to the dose. A reduction in urinary cystine of 250-350 mg/day at a THIOLA® dosage of 1 g/day, and a decline of approximately 500 mg/day at a dosage of 2 g/day, might be expected. THIOLA® causes a sustained reduction in cystine excretion without apparent loss of effectiveness. THIOLA® has a rapid onset and offset of action, showing a fall in cystine excretion on the first day of administration and a rise on the first day of drug withdrawal.

INDICATIONS AND USAGE: THIOLA® is indicated for the prevention of cystine (kidney) stone formation in patients with severe homozygous cystinuria with urinary cystine greater than 500 mg/day, who are resistant to treatment with conservative measures of high fluid intake, alkali and diet modification, or who have adverse reactions to d-penicillamine.

Cystine stones typically occur in approximately 10,000 persons in the United States who are homozygous for cystinuria. These persons excrete abnormal amounts of cystine in urine of over 250 mg/g creatinine, as well as excessive amounts of other dibasic amino acids (lysine, arginine and ornithine). In addition, they show varying intestinal transport defects for these same amino acids. The stone formation is the result of poor aqueous solubility of cystine.

Since there are no known inhibitors of the crystallization of cystine, the stone formation is determined primarily by the urinary supersaturation of cystine. Thus, cystine stones could theoretically form whenever urinary cystine concentration exceeds the solubility limit. Cystine solubility in urine is pH-dependent, and ranges from 170-300 mg/liter at pH 5, 190-400 mg/liter at pH 7 and 220-500 mg/liter at pH 7.5.

The goal of therapy is to reduce urinary cystine concentration below its solubility limit. It may be accomplished by dietary means aimed at reducing cystine synthesis and by a high fluid intake in order to increase urine volume and thereby lower cystine concentration.

Unfortunately, the above conservative measures alone may be ineffective in controlling cystine stone formation in some homozygous patients with severe cystinuria (urinary cystine exceeding 500 mg/day). In such patients, d-penicillamine has been used as an additional therapy. Like THIOLA®, d-penicillamine undergoes thiol-disulfide exchange with cystine, thereby lowering the amount of sparingly soluble cystine in urine.

However, d-penicillamine treatment is frequently accompanied by adverse reactions, such as dermatologic complications, hypersensitivity reactions, hematologic abnormalities and renal disturbances. THIOLA® may have a particular therapeutic role in such patients.

CONTRAINDICATIONS: The use of THIOLA® during pregnancy is contraindicated, except in those with severe cystinuria where the anticipated benefit of inhibited stone formation clearly outweighs possible hazards of treatment (see PRECAUTIONS).

THIOLA® should not be begun again in patients with a prior history of developing agranulocytosis, aplastic anemia or thrombocytopenia on this medication.

Mothers maintained on THIOLA® treatment should not nurse their infants.

WARNINGS: Despite apparent lower toxicity of THIOLA®, THIOLA® may potentially cause all the serious adverse reactions reported for d-penicillamine. Thus, although no death has been reported to result directly from THIOLA® treatment, a fatal outcome from THIOLA® is possible, as has been reported with d-penicillamine therapy from such complications as aplastic anemia, agranulocytosis, thrombocytopenia, Goodpasture's syndrome or myasthenia gravis.

Leukopenia of the granulocytic series may develop without eosinophilia. Thrombocytopenia may be immunologic in origin or occur on an idiosyncratic basis. The reduction in peripheral blood white count to less than 3500/cubic mm or in platelet count to below 100,000 cubic mm mandates cessation of therapy. Patients should be instructed to report promptly the occurrence of any symptom or sign of these hematological abnormalities, such as fever, sore throat, chills, bleeding or easy bruisability.

Proteinuria, sometimes sufficiently severe to cause nephrotic syndrome, may develop from membranous glomerulopathy. A close observation of affected patients is mandatory.

The following complications, though rare, have been reported during d-penicillamine therapy and could occur during THIOLA® treatment. When there are abnormal urinary findings associated with hemoptysis and pulmonary infiltrates suggestive of Goodpasture's syndrome, THIOLA® treatment should be stopped. Appearance of myasthenic syndrome or myasthenia gravis requires cessation of treatment. When pemphigus-type reactions develop, THIOLA® therapy should be stopped. Steroid treatment may be necessary.

