**FIRST AND ONLY** | CTEXLI is the **first and only** FDA-approved treatment for cerebrotendinous xanthomatosis (CTX) in adults.[1]

**CTX leaves a critical gap in the body's bile acid levels. CTEXLI helps to replenish the deficient bile acid pool.**[1]

# CTEXLI HELPS PUT BACK WHAT CTX TAKES AWAY

## INDICATION

CTEXLI is indicated for the treatment of cerebrotendinous xanthomatosis (CTX) in adults.

## IMPORTANT SAFETY INFORMATION

### WARNINGS AND PRECAUTIONS

**Hepatotoxicity:** Chenodiol, including CTEXLI, has been associated with hepatotoxicity. Patients with preexisting liver disease or bile duct abnormalities may be at a higher risk for hepatotoxicity during treatment.

**Please see Important Safety Information throughout and accompanying full Prescribing Information.**

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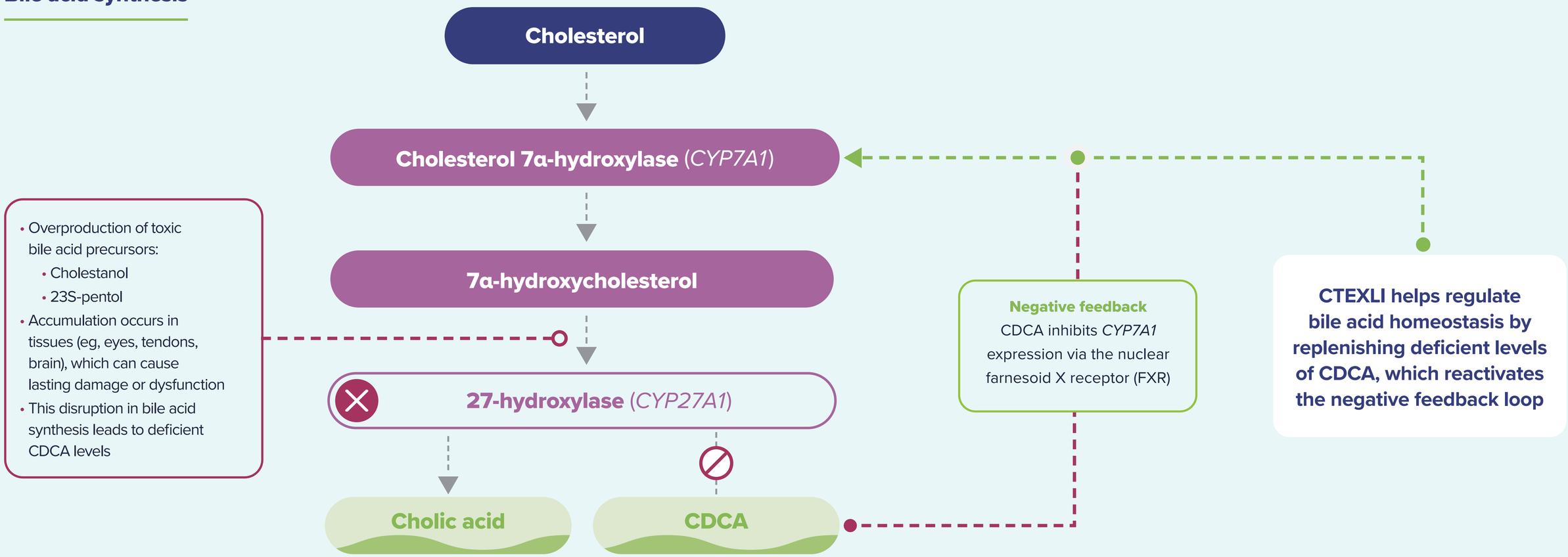
# CTX takes away CDCA[1-7]

