RXADVANCE
136 Turnpike Road
Southborough, MA 01772

Clinical Policy Title:	cholic acid
Policy Number:	RxA.067
Drug(s) Applied:	Cholbam®
Original Policy Date:	02/07/2020
Last Review Date:	03/09/2021
Line of Business Policy Applies to:	All lines of business

Background

Cholic acid is a bile acid indicated for:

- Treatment of bile acid synthesis disorders due to single enzyme defects (SEDs)
- Adjunctive treatment of peroxisomal disorders (PDs) including Zellweger spectrum disorders in patients who exhibit manifestations of liver disease, steatorrhea or complications from decreased fat-soluble vitamin absorption (A, D, E, K)

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
cholic acid (Cholbam®)	Bile acid synthesis disorders due to SED, PD including Zellweger spectrum disorders	10 to 15 mg/kg/day administered PO in one or two divided doses For concomitant familial hypertriglyceridemia: 11 to 17 mg/kg/day PO in one or two divided doses	17 mg/kg/day

Dosage Forms

- Capsules: 50 mg, 250 mg

Clinical Policy

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

I. Initial Approval Criteria

A. Bile Acid Synthesis Disorders or Peroxisomal Disorders (must meet all):

1. Member has one of the following diagnoses (a or b):
   a. Bile acid synthesis disorders due to SEDS confirmed by one of the following (i or ii):
      i. Abnormal urinary bile acid consistent with a bile acid synthesis disorder as confirmed by Fast Atom Bombardment ionization-Mass Spectrometry (FAB-MS analysis); or
      ii. Molecular genetic testing consistent with the diagnosis (e.g., biallelic pathogenic variants in *ABCD3, AKR1D1, AMACR, HSD3B7, CYP27A1,* or *CYP7B*);
   b. PDs, including Zellweger spectrum disorders, and all of the following (i and ii):

i. Member has PDs confirmed with at least one of the following criteria (a or b):
   a) An abnormal urinary bile acid analysis consistent with Zellweger spectrum disorder as confirmed by FAB-MS analysis (e.g., increased C27 bile acid intermediates trihydroxycholestanoic acid and dihydroxycholestanoic acid concentrations); or
   b) Molecular genetic testing consistent with the diagnosis (e.g., biallelic pathogenic variants in one of the *PEX* variants);
ii. Member has liver disease, steatorrhea, or complications from decreased fat-soluble vitamin absorption (e.g., rickets);

2. Prescribed by or in consultation with a hepatologist, metabolic specialist, or gastroenterologist;
3. Dose does not exceed 17 mg/kg/day

Approval Duration
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

A. Bile Acid Synthesis Disorders or Peroxisomal Disorders (must meet all):

1. Member is currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy
2. Member is responding positively to therapy as demonstrated by one of the following (a or b):
   a. For bile acid synthesis disorders due to SEDS (i and ii):
      i. Improvement in liver function tests;
      ii. Member does not have complete biliary obstruction;
   b. For PDs, including Zellweger spectrum disorders (i and ii):
      i. Improvements in liver function tests and/or steatorrhea;
      ii. Member does not have complete biliary obstruction;
3. If request is for a dose increase, new dose does not exceed 17 mg/kg/day.

Approval Duration
Commercial: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
FAB-MS: Fast Atom Bombardment ionization-Mass Spectrometry
FDA: Food and Drug Administration
PDs: Peroxisomal Disorders
SEDs: Single Enzyme Defects

APPENDIX B: Therapeutic Alternatives
Not applicable

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - None reported
- Boxed Warning(s):
  - None reported

APPENDIX D: General Information

- Treatment should be initiated and monitored by a hepatologist, metabolic specialist, or gastroenterologist.
- Discontinue cholic acid if liver function does not improve within 3 months of starting treatment or complete biliary obstruction develops.
- Discontinue treatment with cholic acid at any time if there are persistent clinical or laboratory indicators of worsening liver function or cholestasis.
- The safety and effectiveness of cholic acid on extrahepatic manifestations of bile acid synthesis disorders due to SEDs or PDs including Zellweger spectrum disorders have not been established.

References

1. Cholbam® (cholic acid) capsules, for oral use Prescribing Information. San Diego, CA: Retrophin, Inc.; March 2015. Available at: https://www.cholbam.com/pdf/Cholbam-PI.pdf. Accessed January 14, 2021.
2. Clinical Pharmacology [database online] powered by ClinicalKey. Tampa, FL: Elsevier, 2021. Accessed with subscription at: http://www.clinicalkey.com. Updated March 23, 2015. Accessed January 14, 2021.
3. Cholic acid. Micromedex Solutions. Truven Health Analytics, Inc. Ann Arbor, MI; 2019, November 6. Accessed with subscription at: http://www.micromedexsolutions.com. Accessed January 14, 2021.

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy was established	01/2020	02/07/2020
Policy was reviewed: 1. References updated. 2. Grammatical update in indications and add types of fat-soluble vitamins	05/2020	05/21/2020
Policy was reviewed: 1. Clinical policy title & lines of business updated. 2. Line of Business Policy Applies to was updated to “All lines of business”. 3. Clinical criteria for initial approval and continued therapy updated. 4. Initial and continued approval duration updated. 5. Continued therapy criteria II.A.1 was rephrased to “Currently receiving medication that has been authorized by RxAdvance…”. 6. References updated.	01/14/2021	03/09/2021