09-J5000-16

Original Effective Date: 07/01/25

Reviewed: 05/14/25

Revised: 00/00/00

Subject: Chenodiol (Ctexli) Tablets

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

DESCRIPTION:

Cerebrotendinous xanthomatosis (CTX) is a rare, autosomal recessive lipid storage disorder caused by a mutation in the *CYP27A1* gene, leading to sterol 27-hydroxylase deficiency. This results in reduced primary bile acid synthesis, particularly chenodeoxycholic acid (CDCA) levels, abnormal deposition of cholesterol and cholestanol in the tissues, and increased excretion of bile alcohols in the urine. CTX occurs more frequently in females than males and has an estimated prevalence worldwide of fewer than 5 cases per 100,000 individuals. Clinical presentation can occur in childhood and consists of xanthomas in lungs, tendons, bone or the central nervous system, developmental delays, infantile-onset diarrhea, and childhood-onset cataracts. Adults may present with the same signs and symptoms as children but with increased severity including adult-onset progressive neurologic dysfunction, dementia, psychiatric disturbances, pyramidal or cerebellar signs, dystonia, atypical parkinsonism, peripheral neuropathy, and seizures. Until recently, treatment options included the off-label use of synthetic chenodeoxycholic acid known as chenodiol (Chenodal), which is FDA-approved for the treatment of gallstones, and cholic acid (Cholbam), another bile acid therapy.

On February 21, 2025, the FDA approved chenodiol (Ctexli) for treatment of CTX in adults, which is used to replace deficient levels of the endogenous bile acid CDCA. Increased chenodiol levels in the enterohepatic bile acid pool restore the activation of farnesoid X receptor (FXR) and downregulate CYP7A1 leading to suppression and reduction of atypical bile acids and bile alcohols including cholestanol and 23S-pentol.

According to the manufacturer prescribing information, the efficacy of chenodiol (Ctexli) for the treatment of patients with CTX was evaluated in a randomized, double-blind, placebo controlled, 2-period with 2-treatment crossover trial in patients ≥16 years of age (NCT 04270682). Fourteen patients were enrolled, and 13 patients were randomized and treated in a crossover withdrawal design to

receive either chenodiol (Ctexli) 250 mg or placebo orally three times daily for 4 weeks during 2 double-blind treatment periods. The study also included treatment with chenodiol (Ctexli) 250 mg three times daily during an 8-week run-in period and an 8-week open label period in between the 2 double-blind withdrawal periods. The total duration of study treatment was 24 weeks. Of the 13 randomized patients, 62% were male and 39% were female. The baseline median age was 42 years (16-55) and median age at diagnosis was 35 years (15-55). The patient population consisted of 62% White, 15% Asian, and 23% Other. Ethnicity consisted of 15% Hispanic or Latino, 54% not Hispanic or Latino, and 31% unknown. Plasma cholestanol and urine 23S-pentol were assessed at multiple time points. For plasma cholestanol, the estimated mean change from baseline at day 29 was -2.3 µg/mL when patients continued chenodiol (Ctexli) treatment and 6.2 µg/mL when patients received placebo. The estimated treatment difference was -8.5 µg/mL (95% CI: -13.2, -3.9). For urine 23S-pentol, the estimated mean change from baseline at day 29 was 185 ng/mL when patients continued chenodiol (Ctexli) treatment and 29506 ng/mL when patients received placebo. The estimated treatment difference was -29321 ng/mL (95% CI: -45701, -12941). A summary of results for plasma cholestanol and urine 23S pentol is provided in Table 1.

Table 1: Results for plasma cholestanol and urine 23S pentol

	Mean (SD)	**Chenodiol (Ctexli) (N = 13)**	**Placebo (N = 13)**
Plasma Cholestanol (µg/mL)	Baseline	10.8 (10.0)	8.8 (7.8)
	Day 29	8.5 (7.0)	15.1 (8.8)
	Change from Baseline at Day 29	-2.3 (3.9)	6.2 (5.6)
	Treatment Difference	-8.5 (95% CI: -13.2, -3.9)	
Urine 23SPentol (ng/mL)	Baseline	1811 (1693)	1773 (1940)
	Day 29	1996 (1341)	31279 (27595)
	Change from Baseline at Day 29	185 (1479)	29506 (27257
	Treatment Difference	-29321 (95% CI: -45701, -12941)	

For each study treatment [placebo or chenodiol (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; and the mean value at Day 29 was calculated as the mean of the measurements at Day 29 at the end of the study treatment.