- Cerebrotendinous xanthomatosis (CTX) stems from a **mutated *CYP27A1* gene**, which causes a deficiency in an enzyme (sterol 27-hydroxylase) needed for bile acid synthesis, including chenodeoxycholic acid (CDCA) synthesis[1,2]
- Without sufficient CDCA, negative feedback mechanisms that regulate bile acid synthesis are inhibited. This causes an **overproduction of toxic bile acid precursors** (eg, 23S-pentol, cholestanol)[2,3]

## Bile acid synthesis[1-7]




**IMPORTANT SAFETY INFORMATION** (cont'd)

**WARNINGS AND PRECAUTIONS**

**Hepatotoxicity:** Before initiating CTEXLI, obtain baseline liver transaminase (alanine aminotransferase [ALT] and aspartate aminotransferase [AST]) and total bilirubin levels in all patients.



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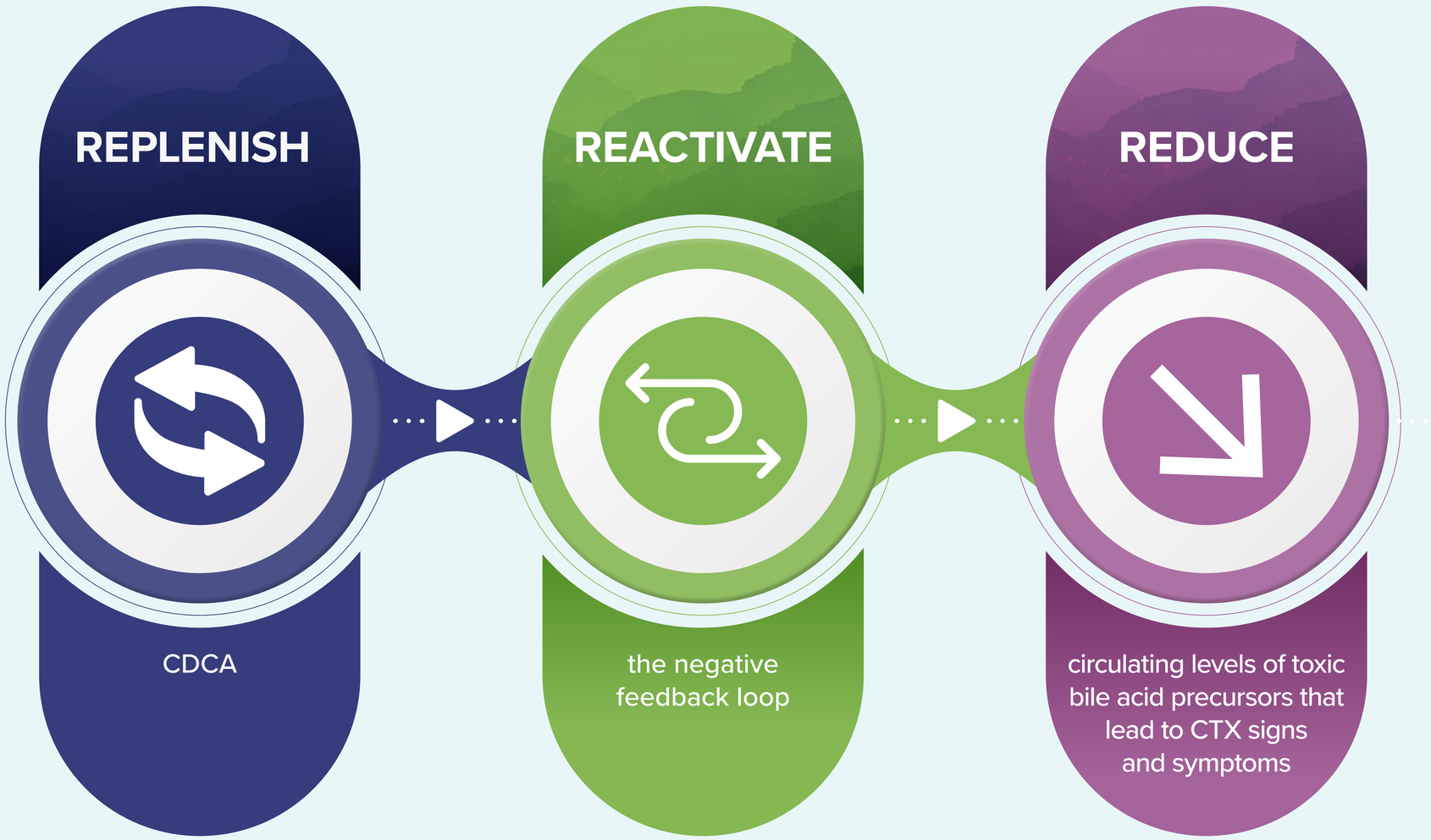
# CTEXLI helps regulate bile acid homeostasis[1,4]




