Drug Coverage Policy

Effective Date.....9/15/2025
Coverage Policy Number IP0289
Policy Title..... Cholbam

Cholbam

- Cholbam® (cholic acid capsules – Travere)

INSTRUCTIONS FOR USE

The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

OVERVIEW

Cholbam, a bile acid, is indicated for the following uses:[1]

- **Bile acid synthesis disorders due to single enzyme defects (SEDs)**.
- **Peroxisomal disorders (PDs), including Zellweger spectrum disorders**, as adjunctive treatment in patients who exhibit manifestations of liver disease, steatorrhea, or complications from decreased fat soluble vitamin absorption.

The effects of Cholbam on extrahepatic manifestations (e.g., neurologic symptoms) of bile acid synthesis disorders due to SEDs or PDs have not been established.[1] The prescribing information states that treatment with Cholbam should be discontinued if liver function does not improve within 3 months of the start of treatment or if complete biliary obstruction develops.

Bile Acid Synthesis Disorders

Bile acids are found in the liver and have several biological roles, including promotion of bile flow and intestinal absorption of fat and fat soluble vitamins.[2] The two primary bile acids are cholic acid and chenodeoxycholic acid (available as Chenodal® [chenodiol tablets]). Bile acids are formed from cholesterol; inadequate bile acid production leads to accumulation of cholesterol in the body, as well as other intermediary metabolites. This can result in damage to various organ systems. Severe cases may progress to cirrhosis and liver failure. Progressive neurologic disease may also occur, even in the absence of liver disease.

There are at least 17 known enzymes involved in bile acid synthesis. Primary bile acid synthesis disorders may be caused by a defect in the gene encoding any one of these enzymes. Enrollment criteria in the pivotal studies with Cholbam were based on abnormal urinary bile acids analysis by Fast Atom Bombardment ionization – mass spectrometry (FAB-MS).[1] However, gene sequencing is now available for many of the affected enzymes.

Peroxisomal Disorders (PDs)

PDs occur due to genetic mutations to genes that are essential to the proper formation of peroxisomes.[3] Among their many roles, peroxisomes are vital to the production of bile acids, as well as for neurologic function. Zellweger spectrum disorder is a type of PD and may be severe (Zellweger syndrome) or intermediate/milder (previously called neonatal adrenoleukodystrophy, infantile Refsum disease, or Heimler syndrome).[4] Enrollment criteria in the pivotal trials were based on abnormal urinary bile acids analysis by FAB-MS and a neurologic exam.[1] However, molecular genetic testing is now available.[4]

GUIDELINES

A joint guideline by the North American and European Societies for Pediatric Gastroenterology, Hepatology, and Nutrition is available (2017).[5] The guideline, which briefly addresses evaluation of cholestatic jaundice in infants, provides recommendations for diagnosis of bile acid synthesis disorders. While it is possible to perform rapid diagnosis of potential inborn errors in bile acid synthesis from urinary bile acid analysis, FAB-MS of urine is recommended. The guideline also notes that molecular techniques identify the specific mutations in genes encoding enzymes responsible for bile acid synthesis.

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POLICY STATEMENT

Prior Authorization is required for benefit coverage of Cholbam. All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with Cholbam as well as the monitoring required for adverse events and long-term efficacy,

approval requires Cholbam to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Documentation: Documentation is required where noted in the criteria as **[documentation required]**. Documentation may include, but is not limited to, chart notes, laboratory tests, claims records, and/or other information.

Cholbam is considered medically necessary when the following is met:

FDA-Approved Indications

1. **Bile Acid Synthesis Disorders Due to Single Enzyme Defects (SEDs).** Approve for the duration noted if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve for 3 months if the patient meets BOTH of the following (i and ii):
     - **i.** Patient has at least ONE of the following (a or b):
       - **a)** An abnormal urinary bile acid as confirmed by Fast Atom Bombardment ionization – Mass Spectrometry (FAB-MS) analysis **[Documentation Required]**; OR
       - **b)** Molecular genetic testing consistent with the diagnosis **[Documentation Required]**; AND
     - **ii.** The medication is prescribed by or in consultation with a hepatologist, metabolic specialist, or gastroenterologist; OR
   - **B)** Patient is Currently Receiving Cholbam. Approve for 1 year if the patient meets ALL of the following (i, ii, and iii):
     - **i.** Patient has responded to initial Cholbam therapy with an improvement in liver function tests (e.g., aspartate aminotransferase [AST], alanine aminotransferase [ALT], bilirubin levels); AND
     - **ii.** Patient does not have complete biliary obstruction; AND
     - **iii.** The medication is prescribed by or in consultation with a hepatologist, metabolic specialist, or gastroenterologist.