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

The most common adverse reactions with chenodiol (Ctexli) (incidence > 14%) are diarrhea, headache, abdominal pain, constipation, hypertension, muscular weakness, and upper respiratory tract infection.

POSITION STATEMENT:

Comparative Effectiveness

The Food and Drug Administration has deemed the drug(s) or biological product(s) in this coverage policy to be appropriate for self-administration or administration by a caregiver (i.e., not a healthcare professional). Therefore, coverage (i.e., administration) in a provider-administered setting such as an outpatient hospital, ambulatory surgical suite, physician office, or emergency facility is not considered medically necessary.

Initiation of chenodiol (Ctexli) **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. Member is at least 18 years of age
2. Diagnosis of cerebrotendinous xanthomatosis (CTX) confirmed by genetic test demonstrating pathogenic variants in the *CYP27A1* gene – Genetic test documentation must be submitted
3. Clinical findings consistent for CTX (e.g., xanthomas in lungs, tendons, bone or central nervous system, infantile-onset diarrhea, childhood-onset cataracts, adult-onset progressive neurologic dysfunction including dementia, psychiatric disturbances, pyramidal or cerebellar signs, dystonia, atypical parkinsonism, peripheral neuropathy, seizures) - Documentation must be submitted
4. **BOTH** of the following: - Laboratory documentation within the last 6 months must be submitted
    a. Elevated plasma cholestanol (i.e., greater than or equal to 5-times the upper limit of normal)
    b. Urine positive for bile alcohols
5. Baseline liver transaminase (i.e., ALT, AST) and total bilirubin labs are obtained prior to initiating chenodiol (Ctexli)
6. **NOT** prescribed in combination with chenodiol (Chenodal), cholic acid (Cholbam), bile acid sequestering agents (e.g., cholestyramine, colestipol) or aluminum-based antacids
7. Prescribed by a specialist who treats patients with CTX such as a neurologist, gastroenterologist, hepatologist, or geneticist.
8. Dose does NOT exceed 250 mg orally three times daily

Approval duration: 6 months

Chenodiol (Ctexli) is considered experimental or investigational for any other indications due to insufficient evidence in the peer-reviewed medical literature to support safety, efficacy, and net health outcome.

Continuation of chenodiol (Ctexli) **meets the definition of medical necessity** for members meeting the following criteria:

1. Authorization/reauthorization for the requested agent has been previously approved by Florida Blue or another health plan in the past 2 years (if another health plan, documentation of a

health plan-paid claim during the 90 days before the authorization request must be submitted), OR the member has previously met ALL indication-specific initiation criteria.

2. Member has a clinical meaningful response (e.g., improvement or stabilization in clinical findings associated with CTX, reduction in plasma cholestanol and bile alcohols in the urine) - Documentation must be submitted
3. Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) are less than 3-times the upper limit of normal (ULN) and total bilirubin is less than 2-times the ULN
4. **NOT** prescribed in combination with chenodiol (Chenodal), cholic acid (Cholbam), bile acid sequestering agents (e.g., cholestyramine, colestipol) or aluminum-based antacids
5. Prescribed by a specialist who treats patients with CTX such as a neurologist, gastroenterologist, hepatologist, or geneticist.
6. Dose does NOT exceed 250 mg orally three times daily