CDCA=chenodeoxycholic acid; CTX=cerebrotendinous xanthomatosis.

## IMPORTANT SAFETY INFORMATION (cont'd)

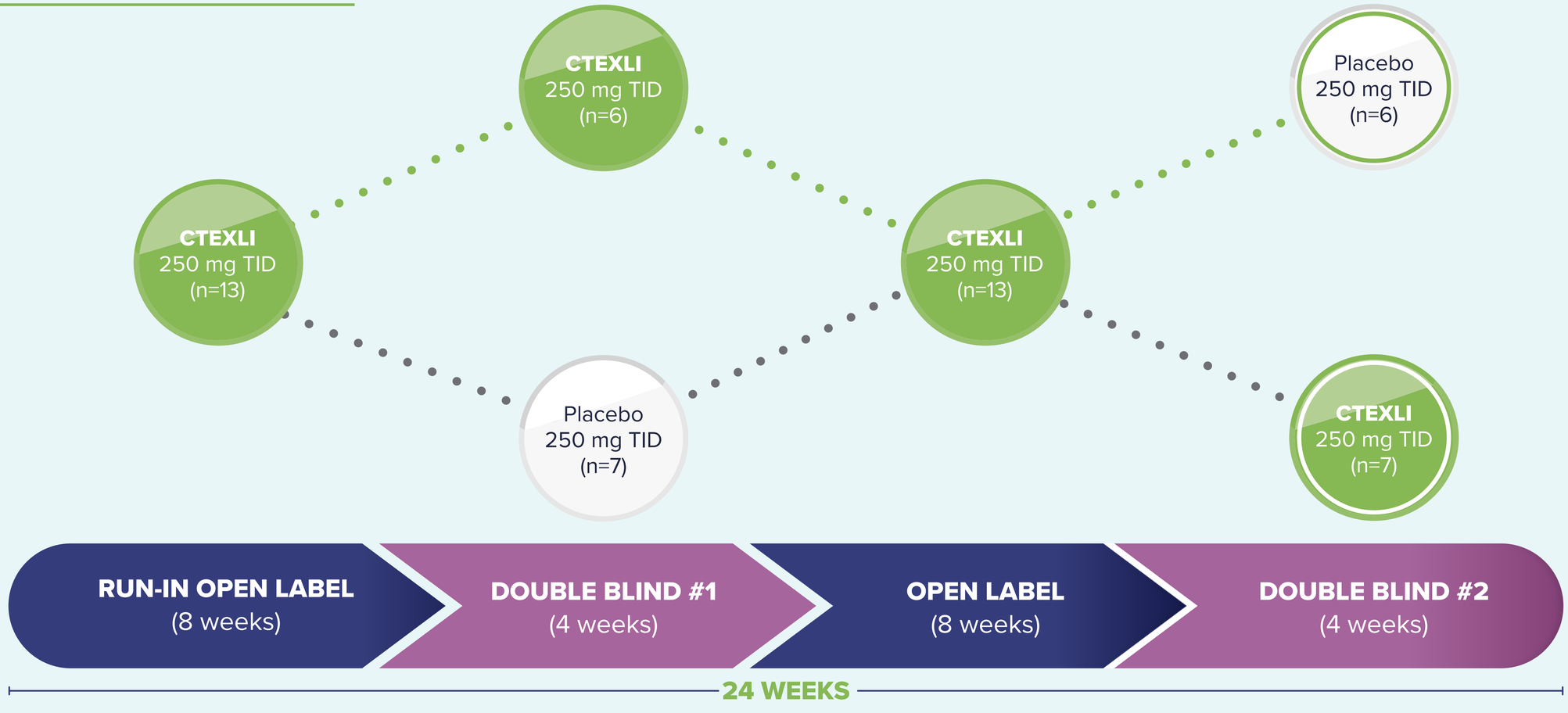
### WARNINGS AND PRECAUTIONS

**Hepatotoxicity:** Monitor liver transaminase (ALT, AST) and total bilirubin levels yearly and as clinically indicated. If liver transaminase levels are elevated >3 times the upper limit of normal (ULN) or total bilirubin level is >2 times ULN, interrupt treatment until the levels have returned to baseline values. For persistent or recurrent liver test abnormalities, consider discontinuing CTEXLI.

# The efficacy of CTEXLI was evaluated in the RESTORE study[1]

- Randomized, double-blind, placebo-controlled, crossover trial in patients with cerebrotendinous xanthomatosis (CTX)
- 14 patients enrolled, 13 randomized to receive either CTEXLI 250 mg or matching placebo TID for 4 weeks
- A 4-phase study including 2 separate 4-week, double-blind withdrawal periods*

