Clinical Policy: Chenodiol (Chenodal)

Reference Number: ERX.NPA.78
Effective Date: 09.01.18
Last Review Date: 08.20
Line of Business: Commercial, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Chenodiol (Chenodal®) is a naturally occurring human bile acid.

FDA Approved Indication(s)
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.

Limitation(s) of use: Safety of use beyond 24 months is not established. The likelihood of successful dissolution is far greater if the stones are floatable or small. For patients with non-floatable stones, dissolution is less likely and added weight should be given to the risk that more emergent surgery might result from a delay due to unsuccessful treatment. Chenodiol will not dissolve calcified (radiopaque) or radiolucent bile pigment stones.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Chenodal is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Radiolucent Gallstones (must meet all)**:**

1. Presence of radiolucent stones in well-opacifying gallbladders;
2. Age ≥ 18 years;
3. Failure of a 6-month trial of ursodiol, unless contraindicated or clinically significant adverse effects are experienced;
4. Member is not a candidate for surgery (e.g., due to systemic disease or age);
5. Dose does not exceed 18 mg/kg per day.

Approval duration: 12 months

B. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Radiolucent Gallstones (must meet all)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. Total treatment duration does not exceed 24 months.
4. If request is for a dose increase, new dose does not exceed 18 mg/kg per day.

Approval duration: 12 months (up to 24 months total treatment)

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
ursodiol (Actigall®)	8-10 mg/kg/day PO in 2-3 divided doses	Not available

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings
- Contraindication(s):
  - Presence of known hepatocyte dysfunction or bile ductal abnormalities such as intrahepatic cholestasis, primary biliary cirrhosis or sclerosing cholangitis; a gallbladder confirmed as non-visualizing after two consecutive single doses of dye; radiopaque stones; gallstone complications or compelling reasons for gallbladder surgery (e.g., unremitting acute cholecystitis, cholangitis, biliary obstruction, gallstone pancreatitis, biliary gastrointestinal fistula)
  - Use in pregnancy or in women who can become pregnant
- Boxed warning(s): due to potential hepatoxicity, poor response rate and increase rate of a need for cholecystectomy was seen in some Chenodiol treated patients therefore it is not an appropriate treatment for many patients with gallstones. Chenodiol should be reserved for carefully selected patients, accompanied with liver function alternations.

Appendix D: General Information
- Oral cholecystograms or ultrasonograms are recommended at 6 to 9 month intervals to monitor response. Complete dissolutions should be confirmed by a repeat test after 1 to 3 months continued administration of Chenodal. Most patients who eventually achieve complete dissolution will show partial (or complete) dissolution at the first on-treatment test. If partial dissolution is not seen by nine to 12 months, the likelihood of success of treating longer is greatly reduced.
- Stone recurrence can be expected within 5 years in 50% of cases. After confirmed dissolution, treatment generally should be stopped. Serial cholecystograms or ultrasonograms are recommended to monitor for recurrence, keeping in mind that radiolucency and gallbladder function should be established before starting another course of Chenodal.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Treatment of cholelithiasis via the dissolution of radiolucent cholesterol gallstones	The recommended range is 13 to 16 mg/kg/day PO in two divided doses, morning and night, starting with 250 mg BID the first two weeks and increasing by 250 mg/day each week thereafter until the recommended or maximum tolerated dose is reached. Chenodiol should be discontinued if there is no response by 18 months. Safety of use beyond 24 months is not established.	Not available

VI. Product Availability

Tablet: 250 mg

VII. References

1. Chenodal Prescribing information. Irvine, CA: Nexgen Pharma, Inc.; September 2019. Available at https://dailymed.nlm.nih.gov/dailymed/. Accessed May 8, 2020.
2. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2020. Available at: http://www.clinicalpharmacology-ip.com/.
3. Petroni M, Jazrawi R, Pazzi P. Ursodeoxycholic acid alone or with chenodeoxycholic acid for dissolution of cholesterol gallstones: a randomized multi-center trial. Aliment Pharmcol Ther. 2004;15:123-128. https://onlinelibrary.wiley.com/doi/pdf/10.1046/j.1365-2036.2001.00853.x

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created: adapted from ERX.ST.03; no significant changes; diagnosis added to mirror the FDA indication; pregnancy contraindication added per safety guidance endorsed by Medical Affairs; positive response requirement added; references reviewed and updated.	05.01.18	08.18
3Q 2019 annual review: no significant changes; removed pregnancy contraindication per current safety approach; added maximum dosing requirements; references reviewed and updated.	05.21.19	08.19
3Q 2020 annual review: no significant changes; references reviewed and updated.	05.08.20	08.20

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.