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| <b>Section:</b>    | Prescription Drugs      | <b>Effective Date:</b>       | April 1, 2021    |
| <b>Subsection:</b> | Gastrointestinal Agents | <b>Original Policy Date:</b> | October 30, 2015 |
| <b>Subject:</b>    | Cholbam                 | <b>Page:</b>                 | 1 of 4           |

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**Last Review Date:** March 12, 2021

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## Cholbam

### Description

#### Cholbam (cholic acid)

#### Background

Cholbam is the first FDA approved treatment for pediatric and adult patients with rare bile acid synthesis disorders due to single enzyme defects, and for patients with peroxisomal disorders (including Zellweger spectrum disorders). Patients with these rare, genetic, metabolic conditions exhibit manifestations of liver disease, steatorrhea (presence of fat in the stool) and complications from decreased fat-soluble vitamin absorption. Individuals with these rare disorders lack the enzymes necessary to produce cholic acid, a primary bile acid synthesized by the liver from cholesterol (1).

The mechanism of action of cholic acid has not been fully established. Endogenous bile acids including cholic acid enhance bile flow, provide the physiologic feedback inhibition of bile acid synthesis, and regulate bile acid circulation (1).

#### Regulatory Status

FDA-approved indications: Cholbam (cholic acid) is a bile acid indicated for: (1)

1. Treatment of bile acid synthesis disorders due to single enzyme defects (SEDs).
2. 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.

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|--------------------|-------------------------|------------------------------|------------------|
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| <b>Subject:</b>    | Cholbam                 | <b>Page:</b>                 | 2 of 4           |

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## Limitations of Use:

The safety and effectiveness of Cholbam on extrahepatic manifestations of bile acid synthesis disorders due to SEDs or PDs including Zellweger spectrum disorders have not been established (1).

Treatment with Cholbam should be initiated and monitored by an experienced hepatologist or pediatric gastroenterologist (1).

The Cholbam label includes a warning for exacerbation of liver impairment. Patients should be monitored every month for the first 3 months for serum aspartate aminotransferase (AST), serum alanine aminotransferase (ALT), serum gamma glutamyltransferase (GGT), alkaline phosphatase (ALP), bilirubin and INR levels then every 3 months for the next 9 months, every 6 months during the subsequent three years and annually thereafter; or more frequently during periods of rapid growth, concomitant disease, and pregnancy. Cholbam should be discontinued in patients who develop worsening of liver function or cholestasis while on treatment (1).

The safety and effectiveness of Cholbam has been established in pediatric patients 3 weeks of age and older for the treatment of bile acid synthesis disorders due to SEDs, and for adjunctive treatment of patients with PDs including Zellweger spectrum disorders who exhibit manifestations of liver disease, steatorrhea or complications from decreased fat soluble vitamin absorption (1).

## **Related policies**

### **Policy**

*This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.*

Cholbam may be considered **medically necessary** for the treatment of bile acid synthesis disorders to due single enzyme defects or peroxisomal disorder, including Zellweger spectrum disorders and if the conditions indicated below are met.

Cholbam is considered **investigational** for all other indications.

## **Prior-Approval Requirements**

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|                    |                         |                              |                  |
|--------------------|-------------------------|------------------------------|------------------|
| <b>Section:</b>    | Prescription Drugs      | <b>Effective Date:</b>       | April 1, 2021    |
| <b>Subsection:</b> | Gastrointestinal Agents | <b>Original Policy Date:</b> | October 30, 2015 |
| <b>Subject:</b>    | Cholbam                 | <b>Page:</b>                 | 3 of 4           |

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## Diagnoses

Patient must have **ONE** of the following:

1. Bile acid synthesis disorder due to single enzyme defects (SEDs)
2. Peroxisomal disorder (PD), including Zellweger spectrum disorders
  - a. Prescribed as adjunctive treatment

**AND ALL** of the following:

1. Diagnosis was confirmed by mass spectrometry or other biochemical testing or genetic testing
2. Prescribed by hepatologist, gastroenterologist, or metabolic or biochemical geneticist physician experienced in treating bile acid synthesis disorder/peroxisomal disorder
3. Physician agrees to monitor liver function including AST, ALT, GGT, alkaline phosphatase, bilirubin and INR

## Prior – Approval *Renewal* Requirements

### Diagnoses

Patient must have **ONE** of the following:

1. Bile acid synthesis disorder due to single enzyme defects (SEDs)
2. Peroxisomal disorder (PD), including Zellweger spectrum disorders
  - a. Prescribed as adjunctive treatment

**AND** the following:

1. Physician agrees to monitor liver function including AST, ALT, GGT, alkaline phosphatase, bilirubin and INR

### [Policy Guidelines](#)

## Pre - PA Allowance

None

## Prior - Approval Limits

**Duration** 2 years

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|                    |                         |                              |                  |
|--------------------|-------------------------|------------------------------|------------------|
| <b>Section:</b>    | Prescription Drugs      | <b>Effective Date:</b>       | April 1, 2021    |
| <b>Subsection:</b> | Gastrointestinal Agents | <b>Original Policy Date:</b> | October 30, 2015 |
| <b>Subject:</b>    | Cholbam                 | <b>Page:</b>                 | 4 of 4           |

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## Prior – Approval *Renewal* Limits

Same as above

### Rationale

#### Summary

Cholbam is an oral bile acid therapy approved for treatment of bile acid synthesis disorders and adjunctive treatment of peroxisomal disorders. Cholbam has a warning for possible exacerbation of liver impairment. Patients should be monitored for worsening liver function or cholestasis. More frequent monitoring may be required during periods of rapid growth, concomitant disease, and pregnancy (1).

Prior authorization is required to ensure the safe, clinically appropriate and cost-effective use of Cholbam while maintaining optimal therapeutic outcomes.

#### References

1. Cholbam [package insert] San Diego, CA: Retrophin, Inc.; March 2015.

### Policy History

| Date           | Action   |
|----------------|--|
| October 2015   | Addition to PA   |
| December 2015  | Annual review  |
| September 2016 | Annual editorial review and reference update<br>Policy code changed from 5.09.09 to 5.50.09.                               |
| March 2017     | Annual review  |
| March 2018     | Annual review  |
| March 2019     | Annual review  |
| March 2020     | Annual editorial review. Changed approval duration from lifetime to 2 years. Revised monitoring requirement for initiation |
| March 2021     | Annual review  |

### Keywords

**This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 12, 2021 and is effective on April 1, 2021.**