## RESTORE 24-week crossover study design[1,8,9]




TID=3 times a day.

*The study also included an 8-week, run-in period of CTEXLI 250 mg TID and an 8-week, open-label period between the 2 double-blind withdrawal periods. Total duration of treatment was 24 weeks.[1]

## IMPORTANT SAFETY INFORMATION (cont'd)

### WARNINGS AND PRECAUTIONS

**Hepatotoxicity:** Inform the patient of the symptoms of hepatotoxicity (e.g., abdominal pain, bruising, dark-colored urine, fatigue, bleeding, jaundice, nausea, and pruritus). Have the patient discontinue CTEXLI immediately if clinical signs and symptoms consistent with hepatotoxicity occur.



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# Significant reductions in circulating levels of toxic bile acid precursors[1]

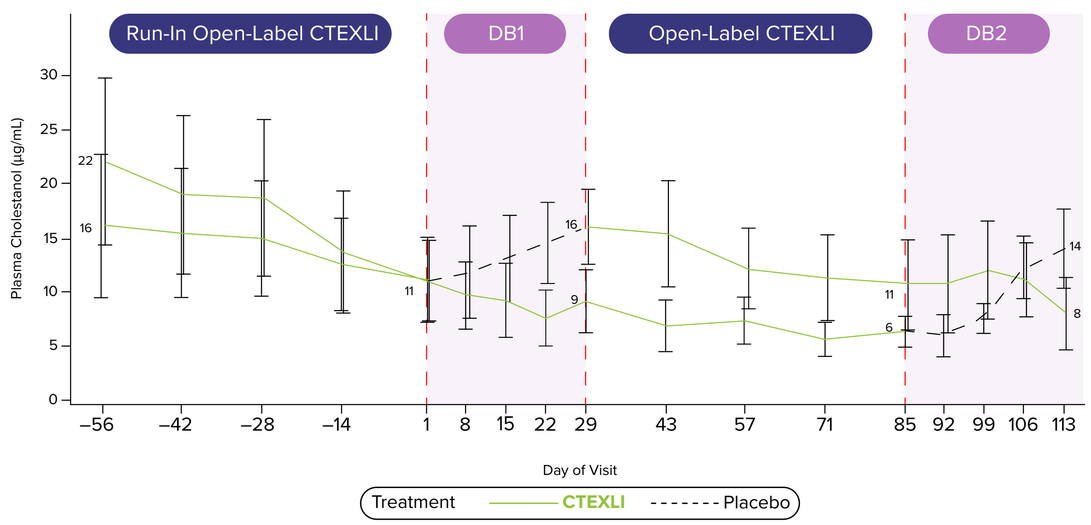
Plasma cholestanol and urine 23S-pentol were assessed at multiple time points over 24 weeks of treatment.