PRECAUTIONS: Patients should be advised of the potential development of complications and to report promptly the occurrence of any symptom or sign of them.

To help monitor potential complications, the following tests are recommended: peripheral blood counts, direct platelet count, hemoglobin, serum albumin, liver function tests, 24-hour urinary protein and routine urinalysis at 3-6 month intervals during treatment. In order to assess effect on stone disease, urinary cystine analysis should be monitored frequently during the first 6 months when the optimum dose schedule is being determined, and at 6-month intervals thereafter. Abdominal roentogenogram (KUB) is advised on a yearly basis to monitor the size and appearance/disappearance of stone(s).

CARCINOGENESIS, MUTAGENESIS, IMPAIRMENT OF FERTILITY: Long-term carcinogenicity studies in animals have not been performed. High doses of THIOLA® in experimental animals have been shown to interfere with maintenance of pregnancy and viability of the fetus.

USE IN PREGNANCY: Pregnancy category C. D-penicillamine has been shown to cause skeletal defects and cleft palates in the fetus when given to pregnant rats at 10 times the dose recommended for human use. A similar teratogenicity might be expected for THIOLA® although no such findings could be related to the drug in studies in mice and rats at doses up to 10 times the highest recommended human dose.

There are no adequate and well-controlled studies in pregnant women. THIOLA® should be used during pregnancy only if the potential benefit justifies potential risk to the fetus.

NURSING MOTHERS: Because THIOLA® may be excreted in milk and because of the potential serious adverse reactions of nursing infants from THIOLA®, mothers taking THIOLA® should not nurse their infants.

PEDIATRIC USE: Safety and effectiveness below the age of 9 have not been established.

ADVERSE REACTIONS: Some patients may develop drug fever, usually during the first month of therapy. THIOLA® treatment should be discontinued until the fever subsides. It may be reinstated at a small dose, with a gradual increase in dosage until the desired level is achieved.

A generalized rash (erythematous, maculopapular or morbilliform) accompanied by pruritis may develop during the first few months of treatment. It may be controlled by antihistamine therapy, typically recedes when THIOLA® treatment is discontinued, and seldom recurs when THIOLA® treatment is restarted at a lower dosage. Less commonly, rash may appear late in the course of treatment (of more than 6 months). Located usually in the trunk, the late rash is associated with intense pruritis, recedes slowly after discontinuing treatment, and usually recurs upon resumption of treatment.

A drug reaction simulating lupus erythematous, manifested by fever, arthralgia and lymphadenopathy may develop. It may be associated with a positive antinuclear antibody test, but not necessarily with nephropathy. It may require discontinuance of THIOLA® treatment.

A reduction in taste perception may develop. It is believed to be the result of chelation of trace metals by THIOLA®. Hypogeusia is often self-limiting.

Unlike during d-penicillamine therapy, vitamin B_6 deficiency is uncommonly associated with THIOLA® treatment.

Some patients may complain of wrinkling and friability of skin. This complication usually occurs after long-term treatment, and is believed to result from the effect of THIOLA® on collagen.

A multiclinic trial involving 66 cystinuric patients in the United States indicated that THIOLA® is associated with fewer or less severe adverse reactions than d-penicillamine. Among those who had to stop taking d-penicillamine due to toxicity, 64.7% could take THIOLA®. In those without prior history of d-penicillamine treatment, only 5.9% developed reactions of sufficient severity to require THIOLA® withdrawal. A review of available literature supports the findings from this trial.

