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Policy Number: C17319-A

Cholbam (cholic acid)

PRODUCTS AFFECTED

Cholbam (cholic acid)

COVERAGE POLICY

Coverage for services, procedures, medical devices, and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any. This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational, or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Bile acid synthesis disorder due to single enzyme defects (SEDs), Peroxisomal disorder including Zellweger spectrum disorder

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by-case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available.

A. BILE ACID SYNTHESIS DISORDERS (BASDs) DUE TO SINGLE ENZYME DEFECTS (SEDs):
   1. Documentation member has a diagnosis of a bile acid synthesis disorder due to a single enzyme defect based on ONE of the following [DOCUMENTATION REQUIRED]:

(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 (for example, biallelic pathogenic variants in ABCD3, AKR1D1, AMACR, HSD3B7, CYP27A1, or CYP7B)
AND

2. Prescriber attests to member having at least ONE of the following: (a) Liver disease manifestations such as: Elevations in AST, ALT, GGT, or ALP, Hepatomegaly, Jaundice, Cirrhosis, Cholestasis, Steatorrhea, OR (b) Complications from decreased fat-soluble vitamin absorption
AND
3. Documentation of member's baseline labs: AST, ALT, GGT, ALP, bilirubin, and INR (within 30 days of request)
AND
4. Prescriber attests that Cholbam (cholic acid) will not be used concurrently with Chenodal (chenodiol)
AND
5. Prescriber attests that therapy will be discontinued if liver function does not improve within 3 months of the start of treatment, OR if liver function worsens, OR if complete biliary obstruction develops, OR if cholestasis develops.

B. PEROXISOMAL DISORDERS (PDs), INCLUDING ZELLWEGER SPECTRUM DISORDERS:

1. Documentation member has a diagnosis of peroxisomal disorder with ONE of the following [DOCUMENTATION REQUIRED]:
   (a) An abnormal urinary bile acid analysis consistent with a Zellweger spectrum disorder by Fast Atom Bombardment ionization – Mass Spectrometry (FAB-MS) (for example, increased concentrations of C27 bile acid intermediates trihydroxycholestanoic acid (THCA) and dihydroxycholestanoic acid (DHCA))
   OR
   (b) Molecular genetic testing consistent with the diagnosis (for example, biallelic pathogenic variants in one of the PEX genes)
   AND
2. Prescriber attests to member having at least ONE of the following: (a) Liver disease manifestations such as: Elevations in AST, ALT, GGT, or ALP, Hepatomegaly, Jaundice, Cirrhosis, Cholestasis, Steatorrhea, OR (b) Complications from decreased fat-soluble vitamin absorption
AND
3. Documentation of member's baseline labs: AST, ALT, GGT, ALP, bilirubin, and INR (within 30 days of request)
AND
4. Prescriber attests that Cholbam (cholic acid) will not be used concurrently with Chenodol (chenodiol)
AND
5. Prescriber attests that therapy will be discontinued if liver function does not improve within 3 months of the start of treatment, OR if liver function worsens, OR if complete biliary obstruction develops, OR if cholestasis develops

CONTINUATION OF THERAPY:

A. ALL INDICATIONS:

1. Documentation of positive clinical response as demonstrated by improvement in baseline liver function tests (e.g., aspartate aminotransferase [AST], alanine aminotransferase [ALT], gamma glutamyl transferase [GGT], alkaline phosphatase [ALP], bilirubin, and INR levels) [DOCUMENTATION REQUIRED]
AND

2. Prescriber attests that member does not have complete biliary obstruction
   AND
3. Adherence to therapy at least 85% of the time as verified by the prescriber or member medication fill history OR adherence less than 85% of the time due to the need for surgery or treatment of an infection, causing temporary discontinuation
   AND
4. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity

DURATION OF APPROVAL:
Initial Authorization: 6 months, Continuation of therapy: 12 months

PRESCRIBER REQUIREMENTS:
Prescribed by or in consultation with a hepatologist, metabolic specialist, or a gastroenterologist [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests]

AGE RESTRICTIONS:
3 weeks of age and older

QUANTITY:
Weight based dosing 10 to 15 mg/kg/day per dosing chart. See Appendix.
Maximum Quantity Limits – 11 to 17 mg/kg/day in patients with concomitant familial hypertriglyceridemia

PLACE OF ADMINISTRATION:
The recommendation is that oral medications in this policy will be for pharmacy benefit coverage and patient self-administered.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Oral

DRUG CLASS:
Bile Acid Synthesis Disorder Agents

FDA-APPROVED USES:
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.

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.