## Significant difference between CTEXLI and placebo seen within 4 weeks[1]

### Plasma Cholestanol

**4x** **lower level of plasma cholestanol with continued CTEXLI treatment** vs placebo (change from baseline to Day 29)[1]

(CTEXLI –2.3 µg/mL vs placebo 6.2 µg/mL; estimated treatment difference: –8.5 µg/mL [95% CI: –13.2, –3.9])

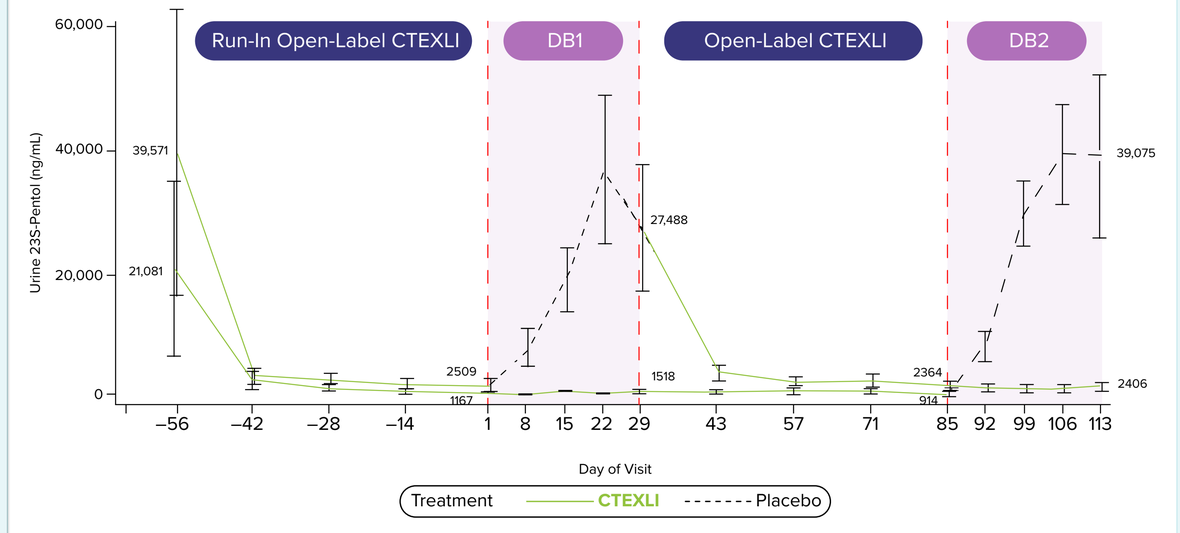



## Significant reductions during the 8-week, open-label CTEXLI phase (*P*=0.0012)[9,10]

### Urine 23S-Pentol

**150x** **lower level of urine 23S-pentol with continued CTEXLI treatment** vs placebo (change from baseline to Day 29)[1]

(CTEXLI 185 ng/mL vs placebo 29,506 ng/mL; estimated treatment difference: –29,321 ng/mL [95% CI: –45,701, –12,941])




For each study treatment (placebo or CTEXLI), the mean value at baseline was calculated as the mean of the measurements obtained prior to receiving the study treatment during the double-blind study duration. The mean value at Day 29 was calculated as the mean of the measurements at Day 29 at the end of the study treatment.[1]

For each patient at each visit, the measurement of urine 23S-pentol was calculated as the geometric mean of the first 3 morning void urine samples collected within 5 days prior to the visit.[1]

**Adherence is critical: significant increases in toxic bile acid precursors were seen within 2 weeks of stopping CTEXLI**[10]
These significant increases were seen when patients switched from CTEXLI to placebo in the double-blind withdrawal periods.