2. **Bile Acid Synthesis Disorders Due to Peroxisomal Disorders (PDs), Including Zellweger Spectrum Disorders.** Approve for the duration noted if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve for 3 months if the patient meets ALL of the following (i, ii, and iii):
     - **i.** Patient has peroxisomal disorders with at least ONE of the following (a or b):
       - **a)** An abnormal urinary bile acid analysis by Fast Atom Bombardment ionization – Mass Spectrometry (FAB-MS) **[Documentation Required]**; OR
       - **b)** Molecular genetic testing consistent with the diagnosis **[Documentation Required]**; AND
     - **ii.** Patient has liver disease, steatorrhea, or complications from decreased fat soluble vitamin absorption (e.g., rickets); AND
     - **iii.** The medication is prescribed by or in consultation with a hepatologist, metabolic specialist, or gastroenterologist; OR
   - **B)** Patient is Currently Receiving Cholbam. Approve for 1 year if the patient meets ALL of the following (i, ii, and iii):
     - **i.** According to the prescriber, patient has responded to initial Cholbam therapy; AND
       Note: Examples of a response to initial Cholbam therapy include improvements in liver enzymes or improvement in steatorrhea.
     - **ii.** Patient does not have complete biliary obstruction; AND
     - **iii.** The medication is prescribed by or in consultation with a hepatologist, metabolic specialist, or gastroenterologist.

Conditions Not Covered

Cholbam for any other use is considered not medically necessary, including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

1. **Concomitant Use with Chenodal or Ctexli.** There are no efficacy data available to support concomitant use of Cholbam and Chenodal or Ctexli.

References

1. Cholbam® capsules [prescribing information]. Foster City, CA: Mirum; October 2024.
2. Bile acid synthesis disorders. National Organization for Rare Diseases. Updated 2024. Available at: https://rarediseases.org/rare-diseases/bile-acid-synthesis-disorders/. Accessed on July 08, 2025.
3. Zellweger spectrum disorders. National Organization for Rare Diseases. Updated 2020. Available at: https://rarediseases.org/rare-diseases/zellweger-spectrum-disorders/. Accessed on July 08, 205.
4. Steinberg SJ, Raymond GV, Braverman NE, et al. Zellweger Spectrum Disorder. 2003 Dec 12 [Updated 2020 Oct 29]. In: Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2021. Updated October 29, 2020. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1448/. Accessed on July 08, 2025.
5. Fawaz R, Baumann U, Ekong U, et al. Guideline for the evaluation of cholestatic jaundice in infants: joint recommendations of the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition and the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition. *J Pediatr Gastroenterol Nutrition*. 2017;64(1):154-168.

Revision Details

Type of Revision	Summary of Changes	Date
Annual Revision	**Updated** coverage policy title from "Cholic Acid" to "Cholbam." **Bile Acid Synthesis Disorders Due to Single Enzyme Defects (SEDs).** Initial Therapy. **Removed** "consistent with a bile acid synthesis disorder" from "an abnormal urinary bile acid as confirmed by Fast Atom Bombardment ionization – Mass Spectrometry analysis." **Removed** the example from "molecular genetic testing consistent with diagnosis" criterion. **Bile Acid Synthesis Disorders Due to Peroxisomal Disorders (PDs), Including Zellweger Spectrum Disorders.** Initial Therapy. **Removed** "analysis consistent with a peroxisomal disorder as confirmed" "an abnormal urinary bile	11/1/2024

	acid by Fast Atom Bombardment ionization – Mass Spectrometry analysis." **Removed** the example from "molecular genetic testing consistent with diagnosis" criterion.	
Annual Revision	**Conditions Not Recommended for Approval**: Ctexli was added as a medication that should not be used concomitantly with Cholbam.	9/15/2025

The policy effective date is in force until updated or retired.