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:

Table 1: Number of CHOLBAM Capsules Needed to Achieve a Recommended Dosage of 10 mg/kg/day

	10 mg/kg/day Dosage	
Body Weight (kg)	Number of 50 mg capsules	Number of 250 mg capsules
4 to 6	1	0
7 to 10	2	0
11 to 15	3	0
16 to 20	4	0
21 to 25	0	1
26 to 30	1	1
31 to 35	2	1
36 to 40	3	1
41 to 45	4	1
46 to 50	0	2
51 to 55	1	2
56 to 60	2	2
61 to 65	3	2
66 to 70	4	2
71 to 75	0	3
76 to 80	1	3

Table 2: Number of CHOLBAM Capsules Needed to Achieve a Recommended Dosage of 15 mg/kg/day

	15 mg/kg/day Dosage	
Body Weight (kg)	Number of 50 mg capsules	Number of 250 mg capsules
4 to 5	1	0
6 to 9	2	0
10 to 13	3	0
14 to 16	4	0
17 to 19	0	1
20 to 23	1	1
24 to 26	2	1
27 to 29	3	1
30 to 33	4	1
34 to 36	0	2
37 to 39	1	2
40 to 43	2	2
44 to 46	3	2
47 to 49	4	2
50 to 53	0	3
54 to 56	1	3
57 to 59	2	3
60 to 63	3	3
64 to 66	4	3
67 to 69	0	4
70 to 73	1	4
74 to 76	2	4
77 to 79	3	4
80	4	4

Patients with newly diagnosed, or a family history of, familial hypertriglyceridemia may have poor absorption of Cholbam from the intestine and require a 10% increase in the recommended dosage to account for losses due to malabsorption. The recommended dosage of Cholbam in patients with concomitant familial hypertriglyceridemia is 11 to 17 mg/kg orally once daily, or in two divided doses. Adequacy of the dosage regimen can be determined by monitoring the patient's clinical response including steatorrhea and laboratory values of serum transaminases, bilirubin, and prothrombin time/international normalized ration (PT/INR).

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:

Bile acids are the product of cholesterol metabolism in the body. The body's mechanism of converting cholesterol to bile acid is essential for maintaining cholesterol homeostasis and preventing an accumulation of cholesterol in the liver and other organs. Bile acids are critical for a variety of functions, including intestinal nutrient absorption and biliary secretion of lipids, toxic metabolites, andxenobiotics.5

Bile acid synthesis disorders are a group of rare metabolic disorders in which there are defects in the synthesis of bile acids. This also leads to a buildup of abnormal bile acids and metabolites which can cause damage in the body.[3] These disorders are estimated to have a prevalence of 1 in 50,000 in the general population.

These disorders can be due to congenital deficiencies in enzymes required for catalyzing bile acids (cholic acid and chenodeoxycholic acid). They may also be due to disorders involved in the transport of bile acids, like low gamma-GT familial intrahepatic cholestasis and MDR3 deficiency, Smith- Lemli-Optiz syndrome, and Zellweger Spectrum disorders.[5]

Diagnosis of bile acid synthesis disorders can be confirmed by interpretation of FAB-MS (fast atom bombardment ionization mass spectrometry) in which samples of urine are tested for the presence of primary bile acid conjugates or primary bile acid. Presence of primary bile acid conjugates in the urine indicates that pathways for normal primary bile acid synthesis are intact, and this rules out a genetic defect. Diagnosis of bile acid synthesis disorders using this technique would then have a clinical presentation as "a condition of cholestasis caused by a loss of primary bile acids."[8]

Zellweger spectrum disorders are a group of rare, genetic disorders characterized by the failure of the body to produce peroxisomes that function properly. Among this group of disorders, Zellweger syndrome is the most severe form. Usually diagnosed at birth, affected newborns will generally have

distinctive facial features, a low seizure threshold, renal cysts, bony stippling, and liver disease that can be severe. The main feature, as it relates to Cholbam therapy, will be the lack of peroxisome production, which affects the final steps of bile acid product in the liver and can ultimately lead to a buildup of abnormal bile acids that can cause damage to hepatocytes.[3,4,6]

Zellweger spectrum disorders: Although included as FDA-approved use in the manufacturer's labeling for use as adjunctive treatment of Zellweger spectrum disorder, the evidence for beneficial effects of cholic acid treatment is too limited to recommend in clinical practice, especially in patients with advanced liver disease. (Klouwer FCC, 2019)

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:

All other uses of Cholbam (cholic acid) are considered experimental/investigational and therefore, will follow Molina's Off-Label policy. Contraindications to Cholbam (cholic acid) include: No labeled contraindications.

OTHER SPECIAL CONSIDERATIONS:

Monitor AST, ALT, GGT, ALP, bilirubin, and INR every month for the first 3 months, every 3 months for the next 9 months, every 6 months during the next 3 years, and annually thereafter. Monitor more frequently during periods of rapid growth, concomitant disease, and pregnancy (per labeling, 2023).

CODING/BILLING INFORMATION

Note: 1) This list of codes may not be all-inclusive. 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

HCPCS CODE	DESCRIPTION
NA	

AVAILABLE DOSAGE FORMS:

Cholbam CAPS 50MG
Cholbam CAPS 250MG

REFERENCES

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9. Klouwer FCC, Koot BGP, Berendse K, et al. The cholic acid extension study in Zellweger spectrum disorders: results and implications for therapy. J Inherit Metab Dis. 2019;42(2):303-312.[PubMed 30793331]10.1002/jimd.12042
10. Bile Acid Synthesis Disorders. (2020, April 24). Retrieved from NORD (National Organization for Rare Disorders) website: https://rarediseases.org/rare-diseases/bile-acid-synthesis-disorders/

SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Required Medical Information Continuation of Therapy Quantity Background References	Q3 2024
REVISION- Notable revisions: Required Medical Information Continuation of Therapy Prescriber Requirements Appendix Contraindications/Exclusions/Discontinuation	Q3 2023
REVISION- Notable revisions: Required Medical Information Continuation of Therapy Prescriber Requirements	Q3 2022
Q2 2022 Established tracking in new format	Historical changes on file