## IMPORTANT SAFETY INFORMATION (cont'd)

### ADVERSE REACTIONS

The most common adverse reactions (≥14%) during CTEXLI treatment were diarrhea, headache, abdominal pain, constipation, hypertension, muscular weakness, and upper respiratory tract infection.



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# CTEXLI has an established safety profile[1]

## Most common adverse reactions (≥14%)[1]

| Adverse Reaction | Incidence |
|---|---|
| Diarrhea | 36% |
| Headache | 21% |
| Abdominal pain* | 14% |
| Constipation | 14% |
| Hypertension | 14% |
| Muscular weakness | 14% |
| Upper respiratory tract infection | 14% |

*Including abdominal pain upper.

**The safety and tolerability profile of CTEXLI was established in the RESTORE study with a mean (SD) CTEXLI exposure of 139.1 (26.7) days.[1]**

## Hepatotoxicity[1]

- Chenodiol, including CTEXLI, has been associated with hepatotoxicity. In the RESTORE study, 1 CTEXLI-treated patient (7%) had increased alanine aminotransferase (ALT) levels >3x upper limit of normal (ULN), which led to treatment interruption. Patients with preexisting liver disease or bile duct abnormalities may be at higher risk for hepatotoxicity during treatment with CTEXLI. Published reports suggest patients who are poor sulfators of lithocholic acid are more likely to develop chenodiol-induced serum aminotransferase elevations

## Monitoring considerations[1]

- Obtain baseline liver transaminase (ALT, aspartate transaminase [AST]) and total bilirubin levels in all patients prior to treatment initiation with CTEXLI. If liver transaminase levels are elevated >3x ULN or total bilirubin level is >2 times ULN, interrupt treatment with CTEXLI until the levels have returned to baseline values. Monitor liver transaminase and total bilirubin levels yearly and as clinically indicated. For persistent or recurrent liver test abnormalities, consider discontinuing CTEXLI
- Inform patients of the symptoms of hepatotoxicity (eg, abdominal pain, bruising, dark-colored urine, fatigue, bleeding, jaundice, nausea, and pruritus). If clinical signs and symptoms consistent with hepatotoxicity occur, discontinue CTEXLI immediately

SD=standard deviation.



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# Daily oral dosing guidance and available support[1]


## Recommended CTEXLI dosage:
## 250 mg orally 3x/day, with or without food[1]

If a dose is missed, advise patients to skip the missed dose and take the next dose as scheduled. **Do not take a double dose.**

Before initiating CTEXLI, obtain baseline liver transaminase (alanine aminotransferase [ALT] and aspartate aminotransferase [AST]) and total bilirubin levels in all patients.

If liver transaminase (ALT, AST) levels are elevated >3x the upper limit of normal (ULN) or total bilirubin level is >2x ULN, interrupt treatment with CTEXLI until the levels have returned to baseline values. Monitor liver transaminase and total bilirubin levels yearly and as clinically indicated.



# Comprehensive patient support

Mirum Access Plus is available with support and resources to help you and your office navigate insurance coverage, as well as assist your patients with treatment costs and prescription fulfillment.

To learn more about Mirum Access Plus, contact us at
**1-855-MRM-4YOU** (1-855-676-4968)
Monday through Friday, 8:00 AM through 8:00 PM ET.

**Visit CTEXLIhcp.com to learn more.**

**IMPORTANT SAFETY INFORMATION** (cont'd)

**DRUG INTERACTIONS**

**Bile acid sequestering agents and aluminum-based antacids:** Avoid concomitant use with CTEXLI. Co-administration of bile acid sequestering agents, such as cholestyramine and colestipol, or aluminum-based antacids may decrease absorption of CTEXLI in the intestine and may result in decreased efficacy.

