Drug Use Research & Management
Oregon State University College of Pharmacy

Abbreviated Drug Review

Drug Product		
Cholbam® (cholic acid) capsule (oral)	Claims: 0	Wholesale Acquisition Cost: $49,650/month for 20 kg patient [based on 50 mg (#90): $24,825]

Indications

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

Dosage

- 10-15 mg/kg/day in 1 or 2 divided doses
- Children 3 weeks of age or older and adults

Background

- Bile acid synthesis is complex requiring at least 17 enzymes.
- Cholic acid is an endogenous bile acid synthesized in the liver facilitates fat absorption, absorption of fat-soluble vitamins, and enhances bile flows.
- Disorders of bile acid synthesis are rare and clinical severity is variable. These disorders can be primary or secondary:
  - SEDs are primary enzyme defects involved in the synthesis of cholic acid and other primary bile acids.
  - PDs are secondary metabolic defects that impact primary bile acid synthesis.
- Impaired bile acid synthesis is associated with insufficient bile acid secretion from the hepatocyte, which results in accumulation of intermediate hepatotoxic bile acids. Accumulation may lead to cholestasis, bile acid plugs, giant cell hepatitis and cirrhosis, or death.

Efficacy

- The primary study is an unpublished, non-randomized, open-label, non-controlled, compassionate-use study (average duration 145 weeks).
- Supplemental data are from a post-hoc subgroup analysis of responders, an extension study, and case series reports.
- Data were evaluated for 50 patients with bile acid synthesis disorders and 29 patients with peroxisomal disorders.
- Blood and urine samples were monitored every 3-6 months; liver biopsy was performed in some patients every 6 months.
- A patient was consider a "Responder" to treatment if they were alive at last follow-up, and
  - **a)** met ≥2 lab criteria; or **b)** met ≥1 lab criterion and had increased body weight by 10% or stable at >50th percentile
- SED: 62% responders; 22% non-responders; 16% data not available
- PD: 0% responders; 76% non-responders; 24% data not available
  - (modified "Responder" criteria that removed lab criteria showed 2/29 patients responded)

Laboratory Criteria

- ALT/AST reduced to <50 U/L, or baseline level reduced by 80%
- Total bilirubin reduced to ≤1 mg/dL
- No evidence of cholestasis on liver biopsy

Safety

- Gastrointestinal: exacerbation of cholestasis (≤14%)
- Hepatic: increased serum bilirubin (≤14%); increased serum transaminases (≤14%)

Evidence Gaps/Limitations

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.

Recommendation

Refer claims to DMAP Medical Director through Prior Authorization.

References

- Center for Drug Evaluation and Research. Medical Review: Application number 205750Orig1s000 http://www.accessdata.fda.gov/scripts/cder/drugsatfda/. Accessed May 23, 2015.
- Cholbam (cholic acid) [prescribing information]. Baltimore, MD: Asklepion Pharmaceuticals; March 2015.

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