

Early and active management: the key to getting to stone-free for Lindsay

Lindsay was able to move from a cystinuria diagnosis to stone-free in less than 1 year by working closely with her doctor and following her management plan, which included being diligent about drinking more fluids, using 24-hour urine tests to regularly monitor her urinary cystine level, and finding the right dosage of THIOLA® (tiopronin) tablets.

Lindsay, 23 years old

Age when first stone appeared:
22 years

Time to diagnosis of cystinuria:
8 months

Number of procedures:
7 in 18 months

Goal of treatment:
*Manage her cystinuria
so she can be stone-free*

Actual patient on THIOLA

Are you ready to potentially become stone-free? Watch Lindsay's video at LindsaysCystinuriaStory.com to hear about her journey and get tips on working with your doctor to find the management plan that's right for you.^a

^aIndividual patient response. Not all patients will respond similarly to the same medical treatment.

Indications:

THIOLA® (tiopronin) tablets are a prescription medicine used to help prevent the formation of cystine (kidney) stones in patients who were not successfully treated with dietary changes and increased fluid intake, or patients who have had side effects with the drug d-penicillamine.

Important Safety Information

THIOLA is not for everyone. You should not take THIOLA if you:

- Are pregnant or plan to become pregnant
- Are breastfeeding or plan to breastfeed
- Have a history of blood disorders including aplastic anemia (your bone marrow does not make enough new cells), agranulocytosis (decrease in certain white blood cells), or thrombocytopenia (decrease in the number of platelets)

Please see additional Important Safety Information and accompanying full Prescribing Information.

Thiola[®]
(tiopronin) tablets
Rx Only

Lindsay's journey to stone-free

Early stone events and diagnosis



At the age of 22, Lindsay was in **extreme pain** and had to be admitted to the emergency department where an ultrasound revealed a **7-mm kidney stone**. She was referred to a kidney stone specialist who treated the stone with shock wave lithotripsy, a procedure used to break up stones to make them easier to pass. This reduced the size of Lindsay's stone but did not eliminate it altogether because cystine stones are typically harder than other kidney stones. **Seven months later, Lindsay was hospitalized for another stone event.** Her doctor couldn't believe she had formed another stone so quickly. After a stone analysis and a 24-hour urine test, Lindsay was **diagnosed with cystinuria**.

The hospitalizations and pain associated with cystine stones caused Lindsay to miss out on work and social events. Talk to your doctor about your treatment options.

Initial management plan



Once diagnosed with cystinuria, Lindsay's kidney stone specialist advised her to **drink more fluids** to help lower her urinary cystine levels. For the next 5 months, Lindsay **continued to form stones**, resulting in **chronic pain, nausea, and weight loss** during and between stone events. After her third stone event, which occurred within 1 year of her first, Lindsay's doctor performed a 24-hour urine test and determined that **dietary changes and increased fluid intake were not enough** to prevent stones from forming. Lindsay's urinary cystine level was still above the line of solubility (generally 250 mg/L), which meant that her cystine was not soluble, or able to dissolve. Lindsay's doctor adjusted her management plan to include **300 mg of THIOLA® (tiopronin) tablets 3 times per day**.

Therapeutic lifestyle changes—such as drinking more fluids—may not be enough to prevent cystine stones. If you're still forming stones, talk to your doctor about adding THIOLA to your management plan.

Finding the right dosage of THIOLA



Three months later, Lindsay was **hospitalized to have a very large stone removed**, suggesting that her treatment plan might need to be adjusted further. Lindsay's doctor **increased her dosage of THIOLA to 400 mg 3 times per day** and advised her to continue drinking **more fluids**. Two months later, a 24-hour urine test showed that Lindsay's urinary cystine level was **still above 250 mg/L**, so her dosage of THIOLA was increased again to **600 mg 3 times per day**.

By using the 24-hour urine test to check Lindsay's urinary cystine level, her doctor was able to see that her cystine was still not where it needed to be, putting her at risk of forming another stone. Don't wait until you have a stone to find out if you're on the right treatment plan. Talk to your doctor about your next 24-hour urine test.

Stone-free for 6+ months



Five months later, Lindsay's dosage of THIOLA was increased one more time to **700 mg 3 times per day** after a 24-hour urine test showed that her urinary cystine level was still too high. By finding the right management plan—which included finding the optimal dosage of THIOLA—and adhering to it, **Lindsay has now been stone-free for more than 6 months**.