**Coumarin and its derivatives:** Monitor prothrombin time and adjust the dosage of coumarin or its derivatives if concomitant use with CTEXLI is unavoidable. Due to potential hepatotoxicity, CTEXLI may affect the pharmacodynamics of coumarin and its derivatives, causing unexpected prolongation of the prothrombin time and hemorrhage.

**DOSING AND ADMINISTRATION**

The recommended dosage of CTEXLI is 250 mg administered orally three times daily, with or without food. Swallow tablets whole.

**FIRST AND ONLY**

**CTX leaves a critical gap in the body's bile acid levels. CTEXLI helps to replenish the deficient bile acid pool.[1]**

# CTEXLI HELPS PUT BACK WHAT CTX TAKES AWAY

**Cerebrotendinous xanthomatosis (CTX) takes away chenodeoxycholic acid (CDCA); CTEXLI helps put it back[1-4]**

- Replenishes CDCA levels
- Reactivates the negative feedback loop to support bile acid homeostasis
- Reduces circulating levels of toxic bile acid precursors that lead to CTX signs and symptoms

**CTEXLI significantly reduced circulating levels of toxic bile acid precursors in the RESTORE study[1]**

- 4x lower level of toxic plasma cholestanol vs placebo
- 150x lower level of toxic urine 23S-pentol vs placebo

**CTEXLI has an established safety profile[1]**

- Most common adverse reactions (≥14%): diarrhea (36%), headache (21%), abdominal pain* (14%), constipation (14%), hypertension (14%), muscular weakness (14%), and upper respiratory tract infection (14%)

*Including abdominal pain upper.

**Visit CTEXLIhcp.com to learn more.**

**References: 1.** CTEXLI™ (chenodiol) tablets. Prescribing Information. Mirum Pharmaceuticals, Inc. **2.** Freedman SF, Brennand C, Chiang J, et al. Prevalence of cerebrotendinous xanthomatosis among patients diagnosed with acquired juvenile-onset idiopathic bilateral cataracts. *JAMA Ophthalmol*. 2019;137(11):1312-1316. doi:10.1001/jamaophthalmol.2019.3639 **3.** Köroğlu M, Karakaplan M, Gündüz E, et al. Cerebrotendinous xanthomatosis patients with late diagnosed in single orthopedic clinic: two novel variants in the *CYP27A1* gene. *Orphanet J Rare Dis*. 2024;19(1):53-65. doi:10.1186/s13023-024-03082-4 **4.** Badura-Stronka M, Hirschfeld AS, Winczewska-Wiktor A, et al. First case series of Polish patients with cerebrotendinous xanthomatosis and systematic review of cases from the 21st century. *Clin Genet*. 2022;101(2):190-207. doi:10.1111/cge.14079 **5.** Fiorucci S, Distrutti E. Chenodeoxycholic acid: an update on its therapeutic applications. *Handb Exp Pharmacol*. 2019;256:265-282. doi:10.1007/164_2019_226 **6.** Ribeiro RM, Vasconcelos SC, Lima PLGSB, et al. Pathophysiology and treatment of lipid abnormalities in cerebrotendinous xanthomatosis: an integrative review. *Brain Sci*. 2023;13(7):1-16. doi:10.3390/brainsci13070979 **7.** Hoeke MO, Heegsma J, Hoekstra M, Moshage H, Faber KN. Human FXR regulates SHP expression through direct binding to an LRH-1 binding site, independent of an IR-1 and LRH-1. *PLOS One*. 2014;9(2):e88011. doi:10.1371/journal.pone.0088011 **8.** Study to evaluate patients with cerebrotendinous xanthomatosis (RESTORE). ClinicalTrials.gov identifier: NCT04270682. Updated October 28, 2024. Accessed January 17, 2025. https://clinicaltrials.gov/study/NCT04270682 **9.** Data on file. REF-01753. Mirum Pharmaceuticals, Inc. **10.** Data on file. REF-01797. Mirum Pharmaceuticals, Inc.

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