Clinical Policy: Chenodiol (Chenodal)

Reference Number: CP.PMN.239
Effective Date: 09.01.20
Last Review Date: 08.22
Line of Business: Commercial, HIM, 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. Safety of use beyond 24 months is not established. Chenodiol will not dissolve calcified (radiopaque) or radiolucent bile pigment stones. 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.

It is the policy of health plans affiliated with Centene Corporation® 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 per kg per day.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):

a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

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

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
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 per kg per day.

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

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

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 policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid 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 hepatotoxicity, 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.	18 mg/kg/day

VI. Product Availability

Tablet: 250 mg

VII. References

1. Chenodal Prescribing information. San Diego, CA: Retropin, Inc.; November 2021. Available at: https://dailymed.nlm.nih.gov/dailymed/. Accessed April 7, 2022.
2. Clinical Pharmacology [database online]. Elsevier; 2022. Available at: https://www.clinicalkey.com/pharmacology/.
3. Micromedex [database online]. Greenwood Village, CO: IBM Corporation; 2021. Available at http://www.micromedexsolutions.com/.
4. 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 previously approved policy CP.CPA.300; retire CP.CPA.300; added HIM and Medicaid lines of business; no significant changes from previously approved policy; references reviewed and updated.	05.08.20	08.20
3Q 2021 annual review: no significant changes; updated reference for HIM off-label use to HIM.PA.154 (replaces HIM.PHAR.21); references reviewed and updated.	05.03.21	08.21
3Q 2022 annual review: no significant changes; references reviewed and updated.	04.07.22	08.22
Template changes applied to other diagnoses/indications and continued therapy section.	10.06.22	

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. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. 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. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.