



PRIOR AUTHORIZATION POLICY

- POLICY:** Cholbam Prior Authorization Policy
- Cholbam® (cholic acid capsules – Travere)

REVIEW DATE: 07/19/2023

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CIGNA NATIONAL FORMULARY COVERAGE:

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.

POLICY STATEMENT

Prior Authorization is recommended for prescription 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.

• Cholbam® (cholic acid capsules – Travele)
is(are) covered as medically necessary when the following criteria is(are) met for fda-approved indication(s) or other uses with supportive evidence (if applicable):

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; OR

b) Molecular genetic testing consistent with the diagnosis; AND

ii. The medication is prescribed by or in consultation with a hepatologist, metabolic specialist, or gastroenterologist.

B) Patient is Currently Receiving Cholbam. Approve for 1 year if the patient meets 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 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); OR

b) Molecular genetic testing consistent with the diagnosis; 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.

B) Patient is Currently Receiving Cholbam. Approve for 1 year if the patient meets the following (i, ii, and iii):

i. Patient has responded to initial Cholbam therapy according to the prescriber; 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® (cholic acid capsules – Traverso)**

is(are) considered experimental, investigational or unproven for ANY other use(s) including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

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

REFERENCES

1. Cholbam® capsules [prescribing information]. San Diego, CA: Travere; March 2023.
2. Bile acid synthesis disorders. National Organization for Rare Diseases. Updated 2020. Available at: <https://rarediseases.org/rare-diseases/bile-acid-synthesis-disorders/>. Accessed on July 11, 2023.
3. Zellweger spectrum disorders. National Organization for Rare Diseases. Updated 2020. Available at: <https://rarediseases.org/rare-diseases/zellweger-spectrum-disorders/>. Accessed on July 11, 2023.
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 11, 2023.
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.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	07/13/2022
Annual Revision	No criteria changes.	07/19/2023

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