Pharmacy Policy Bulletin: J-0690 Chenodiol Products– Commercial and Healthcare Reform	
Number: J-0690	**Category:** Prior Authorization
Line(s) of Business: ☒ Commercial ☒ Healthcare Reform ☐ Medicare	**Benefit(s):** **Commercial:** **Prior Authorization (1.,.):** **1.** Miscellaneous Specialty Drugs Oral = Yes w/ Prior Authorization **Healthcare Reform:** Not Applicable
Region(s): ☒ All ☐ Delaware ☐ New York ☐ Pennsylvania ☐ West Virginia	**Additional Restriction(s):** None
Version: J-0690-011	**Original Date:** 03/03/2010
Effective Date: 04/25/2025	**Review Date:** 04/09/2025

Drugs Product(s):	• Chenodal (chenodiol) • Ctexli (chenodiol)

FDA-Approved Indication(s):	• Chenodal
	  ○ Treatment of radiolucent stones in well-opacifying gallbladders where selective surgery would be undertaken except for the presence of increased surgical risk due to systemic disease or age.
	• Ctexli
	  ○ Treatment of cerebrotendinous xanthomatosis (CTX) in adults.

Background:	• Chenodal is indicated to dissolve certain kinds of gallstones. Chenodal suppresses hepatic synthesis of both cholesterol and cholic acid, gradually replacing the latter and its metabolite, deoxycholic acid, in an expanded bile acid pool. These actions contribute to biliary cholesterol desaturation and gradual dissolution of radiolucent cholesterol gallstones. • The likelihood of successful dissolution is far greater in floatable or small (< 15 mm in diameter) radiolucent stones. For patients with nonfloatable stones, dissolution is less likely and there is a heightened risk that a more emergent surgery may result due to the delay caused by unsuccessful treatment. Chenodal will not dissolve radiopaque (calcified or partially calcified) nor bile pigment stones. • If partial dissolution is not observed by 9 to 12 months, complete dissolution is unlikely, and therapy should be discontinued if no response is observed by 18 months. Safety of use beyond 24 months has not been established. • Ursodiol, even at lower doses, is equally effective and has a lower risk of toxicity when compared to Chenodal. A combination of ursodiol plus Chenodal has been found to be similarly effective to ursodiol monotherapy. • Chenodal received orphan drug designation on March 22, 2010 for the treatment of cerebrotendinous xanthomatosis (CTX) and was recommended as standard of care. On February 21, 2025, Ctexli (chenodiol) was FDA-approved and designated as the first FDA-approved drug to treat CTX.

	• CTX is a rare autosomal recessive genetic disorder caused by a pathogenic variant in the *CYP27A1* gene. CTX is classified as a bile acid synthesis disorder. CTX affects 1:71,677 to 1:148,914 Americans and can lead to serious neurological problems. If left untreated, CTX can lead to seizures, movement disorders, and cognitive decline. Patients with CTX lack the sterol 27-hydroxylase enzyme, which results in accumulation of cholesterol and cholestanol in nerve cells and membranes. This can cause damage to the brain, spinal cord, tendons, lens of the eye and arteries. Ctexli may act to replace deficient levels of the endogenous bile acid chenodeoxycholic acid in patients with CTX. • The hallmark symptoms of CTX – chronic diarrhea, bilateral cataracts, tendon xanthomas, and neurological dysfunction, suggest the presence of CTX. Molecular genetic testing with sequence analysis can detect *CYP27A1* variants and is suggested to confirm the diagnosis of CTX. • Prescribing Considerations: **Chenodal (gallstones)** ○ Chenodal is contraindicated in hepatocyte dysfunction, bile duct abnormalities (e.g., intrahepatic cholestasis, primary biliary cirrhosis, or sclerosing cholangitis), or bile acid agent hypersensitivity. ○ Chenodal is contraindicated in women who are pregnant or may become pregnant as it may cause fetal harm. ○ The safety and effectiveness of Chenodal in children have not been established. ○ The recommended dose range for dissolving gallstones with Chenodal is 13-16 mg/kg/day in two divided doses, morning and night, however, dosages less than 10 mg/kg/day are not recommended as they are usually ineffective and may increase the risk of cholecystectomy. ○ Avoid concomitant use of bile acid sequestering agents or aluminum-based antacids with Chenodal. Due to potential hepatotoxicity, chenodiol may affect the pharmacodynamics of coumarin and its derivatives, causing unexpected prolongation of the prothrombin time and hemorrhage. If concomitant use of chenodiol with coumarin or its derivatives is unavoidable, monitor prothrombin time. **Ctexli (CTX)** ○ The recommended dose of Ctexli in the treatment of CTX in adults is 250 mg orally three times a day, with or without food. Swallow tablets whole. ○ The safety and effectiveness of chenodiol in children have not been established. ○ Before initiation of Ctexli obtain baseline liver transaminase (alanine aminotransferase [ALT] and aspartate aminotransferase [AST] and total bilirubin levels. ○ Avoid concomitant use of bile acid sequestering agents or aluminum-based antacids with chenodiol. Due to potential hepatotoxicity, chenodiol may affect the pharmacodynamics of coumarin and its derivatives, causing unexpected prolongation of the prothrombin time and hemorrhage. If concomitant use of chenodiol with coumarin or its derivatives is unavoidable, monitor prothrombin time.

