PRIOR AUTHORIZATION POLICY

POLICY: Chenodiol Products Prior Authorization Policy
- Chenodal™ (chenodiol tablets – Travere)
- Ctexli™ (chenodiol tablets – Mirum)

REVIEW DATE: 03/19/2025

INSTRUCTIONS FOR USE

THE FOLLOWING COVERAGE POLICY APPLIES TO HEALTH BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. CERTAIN CIGNA COMPANIES AND/OR LINES OF BUSINESS ONLY PROVIDE UTILIZATION REVIEW SERVICES TO CLIENTS AND DO NOT MAKE COVERAGE DETERMINATIONS. REFERENCES TO STANDARD BENEFIT PLAN LANGUAGE AND COVERAGE DETERMINATIONS DO NOT APPLY TO THOSE CLIENTS. COVERAGE POLICIES ARE INTENDED TO PROVIDE GUIDANCE IN INTERPRETING CERTAIN STANDARD BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. PLEASE NOTE, THE TERMS OF A CUSTOMER'S PARTICULAR BENEFIT PLAN DOCUMENT [GROUP SERVICE AGREEMENT, EVIDENCE OF COVERAGE, CERTIFICATE OF COVERAGE, SUMMARY PLAN DESCRIPTION (SPD) OR SIMILAR PLAN DOCUMENT] MAY DIFFER SIGNIFICANTLY FROM THE STANDARD BENEFIT PLANS UPON WHICH THESE COVERAGE POLICIES ARE BASED. FOR EXAMPLE, A CUSTOMER'S BENEFIT PLAN DOCUMENT MAY CONTAIN A SPECIFIC EXCLUSION RELATED TO A TOPIC ADDRESSED IN A COVERAGE POLICY. IN THE EVENT OF A CONFLICT, A CUSTOMER'S BENEFIT PLAN DOCUMENT ALWAYS SUPERSEDES THE INFORMATION IN THE COVERAGE POLICIES. IN THE ABSENCE OF A CONTROLLING FEDERAL OR STATE COVERAGE MANDATE, BENEFITS ARE ULTIMATELY DETERMINED BY THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT. COVERAGE DETERMINATIONS IN EACH SPECIFIC INSTANCE REQUIRE CONSIDERATION OF 1) THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT IN EFFECT ON THE DATE OF SERVICE; 2) ANY APPLICABLE LAWS/REGULATIONS; 3) ANY RELEVANT COLLATERAL SOURCE MATERIALS INCLUDING COVERAGE POLICIES AND; 4) THE SPECIFIC FACTS OF THE PARTICULAR SITUATION. EACH COVERAGE REQUEST SHOULD BE REVIEWED ON ITS OWN MERITS. MEDICAL DIRECTORS ARE EXPECTED TO EXERCISE CLINICAL JUDGMENT AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. COVERAGE POLICIES RELATE EXCLUSIVELY TO THE ADMINISTRATION OF HEALTH BENEFIT PLANS. COVERAGE POLICIES ARE NOT RECOMMENDATIONS FOR TREATMENT AND SHOULD NEVER BE USED AS TREATMENT GUIDELINES. IN CERTAIN MARKETS, DELEGATED VENDOR GUIDELINES MAY BE USED TO SUPPORT MEDICAL NECESSITY AND OTHER COVERAGE DETERMINATIONS.

CIGNA NATIONAL FORMULARY COVERAGE:

OVERVIEW

Chenodiol products are naturally occurring bile acids. **Chenodal** is indicated for patients with **radiolucent stones** in well-opacifying gallbladders, in whom selective surgery would be undertaken except for the presence of increased surgical risk due to systemic disease or age.[1] **Ctexli** is indicated for the treatment of **cerebrotendinous xanthomatosis** in adults.[2]

Disease Overview

Gallstones

The most widely used treatment for symptomatic gallstones is cholecystectomy.[3] Two naturally occurring bile acids are used in the treatment of gallstones: ursodeoxycholic acid (UrsoForte®, Urso-250®, [ursodiol tablets, generic], Actigall® [ursodiol capsules, generic]) and chenodeoxycholic acid/chenodiol (Chenodal).[4] These agents reduce biliary cholesterol; however, their exact mechanisms differ. Both Chenodal and ursodiol promote the gradual dissolution of radiolucent gallstones over a period of 6 months to 2 years.[3]

Cerebrotendinous xanthomatosis (CTX)