Approval duration: 1 year

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

- Chenodiol (Ctexli) is a bile acid indicated for treatment of cerebrotendinous xanthomatosis (CTX) in adults.
- The recommended dosage is 250 mg orally three times daily.
- Co-administration of bile acid sequestering agents, such as cholestyramine and colestipol, or aluminum-based antacids may decrease absorption of chenodiol (Ctexli) in the intestine and may result in decreased efficacy of chenodiol (Ctexli). Avoid concomitant use of bile acid sequestering agents or aluminum-based antacids with chenodiol (Ctexli).
- Chenodiol (Ctexli) may affect the pharmacodynamics of coumarin and its derivatives, causing unexpected prolongation of the prothrombin time and hemorrhage. If concomitant use of chenodiol (Ctexli) with coumarin or its derivatives is unavoidable, monitor prothrombin time. Adjust the dosage of coumarin or its derivatives in accordance with its approved product labeling.

Dose Adjustments

- None

Drug Availability

- Chenodiol (Ctexli) tablets are supplied as 250 mg white film-coated tablets imprinted with "MP" on one side and "250" on the other side (NDC 79378-310-90: 100 count bottle)

PRECAUTIONS:

Boxed Warning

- None

Contraindications

- None

Precautions/Warnings

- **Hepatotoxicity:** Chenodiol, including Ctexli, has been associated with hepatotoxicity. In Trial 1, one chenodiol-treated patient (7%) had increased ALT levels > 3 times ULN, which led to treatment interruption. Patients with pre-existing liver disease or bile duct abnormalities may be at higher risk for hepatotoxicity during treatment with chenodiol (Ctexli). Published reports suggest patients who are poor sulfators of lithocholic acid are more likely to develop chenodiol-induced serum aminotransferase elevations. Obtain baseline liver transaminase (ALT, AST) and total bilirubin levels in all patients prior to treatment initiation with chenodiol (Ctexli). If liver transaminase levels are elevated > 3 times ULN or total bilirubin level is >2 times ULN, interrupt treatment with chenodiol (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 chenodiol (Ctexli). Inform the patient of the symptoms of hepatotoxicity (e.g., abdominal pain, bruising, dark-colored urine, fatigue, bleeding, jaundice, nausea, and pruritus). If clinical signs and symptoms consistent with hepatotoxicity occur, have the patient discontinue chenodiol (Ctexli) immediately.

BILLING/CODING INFORMATION:

The following codes may be used to describe:

HCPCS Coding

J8499	Prescription drug, oral, non-chemotherapeutic, not otherwise specified

ICD-10 Diagnosis Codes That Support Medical Necessity

E75.5	Other lipid storage disorders
E75.6	Lipid storage disorder, unspecified

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: The following National Coverage Determination (NCD) was reviewed on the last guideline revised date: Self-administered Drug List (A54770). No Local Coverage Determination (LCD) was found at the time of the last guideline revised date.

If this Medical Coverage Guideline contains a step therapy requirement, in compliance with Florida law 627.42393, members or providers may request a step therapy protocol exemption to this requirement if based on medical necessity. The process for requesting a protocol exemption can be found at Coverage Protocol Exemption Request.

DEFINITIONS:

None

RELATED GUIDELINES:

None

OTHER:

None

REFERENCES:

1. Clinical Pharmacology powered by ClinicalKey [Internet]. Tampa, FL: Elsevier.; 2025. Available at: https://www.clinicalkey.com/pharmacology/. Accessed 5/1/25.
2. Ctexli (chenodiol) [package insert]. Foster City, CA: Mirum Pharmaceuticals, Inc.; February 2025.
3. DRUGDEX System [Internet]. Greenwood Village (CO): Thomson Micromedex; Updated periodically [cited 2025 May 1].
4. DynaMed [database online]. Ipswich, MA: EBSCO Information Services.; 2025. URL http://www.dynamed.com. Accessed 5/1/25.
5. Orphan Drug Designations and Approval [Internet]. Silver Spring (MD): US Food and Drug Administration; 2025 [cited 2025 May 1]. Available from: http://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm/.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 05/14/25.

GUIDELINE UPDATE INFORMATION:

07/01/25	New Medical Coverage Guideline: Chenodiol (Ctexli), a bile acid, for the treatment of cerebrotendinous xanthomatosis (CTX) in adults.