Approval Criteria

I. Chenodal

A. Initial Authorization

When a benefit, coverage of Chenodal may be approved when all of the following criteria are met **(1., 2., and 3.)**:

A. The member is 18 years of age or older.
B. The member is receiving Chenodal for the treatment of small (< 15 mm in diameter) or floatable radiolucent gallstones (ICD-10: K80).
C. The member has experienced therapeutic failure, contraindication, or intolerance to plan-preferred ursodiol therapy.

B. Reauthorization
When a benefit, reauthorization of Chenodal may be approved when the following criterion is met **(1.)**:
1. The member has experienced at least partial dissolution of gallstones.

II. Ctexli

A. Initial Authorization
When a benefit, coverage of Ctexli may be approved when all of the following criteria are met (**1., 2., and 3.):**
1. The member is 18 years of age or older.
2. The prescriber is a specialist who focuses on the treatment of CTX or the prescriber is acting in consultation with a specialist who focuses on the treatment of CTX.
3. The member has a diagnosis of CTX confirmed with genetic testing (ICD-10: E75.5).

B. Reauthorization
When a benefit, reauthorization of Ctexli may be approved when the following criterion is met **(1.)**:
1. The member experiences improvement in one of the following **(a., b., or c.):**
a. Normalization of elevated serum or urine 23S-pentol (bile alcohols).
b. Normalization of elevated serum cholestanol levels.
c. Improvement in neurologic and psychiatric symptoms (dementia, pyramidal tract, and cerebellar symptoms).

III. An exception to some or all of the criteria above may be granted for select members and/or circumstances based on state and/or federal regulations.

Limitations of Coverage

I. Coverage of drug(s) addressed in this policy for disease states outside of the FDA-approved indications should be denied based on the lack of clinical data to support effectiveness and safety in other conditions unless otherwise noted in the approval criteria.
II. For Commercial or HCR members with a closed formulary, a non-formulary product will only be approved if the member meets the criteria for a formulary exception in addition to the criteria outlined within this policy.

Authorization Duration

Initial Authorization

- Commercial and HCR Plans: If approved, up to a 12 month authorization may be granted.

Reauthorization

- Commercial and HCR Plans: If approved, up to an additional 12 month authorization may be granted.
    - **Chenodal**: Approval beyond 2 years (24 months) will not be granted, as safety and efficacy of this product beyond 2 years has not been evaluated.

Automatic Approval Criteria

None

References:

1. Chenodal [package insert]. San Diego, CA: Retrophin, Inc.; December 2024.
2. Schoenfield LJ, Lachin JM. Chenodiol (chenodeoxycholic acid) for dissolution of gallstones: The National Cooperative Gallstone Study. A controlled trial of efficacy and safety. *Ann Intern Med*. 1981; 95:257-282.
3. Abraham S, Rivero HG, Erlikh IV, Griffith LF, Kondamudi VK. Surgical and nonsurgical management of gallstones. *Am Fam Physician*. 2014;89(10):795-802. Available at: https://www.aafp.org/afp/2014/0515/p795.html. Accessed October 11, 2024.
4. LiverTox: Clinical and Research Information on Drug-Induced Liver Injury [Internet]. Bethesda (MD): National Institute of Diabetes and Digestive and Kidney Diseases; 2012–. Chenodiol (Chenodeoxycholic Acid). 2016. Available at: https://www.ncbi.nlm.nih.gov/books/NBK547907/. Accessed October 11, 2024.
5. Hofmann AF. Medical dissolution of gallstones by oral bile acid therapy. *Am J Surg*. 1989 Sep;158(3):198-204.
6. Patni N, Wilson DP. Cerebrotendinous Xanthomatosis. In: Feingold KR, Anawalt B, Boyce A, et al., editors. Endotext [Internet]. South Dartmouth (MA): MDText.com, Inc.; Updated 2023 Mar 8. Available from: https://www.ncbi.nlm.nih.gov/books/NBK395578/. Accessed October 11, 2024.
7. NORD. Cerebrotendinous Xanthomatosis. Available at: https://rarediseases.org/rare-diseases/cerebrotendinous-xanthomatosis/. Accessed March 11, 2025.
8. Patel H, Jepsen J. Gallstone Disease: Common Questions and Answers. *Am Fam Physician*. 2024;109(6):518-524.
9. UpToDate. Cerebrotendinous Xanthomatosis. Available at: https://www.uptodate.com. Accessed March 19, 2025.