CTX is a lipid storage and bile acid synthesis disorder with various clinical manifestations including juvenile cataracts, tendon xanthomas, premature atherosclerosis, and progressive neurologic disturbance (e.g., ataxia, seizures, psychiatric disorders, and peripheral neuropathy).[5] Other conditions associated with CTX include osteoarthritis, skeletal fractures, pulmonary insufficiency, renal and hepatic calculi, and childhood chronic diarrhea. CTX is caused by pathogenic variants in the cytochrome P450 (*CYP)27A1* gene.[7] This gene encodes for sterol 27-hydroxylase, an enzyme responsible for the conversion of cholesterol to cholic acid and chenodeoxycholic acid (primary bile acids). Mutations in this gene lead to 27-hydroxylase deficiency and a subsequent reduction in primary bile acid synthesis. In CTX, reduced synthesis of cholic and chenodeoxycholic acids results in failed feedback inhibition of cholesterol production, in turn leading to hallmark laboratory findings of the disorder: increased serum cholestanol, a cholesterol metabolite, and elevated urinary bile alcohols, like 23S-pentol.[6] Replacement therapy with chenodiol inhibits abnormal bile acid synthesis and is most effective in reducing elevated plasma cholestanol concentrations and eliminating bile alcohols.[5] As such, a CTX expert treatment panel concluded that treatment with chenodiol is necessary to improve/stabilize prognosis in the majority of patients, regardless of age or the presence of symptoms.[7] Alongside the clinical manifestations, biochemical and molecular genetic tests are typically used to diagnose CTX. Diagnostic biochemical tests include detection of elevated serum cholestanol levels while genetic tests include identification of pathogenic variants in the *CYP27A1* gene.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of chenodiol products. All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with chenodiol products as well as the monitoring required for adverse events and long-term efficacy, approval requires chenodiol products to be prescribed by or in consultation with a physician who specializes in the condition being treated.

I. Chenodal™ (chenodiol tablets - Travere) is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):

FDA-Approved Indication

1. **Gallstones.** Approve for 1 year if the patient meets ONE of the following (A or B):
   A) Patient has tried an ursodiol product; OR
   B) Patient is currently receiving an ursodiol product.

II. Ctexli™ (chenodiol tablets – Mirum)
is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):

FDA-Approved Indication

1. **Cerebrotendinous Xanthomatosis.** Approve for 1 year if the patient meets BOTH of the following (A and B):
   A) The diagnosis is established by ONE of the following (i or ii):
      i. Patient has a molecular genetic test demonstrating a pathogenic variant in the cytochrome P450 27A1 *(CYP27A1)* gene; OR
      ii. Patient has a laboratory test demonstrating elevated serum cholestanol levels; AND
   B) The medication is prescribed by or in consultation with a geneticist, neurologist, ophthalmologist, metabolic specialist who treats patients with cerebrotendinous xanthomatosis or a specialist who focuses in the treatment of cerebrotendinous xanthomatosis.

CONDITIONS NOT COVERED

- **Chenodal™ (chenodiol tablets - Travere)**
- **Ctexli™ (chenodiol tablets – Mirum)**

is(are) considered experimental, investigational or unproven for ANY other use(s) including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

1. **Combination Therapy with Cholbam (cholic acid capsules)**. There are no efficacy data available to support concomitant use.

REFERENCES

1. Chenodal™ tablets [prescribing information]. San Diego, CA: Travere; May 2021.
2. Ctexli™ tablets [prescribing information]. Foster City, CA: Mirum; February 2025.
3. Gaby AR. Nutritional approaches to prevention and treatment of gallstones. *Altern Med Rev.* 2009;14(3):258-267.
4. Abraham S, Rivero HG, Erlikh IV, Griffith LF, and Hondamudi VK. Surgical and nonsurgical management of gallstones. *Am Fam Physician*. 2014;89(10):795-802.
5. Moghadasian MH, Salen G, Frohlich JJ, et al. Cerebrotendinous xanthomatosis. *Arch Neurol*. 2002;59:527-529.
6. Lorincz MT, Rainier S, Thomas D and Fink JK. Cerebrotendinous xanthomatosis: possible higher prevalence than previously recognized. *Arch Neurol.* 2005;62:1459-1463.
7. Stelten B, Dotti M., Verrips A, et al. Expert opinion on diagnosing, treating and managing patients with cerebrotendinous xanthomatosis (CTX): a modified Delphi study. *Orphanet J Rare Dis* 16, 353 (2021). Available at: https://doi.org/10.1186/s13023-021-01980-5. Accessed on: March 12, 2025.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	08/23/2023
Annual Revision	No criteria changes.	08/28/2024
Early Annual Revision	The policy name was changed from "Chenodal" to "Chenodiol Products," with the addition of Ctexli tablets to the policy. Also, divided criteria based on specific agent intended for approval. **Chenodal:** Removed condition of approval for cerebrotendinous xanthomatosis (CTX) from other uses with supportive evidence. **Ctexli:** Added new condition of approval for CTX.	03/19/2025