chenodiol (Chenodal®)

EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO200

Description

Chenodiol (Chenodal®) suppresses hepatics synthesis of cholesterol and cholic acid, which leads to biliary cholesterol desaturation and gradual dissolution.

Length of Authorization

- Initial: Six months
- Renewal: up to 24 months (Maximum of **24** fills total)
    - Renewals are approved at six-month intervals

Quantity Limits

Product Name	Dosage Form	Indication	Quantity Limit
chenodiol (Chenodal)	250mg tablet	radiolucent gallstones	16 mg/kg/day

Initial Evaluation

I. Chenodiol (Chenodal) may be considered medically necessary when the following criteria are met:
   A. Member is 18 years of age or older; **AND**
   B. Medication is prescribed by, or in consultation with, a gastroenterologist; **AND**
   C. Treatment with ursodiol (for at least six months) has been ineffective, contraindicated, or not tolerated; **AND**
   D. Member will not have received treatment with chenodiol (Chenodal) for more than two years during their lifetime; **AND**
   E. Medication will **NOT** be used for prophylaxis; **AND**
   F. A diagnosis of **radiolucent gallstones** when the following are met:
      1. Provider attests that member's symptoms effect quality of life (e.g. biliary colic, pain); **AND**
      2. Provider attests that the member is not a candidate for surgery (e.g. laparoscopic cholecystectomy).

II. Chenodiol (Chenodal) is considered investigational when used for all other conditions, including but not limited to:
   A. Cerebrotendinous xanthomatosis (CTX)

Renewal Evaluation

I. Member has received a previous prior authorization approval for this agent through this health plan; **AND**
II. Member is not continuing therapy based off being established on therapy through samples, manufacturer coupons, or otherwise. Initial policy criteria must be met for the member to qualify for renewal evaluation through this health plan; **AND**
III. Member has not received treatment with chenodiol (Chenodal) for more than a total of **two** years (i.e., the maximum treatment duration is two years during a lifetime); **AND**
IV. Member has exhibited improvement or stability of disease symptoms [e.g., member doesn't exhibit biliary colic, has a loss of discomfort and pain].

Supporting Evidence

I. The safety and efficacy of chenodiol (Chenodal) was studied in a double blind, placebo controlled National Cooperative Gallstone Study (NCGS) involving 916 adult patients with radiolucent gallstones who were randomly assigned to the three treatment groups (placebo and chenodiol dosages of 375 mg and 750 mg) and followed for 24 months.
    - The placebo and chenodiol 375mg and 750mg per day treatment groups were associated with a 0.8%, 5.2%, and 13.5% complete stone dissolution, respectively. Chenodiol treatment (750 mg/day) compared to placebo was associated with a significant reduction in both biliary pain and the cholecystectomy rates in the group with floatable stones (27% versus 47% and 1.5% versus 19%, respectively). For patients with small (less than 15 mm in diameter) radiolucent stones, the observed rate of complete dissolution was approximately 20% on 750 mg/day.
II. The recommended dose range for chenodiol (Chenodal) is 13 to 16 mg/kg/day in two divided doses, or seven tablets a day. A maximum tolerated dose has not been well established.
III. The use of chenodiol (Chenodal) in pediatric patients has not been established in randomized controlled trials. There is no safety and efficacy data to support the use.
IV. In the absence of direct comparative trials there is no evidence to conclude that one product is safer or more effective than another. Ursodiol has been the standard of care in this space.
V. There is a lack of strong scientific evidence from randomized controlled trials supporting safety and efficacy of chenodiol (Chenodal) beyond two years in a lifetime. Chenodiol should be discontinued if there is no response by 18 months.

VI. Chenodiol (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. Surgery (laparoscopic cholecystectomy) is the standard of care for gallstones and offers immediate and permanent stone removal.

VII. Per the American Association of Family Physician (AAFP) guidelines, no medical therapy aside from pain control is recommended for asymptomatic pigmented or calcified gallstones.

VIII. When a symptomatic patient is not a candidate for surgery, extracorporeal shock wave lithotripsy is a noninvasive therapeutic alternative, per the AAFP guidelines. Recent studies demonstrated efficacy of extracorporeal shock wave lithotripsy for large common bile duct (CBD) stones followed by ERCP, with results comparable to those of surgery with regard to pain relief and duct clearance. Complete clearance of the CBD was achieved in 84.4% of and partial clearance in 12.3% of 283 patients.

IX. At therapeutic doses, chenodiol suppresses hepatic synthesis of both cholesterol and cholic acid and contributes to biliary cholesterol desaturation and gradual dissolution of radiolucent cholesterol gallstones. Chenodiol has no effect on radiopaque (calcified) gallstones or on radiolucent bile pigment stones.

X. Ultrasound remains the first line and best imaging modality to diagnose gallstones. A systematic review estimated that the sensitivity was 84% and specificity was 99% better than other modalities. If an ultrasound study is not equivocal for ruling out acute cholecystitis, then a nuclear medicine cholescintigraphy scan, also known as a HIDA scan, can be performed.

Investigational or Not Medically Necessary Uses

I. Chenodiol (Chenodal) has not been FDA-approved, or sufficiently studied for safety and efficacy for the conditions or settings listed below:
   A. Cerebrotendinous xanthomatosis (CTX)
      i. Two-cohort studies, one for adult patients with a double-blind placebo withdrawal (with CDCA rescue) crossover in patients 16 years of age or older and second will dose titrate pediatric patients (one month of age to less than 16 years of age) into a stable, open-label treatment. The study is still recruiting as of November 2020 and there is a lack of safety and efficacy data to support the use.

References

1. Chenodal [Prescribing Information]. Retrophin, Inc. San Diego, CA. June 2015.
2. S M Grundy, et al. The effects of chenodiol on biliary lipids and their association with gallstone dissolution in the National Cooperative Gallstone Study (NCGS). J Clin Invest. 1984 Apr;73(4):1156-66. doi: 10.1172/JCI111301.
3. Jasmin Tanaja, et al. Cholelithiasis. StatPearls Publishing; 2020

4. Diehl AK, Sugarek NJ, Todd KH. Clinical evaluation for gallstone disease: usefulness of symptoms and signs in diagnosis. *Am J Med*. 1990;89(1):29-33. doi:10.1016/0002-9343(90)90094-t
5. Sherly Abraham, MD, et al. Surgical and Nonsurgical Management of Gallstones. Am Fam Physician. 2014 May 15;89(10):795-802.
6. Tandan M, Reddy DN. Extracorporeal shock wave lithotripsy for pancreatic and large common bile duct stones. *World J Gastroenterol*. 2011;17(39):4365–437
7. Retrophin, Inc. Study to Evaluate Patients With Cerebrotendinous Xanthomatosis. ClinicalTrials.gov Identifier: NCT04270682

Policy Implementation/Update:

Action and Summary of Changes	Date
Criteria updated to policy format. Removal of assessments on pregnancy or liver disease history. Addition of the following: limited treatment with chenodiol (Chenodal) for more than two years during member lifetime; required confirmation that medication will NOT be used for prophylaxis; provider attestation that member's symptoms effect quality of life	11/2020
Criteria created	02/2014