Despite this apparent reduced toxicity to THIOLA® relative to d-penicillamine, THIOLA® treatment may potentially be associated with all the adverse reactions reported with d-penicillamine. They include:

Gastrointestinal side-effects (nausea, emesis, diarrhea or softstools, anorexia, abdominal pain, bloating or flatus) in about 1 in 6 patients;

Impairment in taste and smell in about 1 in 25 patients;

Dermatologic complications (pharyngitis, oral ulcers, rash, ecchymosis, prurites, uritcaria, warts, skin wrinkling, pemphigus, elastosis perforans serpiginosa) in about 1 in 6 patients;

Hypersensitivity reactions (laryngeal edema, dyspnea, respiratory distress, fever, chills, arthralgia, weakness, fatigue, myalgia, adenopathy) in about 1 in 25 patients;

Hematologic abnormalities (increased bleeding, anemia, leukopenia, thrombocytopenia, eosinophilia) in about 1 in 25 patients;

Renal complications (proteinuria, nephrotic syndrome, hematuria) in about 1 in 20 patients;

Pulmonary manifestations (bronchiolitis, hemoptysis, pulmonary infiltrates, dyspnea) in about 1 in 50 patients;

Neurologic complications (myasthenic syndrome) in about 1 in 50 patients.

These reactions are more likely to develop during THIOLA® therapy among patients who had previously shown toxicity to d-penicillamine.

In patients who had previously manifested adverse reactions to d-penicillamine, adverse reactions to THIOLA® are more likely to occur than in patients who took THIOLA® for the first time. A close supervision with a careful monitoring of potential side effects is mandatory during THIOLA® treatment. Patients should be told to report promptly any symptoms suggesting toxicity. The treatment with THIOLA® should be stopped if severe toxicity develops.

Jaundice and abnormal liver function tests have been reported during THIOLA® therapy for non-cystinuric conditions. A direct cause and effect relationship, based upon these foreign reports, has not been established. Although such complications were not encountered in the small multi-center trials in the United States, patients should be carefully monitored and if any abnormalities are noted, the drug should be discontinued and the patient treated by appropriate measures.

DOSAGE AND ADMINISTRATION: It is recommended that a conservative treatment program should be attempted first. At least 3 liters of fluid (10-10 oz. glassfuls) should be provided, including two glasses with each meal and at bedtime. The patients should be expected to awake at night to urinate; they should drink two more glasses of fluids before returning to bed. Additional fluids should be consumed if there is excessive sweating or intestinal fluid loss. A minimum urine output of 2 liters/day on a consistent basis should be sought. A modest amount of alkali should be provided in order to maintain urinary pH at a high normal range (6.5-7.0). Potassium alkali are advantageous over sodium alkali, because they do not cause hypercalciuria and are less likely to cause the complication of calcium stones.

Excessive alkali therapy is not advisable. When urinary pH increases above 7.0 with alkali therapy, the complication of calcium phosphate nephrolithiasis may ensue because of the enhanced urinary supersaturation of hydroxyapatite in an alkaline environment.

In patients who continue to form cystine stones on the above conservative program, THIOLA® may be added to the treatment program. THIOLA® may also be substituted for d-penicillamine in patients who have developed toxicity to the latter drug. In both situations, the conservative treatment program should be continued.

The dose of THIOLA® should not be arbitrary but should be based on that amount required to reduce urinary cystine concentration to below its solubility limit (generally <250 mg/liter). The extent of the decline in cystine excretion is generally dependent on the THIOLA® dosage.

THIOLA® may be begun at a dosage of 800 mg/day in adult patients with cystine stones. In a multiclinic trial, average dose of THIOLA® was about 1000 mg/day. However, some patients require a smaller dose. In children, initial dosage may be based on 15 mg/kg/day. Urinary cystine should be measured at 1 month after THIOLA® treatment, and every 3 months thereafter. THIOLA® dosage should be readjusted depending on the urinary cystine value. Whenever possible, THIOLA® should be given in divided doses 3 times/day at least one hour before or 2 hours after meals.

In patients who had shown severe toxicity to d-penicillamine, THIOLA® might be begun at a lower dosage.

HOW SUPPLIED: THIOLA® (NDC 0178-0900-01), is available for oral administration as 100 mg. round, white, sugar coated tablets in bottles of 100 tablets each. Each tablet is imprinted in red with “M” on one side and blank on the other side. Store at 25°C (77°F); excursions permitted to 15-30°C (59-86°F) [see USP Controlled Room Temperature].

L090001R0616

Mission® PHARMACAL

MISSION PHARMACAL COMPANY
SAN ANTONIO, TX 78230 1355
Toll Free (800) 531-3333

THL_T9360R0617