Once Lindsay was able to get on the right management plan, including finding the dosage of THIOLA that was right for her, she reached her treatment goal of becoming stone-free. Have you reached your treatment goal? If not, talk to your doctor about how to get there.

Learning from Lindsay's journey

Lindsay worked with her doctor to understand the science behind cystinuria and how her disease was affecting her. In 10 months, Lindsay was able to find a treatment plan, which included therapeutic lifestyle changes and the right dosage of THIOLA, to get to her treatment goal of stone-free. Lindsay's journey highlights the importance of learning about your disease and working closely with your doctor to find the treatment plan that works for you. In your own journey, regularly monitor your urinary cystine level by using 24-hour urine tests to see if your management plan is working or if you need to work with your doctor to make changes in order to prevent the next stone from forming.^a

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The safety and effectiveness of THIOLA have not been established in children under 9 years of age, and there are no well-controlled studies in pregnant women. High doses of THIOLA in pregnant laboratory animals have been shown to harm the fetus, so you should talk about these risks with your doctor to determine whether THIOLA is right for you. No long-term animal studies have been performed to see whether THIOLA can cause cancer, so you should discuss these risks with your doctor.

While you are taking THIOLA, your doctor will monitor you closely for signs and symptoms of possible complications. Your doctor will routinely do certain blood and urine tests, and yearly scans of your abdomen to look at the size and appearance of kidney stones. THIOLA should only be used under the close supervision of your doctor.

THIOLA can cause serious side effects or potential complications, and some of these could be fatal. Therefore, it is important to call your doctor right away if you have any side effects.

Side effects associated with THIOLA include a drug-related fever that typically occurs during the first month of treatment. If this occurs, talk with your doctor, who may discontinue treatment until the fever goes away.

You may notice a reduced sense of taste while taking THIOLA, which will eventually go away. Some patients also report wrinkling or thin, fragile skin during long-term treatment.

Other side effects of THIOLA may include an itchy rash that is found on many parts of your body. This typically occurs during the first few months of treatment, and antihistamines can help reduce the itching. The rash will usually disappear once you stop taking THIOLA. Less often, patients who take THIOLA for more than 6 months may develop a rash that is usually located on the upper body and is very itchy. It typically goes away slowly after discontinuing treatment and returns after re-starting treatment.

Some patients may develop a drug hypersensitivity reaction to THIOLA that includes fever, joint pain, and swollen lymph nodes. If this occurs, your doctor may discontinue THIOLA.

THIOLA can cause serious and potentially fatal blood disorders, including aplastic anemia (your bone marrow does not make enough new cells), agranulocytosis (decrease in certain white blood cells), or thrombocytopenia (decrease in the number of platelets). Call your doctor immediately if you have any signs or symptoms such as fever, sore throat, chills, bleeding, or if you are bruising more easily.

Although THIOLA may be less toxic than d-penicillamine, it could potentially cause all of the serious side effects reported for d-penicillamine. No deaths have been reported as a result of THIOLA treatment; however, fatal outcomes have been reported with certain complications of d-penicillamine therapy, including reduced white blood cells, red blood cells, or platelets; Goodpasture's syndrome (an autoimmune disorder that affects the lungs and kidneys); and myasthenia gravis (an autoimmune disorder that causes muscles to weaken). Do not take THIOLA if you have a history of these conditions.

Additional side effects that have been reported during treatment with d-penicillamine and that might occur during THIOLA treatment include: decreased sense of smell, nausea, vomiting, diarrhea or soft stools, loss of appetite, abdominal pain, bloating, gas, sore throat, sores in the mouth, hives, warts, swelling of the throat, difficulty breathing, shortness of breath, fatigue or weakness, muscle or joint pain, swelling in your legs or fluid build-up in the lungs, lung or kidney problems, and blood or high amounts of protein in urine. These side effects are more likely to develop during THIOLA therapy in patients who had previous reactions to d-penicillamine. Talk to your doctor about any unusual side effects.

Seek immediate medical attention and discontinue THIOLA if you notice symptoms such as fever, sore throat, chills, bleeding, easy bruising, coughing up blood, muscle weakness, blistering or raw areas on the skin or mucous membranes, joint pain, swelling of the lymph nodes, or swelling in your legs, as these may be signs of a serious reaction to the drug.

Jaundice (yellow appearance of the skin and whites of the eyes) and abnormal liver function tests have been reported during THIOLA treatment for conditions unrelated to cystine stones.

Call your doctor for medical advice about side effects. You may report negative side effects to Retrophin® Medical Information at 1-877-659-5518, or to the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see accompanying full Prescribing Information.

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